CHEMICAL HERITAGE FOUNDATION

CAROLYN R. BERTOZZI

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Andrea R. Maestrejuan

at

The University of California, Berkeley
Berkeley, California

on

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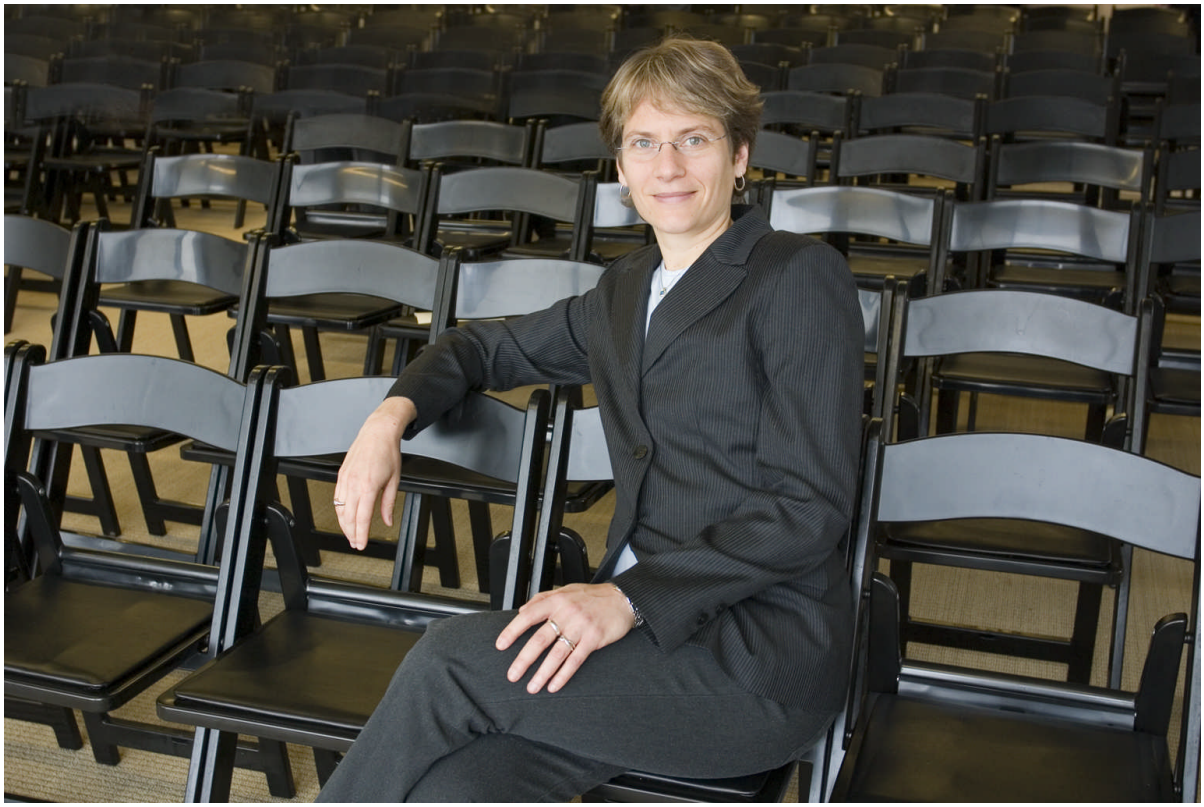

Carolyn R. Bertozzi

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If to Interviewee:

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University of California, Berkeley
Berkeley, California 94720

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UCB Department of Physiology (Address)	Interim Director, Oral History Program (Title)
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Date 8/17/03	Date Sept 22, 2003

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Interviewee's Name

4/15/2022
Date

Chemical Heritage Foundation
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CAROLYN R. BERTOZZI

1966	Born in Boston, Massachusetts on 10 October

Education

1988	A.B. in Chemistry, *summa cum laude*, Harvard University
1993	Ph.D. in Chemistry, University of California, Berkeley

Professional Experience

University of California, San Francisco

1993-1995	Postdoctoral Fellow**,** Program in Immunology and Department of Anatomy
2000-present	Professor of Molecular and Cellular Pharmacology

University of California, Berkeley

1996-1999	Assistant Professor of Chemistry
1999-2002	Associate Professor of Chemistry and Molecular and Cell Biology
2002-present	Professor of Chemistry and Molecular and Cell Biology

Lawrence Berkeley National Laboratory

1996-present	Faculty Associate, Materials Sciences Division
2000-present	Howard Hughes Medical Institute Investigator, Director, Biological Nanostructures Facility of The Molecular Foundry

Honors

1987	Radcliffe Science Research Fellowship
1987	Phi Beta Kappa
1987	Danforth Teaching Award
1988	New England American Institute of Chemists Award
1988	Thomas T. Hoopes Undergraduate Thesis Prize
1988-1991	Office of Naval Research Graduate Fellowship
1988-1993	AT&T Bell Laboratories Graduate Fellowship
1989	Outstanding Graduate Student Instructor Award
1990	Outstanding Graduate Student Instructor Award
1991-1992	American Chemical Society Medicinal Chemistry

	Graduate Fellowship
1992	Bruce Mahan Teaching Award
1993-1995	American Cancer Society Postdoctoral Fellowship
1995	Camille and Henry Dreyfus New Faculty Award
1996	Exxon Education Fund Young Investigator Award
1996-2000	Pew Scholars Award in the Biomedical Sciences
1997	Burroughs Wellcome New Investigator Award in Pharmacology
1997	Alfred P. Sloan Research Fellow
1997	Horace S. Isbell Award in Carbohydrate Chemistry (ACS)
1998	Office of Naval Research Young Investigator Award
1998	Research Corporation Research Innovation Award
1998	Glaxo Wellcome Scholar
1998	Prytanean Faculty Award
1998	Beckman Young Investigator Award
1998-2000	Joel H. Hildebrand Chair in Chemistry
1999	Arthur C. Cope Scholar Award (ACS)
1999	Camille Dreyfus Teacher-Scholar Award
1999	MacArthur Foundation Award
2000	Presidential Early Career Award in Science and Engineering (PECASE)
2000	UC Berkeley Department of Chemistry Teaching Award
2000	Merck Academic Development Program Award
2001	ACS Award in Pure Chemistry
2001	UC Berkeley Distinguished Teaching Award
2001	Donald Sterling Noyce Prize for Excellence in Undergraduate Teaching
2002	Fellow of the American Association for the Advancement of Science
2002	Irving Sigal Young Investigator Award of the Protein Society
2003	Elected member of the American Academy of Arts and Sciences
2004	Iota Sigma Pi Agnes Fay Morgan Research Award
2005	Havinga Medal, Univ. Leiden
2005	T.Z. and Irmgard Chu Distinguished Professorship in Chemistry
2005	Elected member of the National Academy of Science

Selected Publications

Chidsey, C. E. D., Bertozzi, C. R., Putvinski, T. M., Mujsce, A. M, "Coadsorption of Ferrocene-Terminated and Unsubstituted Alkanethiols on Gold: Electroactive Self-Assembled Monolayers," *J. Am. Chem. Soc.* 1990 (112): 4301-4306.

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Immobilization of Glycoproteins, application filed 5/15/02 (Zyomyx, Inc.)

A New Approach to Mineralization of Biocompatible Hydrogel Scaffolds, application filed 2/28/03 (Lawrence Berkeley National Laboratory)

Ceramic/Polymer Composition with Graded Microstructures, application filed (Lawrence Berkeley National Laboratory)

Compositions and Methods for Modification of Biomolecules, application filed 11/1/04 (University of California)

ABSTRACT

Carolyn Bertozzi grew up in Lexington, Massachusetts, the second of three girls. Her father was a nuclear physicist at the Massachusetts Institute of Technology, her mother a secretary in MIT's physics department. Carolyn's father's four siblings, all born in Italy, also went into some branch of science. During the Great Depression Carolyn's maternal grandparents and uncle emigrated from Nova Scotia and established a farm. Carolyn's older sister, a "math genius" now teaches at Duke University, and her younger sister became a psychologist.

It was expected that Carolyn and her sisters would do well in school, and Carolyn did, but she also played soccer in high school and was recruited to Harvard with what would be at any other school an athletic scholarship. She found soccer and later crew too time-consuming, however, and quit sports to devote herself to academics. She began as a biology major but in her second year took an organic chemistry class, which she loved, although she continued to take biology classes, she switched her major to chemistry. She was first in her class and eventually graduated *summa cum laude*, but Harvard's chemistry department was exclusively male at the time. As a result, she went to a lab in the biochemistry department, where Joseph Grabowski, her teacher for a physical organic chemistry class, asked her to work for him during the summer. He was so impressed with her work that he required her to write a graduation thesis, which he then submitted for an award of a substantial amount of money. He convinced her to go to graduate school at University of California at Berkeley.

At Berkeley, she joined Mark Bednarski's bioorganic chemistry laboratory to study carbohydrates. Bednarski was also new, and Carolyn found him enthusiastic, and she wrote a number of grant proposals in his lab. She wrote her doctoral dissertation on the synthesis of carbohydrate analogues for biological applications. Continuing her interest in carbohydrates, and contrary to the advice of other chemists, Carolyn went to work in Steven Rosen's cell biology laboratory at the University of California, San Francisco, for her postdoc. There she studied the role of carbohydrates in inflammation and leukocyte adhesion.

After her postdoctoral work, she accepted an assistant professorship at the University of California at Berkeley and set up her own laboratory. She and Rosen also founded a private company, Thios Pharmaceuticals, Inc. At Berkeley she enjoys teaching, finding her students very intelligent, hard-working, and interesting. In the laboratory she writes (and gets) grants, mentors (particularly women), and sets problems. She has published many journal articles. Her current research interests continue in glycobiology, which she sees as having potentially a wider clinical application. Now a tenured professor, she has a number of academic appointments and steady funding.

UCLA INTERVIEW HISTORY

INTERVIEWER:

Andrea R. Maestrejuan, Interviewer, UCLA Oral History Program, B.S., Biological Sciences, University of California, Irvine, 1986, M.A., History, University of California, Riverside, 1991, C.Phil, History, University of California, Riverside.

TIME AND SETTING OF INTERVIEW:

Place: Bertozzi's office at the University of California, Berkeley.

Dates of sessions: August 17, 2003, August 18, 2003.

Total number of recorded hours: 6

Persons present during interview: Bertozzi and Maestrejuan.

CONDUCT OF INTERVIEW:

This interview is one in a series with Pew Scholars in the Biomedical Sciences conducted by the UCLA Oral History Program in conjunction with the Pew Charitable Trusts's Pew Scholars in the Biomedical Sciences Oral History and Archives Project. The project has been designed to document the backgrounds, education, and research of biomedical scientists awarded four-year Pew scholarships since 1988.

To provide an overall framework for project interviews, the director of the UCLA Oral History Program and three UCLA faculty project consultants developed a topic outline. In preparing for this interview, Maestrejuan held a telephone preinterview conversation with Bertozzi to obtain written background information (curriculum vitae, copies of published articles, etc.) and agree on an interviewing schedule. She also reviewed documentation in Bertozzi's file at the Pew Scholars Program office in San Francisco, including Bertozzi's proposal application, letters of recommendation, and reviews by Pew Scholars Program national advisory committee members.

ORIGINAL EDITING:

Carol Squires edited the interview. She checked the verbatim transcript of the interview against the original tape recordings, edited for punctuation, paragraphing, and spelling, and verified proper names. Words and phrases inserted by the editor have been bracketed.

Bertozzi did not review the transcript. Consequently, some names remain unverified.

Carol Squires prepared the table of contents and TechniType Transcripts compiled the guide to proper names.

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INTERVIEWEE: **Carolyn R. Bertozzi**

INTERVIEWER: **Andrea R. Maestrejuan**

LOCATION: **University of California at Berkeley**

DATE: **17 August 2003**

MAESTREJUAN: It is August 17th, 2003, and I'm Andrea Maestrejuan with Carolyn [Ruth] Bertozzi in her office at the chemistry department at UC [University of California,] Berkeley, for her oral history interview for the Pew Scholars Program in the Biomedical Sciences.

We'll start at the very beginning and I'll ask you where and when you were born.

BERTOZZI: Boston, Massachusetts, 1966.

MAESTREJUAN: Okay. I know from your website that basically science is a family business, so to speak.

BERTOZZI: Yes, that's right.

MAESTREJUAN: Why don't you tell me a little bit about your parents' background, your family background.

BERTOZZI: Well, my dad [William Bertozzi] is the fifth child of immigrants from Italy who came over in the early nineteen-teens, I guess, and landed outside of Boston. Now he's a physics professor at MIT [Massachusetts Institute of Technology] and he was at MIT his entire life, pretty much, he was an undergraduate, graduate student, assistant professor, all the way through, all at MIT. He's in his early seventies, and the oldest child of that family is still alive and he's maybe ninety or so now.

MAESTREJUAN: Wow.

BERTOZZI: Many of those children were scientists. I guess the oldest, my uncle, was a

chemist who worked for Morton Thiokol [Inc.], and one of the intermediate sisters was a junior high school science teacher outside of Boston. She passed away a few years ago. There's another sister that's still alive, and she was a nurse. And there was another brother who died when I was very young, who I didn't really know.

They grew up very poor, on welfare. Basically, my dad's mother [Luigia Maria Madelena Bertozzi], my grandmother, was very active in the Socialist Party in Italy and that's why they fled, actually, because her life was at risk when [Benito] Mussolini came to power. But she was apparently a very progressive, very active, and very literate person. She founded one of the very first childcare centers in Italy for working moms, to help moms become working moms. And again, this is back in the nineteen-teens, this is very early on.

Her husband, who was my grandfather [Eugenio Bertozzi], was not literate. He was a farmer. So when they fled the country, she had to pose as his peasant wife and hide the fact that she was a reader and a writer, because that would have made her suspect.

So when they came to the United States, they had nothing. They basically built a farm and lived on food stamps. Then came the Depression, and so they grew up poor. So all of those kids in that family grew up in an environment where their mom enforced education. So she encouraged them to study hard, work hard, and they are very much believers in the American dream: That if you came to America and you worked really hard, you could make something of yourself, even though you started with nothing.

So, all of them ended up going basically on full scholarships to college. Every single one of those kids went to college, even the women.

[tape recorder off]

As I was saying about my parents, my father's side of the family, so they all went to college. Most of them got higher degrees, and for the women those were degrees in nursing and education. For the men, including my dad, it was like a Ph.D. or a master's degree.

So then my dad was a graduate student at MIT when he met my mother [Norma Gloria Bertozzi], and she was a secretary at MIT.

So then my mom comes from a family that came to the United States from Canada. They're from Nova Scotia, Canada, and they landed in the Boston area, too. So this was kind of a different family because they didn't have this rich tradition of education. My mom has one brother who's about seventeen years older than she, and so she basically grew up as an only child because he was pretty much out of the house by the time she was aware of things. Her father [Stuart Albert Berringer] owned a store, a little corner store, like a Mom and Pop store. I don't remember him very well. All my grandparents died when I was in elementary school, with the exception of my mother's mother [Stella Maude Berringer], who passed away when I was a postdoc [postdoctoral fellow], and she lived to be 100. But the other grandparents I didn't know very well, I only know their stories.

But I remembered my mother's father as being kind of a mean old guy. He had a stroke when I was pretty young, which left him immobilized and kind of making loud noises I couldn't understand. So when you're a kid, you're afraid of stuff like that, so that's kind of how I remember him. And then, thankfully, he died, because he was a tremendous burden on my grandmother, who was just basically waiting on him. They lived in some sort of cheap, low-income housing for the elderly in Watertown, Mass [Massachusetts].

But that grandmother was the grandparent I knew the best because she lived through my early adulthood, or my mid-adulthood, really. And so when I was a kid, she would come over and babysit a lot, stuff like that.

And so my mom, her story is that, again, she's a child of the Depression, so she and my dad both grew up in times when you scrimped and saved every little penny, and education was the most important thing. And the most coveted of all jobs was to be a tenured professor somewhere because your job was secure. Any other job was not secure back then, and so that was part of, I think, the driving force to have this high esteem for academia. But, also, in the Boston area you're just surrounded by it, universities and professors and this very academic environment.

Anecdotally, when I came out to California, that was another surprise to me, because I had grown up in Boston, went to college in Boston, and I came out here and it's very different. The whole environment wasn't dominated by universities. And, in fact, a lot of the students, college students, that I TA'd [teaching assistantship] and then later as a professor taught, had no interest in higher education beyond college. They went to college because they're supposed to, but after that, they just want to get a job. And the jobs in their community that were held in high esteem might have been the local optometrist, right, and they thought of being a professor at a university as a less appealing job because the salary wasn't as high, and so therefore it didn't hold as much esteem in their family, whereas in my family, salary was irrelevant. The fact that it was a secure job is what made it so important. But, again, I think that comes from the Depression.

MAESTREJUAN: Was your dad born in Italy, then?

BERTOZZI: No. His siblings were and he was not.

MAESTREJUAN: He was born in the United States?

BERTOZZI: Yes. He was born shortly after they got here.

MAESTREJUAN: And he was the youngest, then?

BERTOZZI: He may have been conceived in Italy, I don't know. [mutual laughter] He's the youngest of five.

MAESTREJUAN: Did his mother go to the university in Italy?

BERTOZZI: I don't know her educational background. I only know that she had authored a lot of documents and she had written a lot. She was considered an activist of her time, for women's rights.

MAESTREJUAN: And did she stay an activist when she moved to the United States?

BERTOZZI: No, not that I remember. I think she was just trying to survive and feed her family. And again, they had a farm out in Framingham, Massachusetts, which at that time was all farmland. Now it's strip malls. They were on food stamps, they were on welfare, you know. I think at that time when they immigrated here neither of them spoke any English. They never really spoke English. I never heard either of them speak any English, and they both died when I was around eight. And so I don't know if they ever really learned English. So I don't know that it would have been easy for them to work in this country.

And also immigrants—poor immigrants—were just treated like dirt, you know. They weren't religious at all, so they shunned religion. They thought of religion as the opiate of the masses and so on. And at that time, again, in Massachusetts if you didn't have a religion that you subscribed to, you were ostracized by the community. So they settled outside of Boston and they would have the local ministers and priests coming to their house saying, "You've got to bring your children to church. If you don't bring those children to church, they're going to grow up and go to hell," and so on. And my dad's parents didn't want anything to do with it, so they didn't want their kids in religion, they didn't want religion in their house, and so on, and that also further alienated them, not just from the local nonimmigrant culture, but from their own Italian immigrants. Their community is a very Catholic community, and they didn't want anything to do with the Catholic Church.

So my dad grew up as an atheist, and even when I was a kid, he didn't want us to really have much to do with going to church. But my mother came from a family that had a little more tradition, so they were Protestants. So she brought us to church when we were kids, and I got confirmed in the Protestant church and so on. But my dad didn't want anything to do with it.

MAESTREJUAN: Was your mother born in Canada?

BERTOZZI: She was born in the [United] States.

MAESTREJUAN: So her family had come to Canada before that.

BERTOZZI: Yes, they came from Nova Scotia, Canada just to find work, there were no jobs up there. Lunenburg, Nova Scotia, Canada is a little fisherman's town, and, again, the Depression really hit Canada and the United States, I think. Well, the whole world, I guess.

Anyway, so my mom grew up in a family where I think her mother was a little bit older, and I think—well, since this could go on record—it's not clear that she was a planned pregnancy. And so I think she grew up as an only child, basically, and not that close to her parents, kind of out living her own life. She's very independent. She was a very good high school student. She was always at the top of her class and so on in high school. And she wanted to go to college but didn't have the means to go. Her parents, I think, had a style with her, which was they didn't want to give her any money, they thought it was a waste of money to have a girl go to college. Even when she graduated from high school, they started to charge her rent to live in her house. She had to get a job and work.

She had stories that she was pretty good at sports, she wanted to play on the basketball team, but she couldn't because she had to work after school every day to earn the money to stay in her house and buy her clothes and whatever she needed for school. So I think she might have some bitterness about that.

So anyway, her take on education—the message at least I got from her growing up—was that "If you don't go to college and get an education, you're going to end up like me," which is not much choice in life other than to get married and have kids. And that, she felt, was her option in life, was to get married and have kids, and there was no real career option for her.

So, being near the top of her class, and working part time all the time, she was able to put the money together to go to, —I don't know what they would have called it then—sort of secretarial school to learn shorthand and all these things. And then, again, being at the top of her class there, she was able to get one of the best secretarial jobs, which was at MIT. So the top women would get the best secretary jobs, the best nursing jobs.

And MIT was considered kind of top choice because those were the most eligible young men that you would meet. And again, this is late forties, early fifties, after the war when physics reigned, because nuclear physics saved the world, the nuclear bomb. And my dad was a nuclear physicist because that was hot. Just like now everyone wants to solve the human genome, or whatever, and cure cancer, back then everyone wanted to be a nuclear physicist and build bombs and save the world.

And so I think that was considered the best shopping ground for husbands, was in this environment. But my mom also really enjoyed it there because it was stimulating, she got to be around smart people who read books and would talk about them. And also back in those days the secretaries were much more integrated into academic life because those were the only women around. So when men had academic parties, to have any women there at all, you had to invite your secretaries, pretty much. And so she really knew all the professors and the grad [graduate] students, and they'd have outings to the beach on the weekends and stuff. They hung out together. The secretaries were usually these very educated, articulate women who in my day would now be a professor like me. But in that day, that's where they would go.

And so she really, I think, enjoyed working there and having her career as a secretary and getting into the politics. And she's got these old photographs of herself at the beach with Niels [H. D.] Bohr and [J.] Robert Oppenheimer. People like that. She was in that circle. And that's where she met my dad because he was a grad student there. And they got married and so on.

MAESTREJUAN: And what do you think inspired your father's side of the family, that all his siblings and himself went into the sciences?

BERTOZZI: Well, they were good at it. I think people like to do what they're good at, and physics and math came easy to him, so that's why he did it, I think. He never liked chemistry. He said he took organic chemistry in college, maybe, and just didn't understand it, didn't like it. But physics he picked it right up.

MAESTREJUAN: So what were the expectations—you mentioned this briefly before—from both your parents in terms of what you and your siblings should do with your lives in terms of educational opportunities, but also career choices?

BERTOZZI: Well, when we were growing up, there was no question we would go to college, of course. I mean, that was just a foregone conclusion, and we were little five year olds with MIT T-shirts on and so on. I mean, I always got the sense that it was expected of me to major in something having to do with the sciences, but it would be okay to go outside of the sciences as long as it was something practical where you could get a job. That was the emphasis.

I was kind of into music as a kid, and I toyed with the idea in my head of being a music major in college, and I'd sometimes casually mention it to my mom and she'd flip.

MAESTREJUAN: Oh, really?

BERTOZZI: Yes, because you couldn't make a living. And in case there was any doubt of

that, there was evidence in my own family, because I have this older cousin who had majored in music at Harvard [University] and, in fact, couldn't make a living afterwards and was teaching little kiddie violin lessons for a few bucks here and there, and ended up having to go back to school and get a computer degree, and now she's some computer manager at a bank or something. So that was always, "You'll never get a job. You need to major in something where you can get a job." So it could have been journalism. That would have been acceptable, and certainly medical school would have been fine. No matter what the major was. So that's kind of the message that I got, sometimes verbally, sometimes indirectly. All of us got that message, there are three of us.

MAESTREJUAN: Let's talk about your siblings, who they are—I know one of them is a math professor—and what they do.

BERTOZZI: So my older sister, Andrea [Louise Bertozzi], is the math professor now at UCLA [University of California at Los Angeles]. And then I have a younger sister, Diana [Joy Hindermann]. So, Andrea's one year older than I am, Diana's three years younger than I am. Diana is an occupational therapist, and she works at a hospital in New Jersey.

MAESTREJUAN: You all went to college?

BERTOZZI: Yes. So Andrea was one year ahead of me, and so she was kind of the genius of the family, and so the story of my life was always trying to keep up with my older sister. Math is one of those things where I don't think you can learn to be really good at math or work hard to be good at math, you're just either good at it or not, you know. And when you're really good at it, usually that's clear when you're four years old. You know what I mean? So she was one of those little kids who was doing the Rubik's cube in two seconds. And when everyone else was out playing, she was at home doing math puzzles because it was more fun than going out to play. And she was too smart for the math classes in junior high school, they had to ship her off to the high school for math. Stuff like that. Although she wasn't a total geek because she had other things. She played the flute very well in the State Orchestra and all that kind of stuff. And she worked as a lifeguard in the summer, just to be cool, for a period of time.

I was not as smart as she was, at least I didn't have that kind of obvious genius thing going. The junior high school math was just fine for me. Because we were a year apart, I pretty much had the same teachers she had, but a year later, and it was always like, "Oh, it's Andrea's little sister. Are you as smart as your older sister?"

And I just say, "No," and get it out of the way. But I was pretty smart. I just had a different kind of smart than she had.

And then my younger sister totally gave up altogether because she had to follow the

two brainy older sisters. So she had the classic younger sibling "Screw it. I'm just going to screw up in school and go out and party and have fun." So she had rocky spots, like in high school she was pulling Ds and Cs, and in high school that's pretty bad. You don't really have to do much to get a B. I mean, she was hanging out with kind of skuzzy boyfriends and stuff. Then she did go to college.

So my older sister went to Princeton [University] and majored in math, and then stayed at Princeton, went to grad school, and then went to postdoc at University of Chicago for a few years. Then she was hired with tenure immediately at Duke [University] because she was so smart and so on, right.

My younger sister went to Wooster, The College of Wooster college in Ohio— it's a little liberal arts place—for one year, and she failed out. She was partying all the time and not studying at all. And then the you-know-what hit the fan. She had to go back home. In my family, you don't even get a B, much less fail out, and certainly not in college. I mean, this was like the travesty of the family. So it was inconceivable for my parents to have to deal with this.

So she was living at home and working some crappy jobs at the mall, behind the counter and so on, and then my mom talked her into taking some classes at Middlesex Community College, which is a local thing. And, in fact, my mom, at this point, also decided she wanted a college degree. She was in her sixties at the time and she had never been to college, not in the conventional sense. So the way my mom puts it, she said that she decided that she would sign up for some classes at Middlesex to kind of encourage Diana to do these classes at Middlesex and they'd go there together or something. But actually, I think my mom really just wanted to do that herself, with or without Diana, but it was a good excuse for her to do it. Maybe it gave her the extra motivation to do it.

So Diana went and took these classes. So, she screwed up in college, she was young, seventeen, eighteen, and now it's a few years later. She's grown up a bit, and I think she also started to get the sense that working at the Sharper Image [Corporation] behind the counter is just not that fulfilling forever.

So she did pretty well. She got some good grades at Middlesex in some classes, I think psychology-type classes, she was interested in psych [psychology]. And so then she was able to transfer those credits to Northeastern [University]. She got into Northeastern, which is in Boston. It's funny, because when she first went to college, my parents' assumption was that she was less academically motivated and therefore would be better at a small school where they get more attention. But, in fact, that was not the case, because for whatever reason, that small school was too claustrophobic for her or something, and Northeastern's just a big city commuter school, and kids live out wherever and they drive in there. And so it's a much more serious place, actually, because you're not living there getting drunk on weekends, at these frats [fraternity houses]. You know what I mean. These kids are mostly working part time and supporting themselves in school. It's a little older crowd. It's a huge university, but mostly commuter.

I think she got some confidence. She had some better grades at Middlesex than she'd

ever had in high school, or certainly at Wooster where she failed out, and started to feel like she was really good at something. At Northeastern she majored at psych, and she had this one professor who kind of took an interest in her academically and encouraged her to be really good at this, and invited her to kind of work, do research with him kind of on the side, so she did this research project.

Then he said to her, "You should really continue on and get a master's degree in something, because you're really good at this." And it was the first authority figure in academia who said, "You're really good at something," as opposed to, "You're dumber than your two older sisters."

I think even my parents, unfortunately, sent her the message that she was dumber than her two older sisters. Because she would say, "Well, maybe I'll be a doctor when I grow up," and they'd say, "Well, I don't know if you're going to be a doctor, but you could probably be a nurse." They'd say things like that. They would never admit it, but now it's on record. Anyway.

So she did go on. She went to BU [Boston University], got a master's degree in occupational therapy, decided that was her thing. So that's what she does now, she's an OT [occupational therapist].

MAESTREJUAN: How much science was around the house, with your dad being a physicist and your mom working in a physics department and socializing with physicists? How much science was brought home.

BERTOZZI: Well, first of all, when we were born, my mom stopped working, so she was never working when I was a young kid, although she went back a little bit when I was in high school. She had a part-time secretarial job at Harvard, which she hated, and she quit that. So she was really, essentially, not working.

But my dad always had a lot of gadgets around the house, just junk from work that he'd bring home. So the one that made an impression on me was when I was a little kid he had this huge magnet that he brought home, big thing. And it was like this amazing thing where you'd like throw paper clips at it and it would fling them across the room and stuff like that. And we'd stick our dolls to it. When I was a kid, my Christmas present would be an optics kit where you build your own camera, stuff like that. And we used to go hang out at his office sometimes, he'd sometimes bring us in there, and it was all mysterious to us.

But one thing that he did have was a computer. And when we were kids, he brought home this terminal. So this was back in the day— How old are you?

MAESTREJUAN: Your age.

BERTOZZI: Okay, so you know what I'm talking about, then, because my students have no idea what I'm talking about. These terminals, you'd bring them home and plug your phone into the back, and there were two things for the telephone—you'd use an old-fashioned phone—so it would be two holes for the old-fashioned phone, and you dial up a modem and the phone would go "woooo," you'd plug it in, and this thing was a terminal, it was like a typewriter. But this was before anybody could play with a computer, you know. No person actually had access to computers at this point in time. This is in the seventies. A computer was this big thing only at Digital [Equipment Corporation] or Honeywell [International, Inc.], some big-main frames.

And you could program this thing in BASIC [Beginners All-purpose Symbolic Instruction Code] to add two plus two and give you four. You know what I mean? Stuff like that. So that was fun and we'd play with that. And then at his work, they had computers around because he was an experimental physicist who built big instruments. And some of these really early games like Space Wars, we were playing back before anybody else had a computer, so that was kind of cool, in retrospect.

And my dad was a builder. He was really good at building stuff, and for him, physics was all about building instruments, building big beam lines and stuff. So he'd have us in the basement. He had three daughters, he never got his son. They tried. Diana was their last shot, you know. And they were traditional, so they thought the son would be the one that would help dad in the basement building things and the girls would be whatever. So all he had was us, so he had us in the basement helping him build stuff. So we helped build the house. We moved to a new house that we built when I was seven or eight. I put together one of the stone walls, and he showed me how to do the masonry and stuff. So, I mean, that's not really science, but it was like nontraditional things, which I think is maybe more the point for girls.

MAESTREJUAN: A lot of tinkering?

BERTOZZI: Yes. I think for girls growing up who ultimately end up in science, whether or not they were in science as kids is less important than that they were able to do nontraditional things and break out of traditional thinking, I think, is more important.

MAESTREJUAN: Did you go to public schools?

BERTOZZI: Yes.

MAESTREJUAN: In Boston proper?

BERTOZZI: We grew up in Lexington, which, when I grew up, it was a sleepy little boonies town because it was too far away to be commutable. Now it's incredibly a really wealthy town now and very yuppified and the downtown is very commercialized. But that really wasn't true when I was a kid. Now it's very commutable, because what we consider a reasonable commute has expanded so much. So people will drive the forty-five minutes to an hour to Boston from Lexington, but when I was a kid, it was so far out that it was cheap and professors could afford to live out there. So there were a lot of older professors. Young assistant professors could never live in Lexington now, not like my parents did. Like the Bay Area, probably, it's the same thing.

MAESTREJUAN: And you said that you were smart, but in a different way than your sister. In what ways were you smart?

BERTOZZI: Like, she was really a math star, but not so good at maybe other things. I shouldn't say that. She was very good at a lot of things, but she really stood out in math. Like, when you met her and you saw how she lived, it was clear, you could have projected, her whole life would be math. It was absolutely obvious.

And I think that wasn't really my story. It was more, I wasn't sure what I was going to do, but I could do a lot of things pretty well, you know what I mean. But I wasn't like one thing always, which I think actually may be better for me in this job in the sense that I probably have better communication skills with my students. That's maybe important. And I was kind of a jock, and that was the one thing my older sister really never was, was a jock, and I kind of distinguished myself as a jock.

MAESTREJUAN: Doing—

BERTOZZI: Soccer. I went to Harvard, actually, to play soccer. I was kind of recruited onto the team. It's not like I was a dumb jock. I was a pretty hard-working jock, but I wasn't a genius, and I had to work hard to do well. My sister was just effortless.

MAESTREJUAN: Academically, how did you do in junior high and high school?

BERTOZZI: It was fine. I did well. I mean, it was As. In my family, again, you just didn't show up with a B. [laughs] Your life was hell, you know. So I did well in school mostly because I was terrified my parents would kick my butt.

MAESTREJUAN: What would they do? What was the price?

BERTOZZI: You'd sit down every night with Dad and go through it and make sure that on the next test you got an A. It was many evenings at the table after dinner doing math and physics and whatever you had to do to do better. So you learned you don't come home with a bad grade on a test, you get in trouble.

I mean, my parents intervened in our school a lot. In our junior high, for example, my sister had a math teacher who was one of these old assholes of the time that thought that girls do this, boys do that, right? And so she was so smart that she would go to these math classes, just kind of stare out the window because it was like gibberish to her what was going on in the classes. So the math teacher decided that she might have epilepsy. He called my parents and said, "It looks like she's having seizures because she's staring out the window." And really she was bored off of her butt, you know, and she was smarter than her teacher.

And so my parents went in there and taught him a lesson or two, and then my parents said to her "You should probably participate more in class because these teachers think that you have some disease or something."

So she said, "Okay."

And all the answers she just knew, so the teacher would say, "Well, does anyone know?" She'd [gestures], you know.

So then the teacher decided she was answering too many questions, so he called my parents, "She's acting too smart in class, and she's not going to have that many friends if she acts this smart. She's going to have a hard time making friends."

So finally my dad went down there to the principal and got this guy fired. And after that, other teachers were really afraid of my parents, [laughs] they'd come down and kick up a stink, you know. For example, I had a junior high school chemistry teacher who didn't, apparently, know that much chemistry. I had a test, I didn't do that well on it, and it turns out that a lot of those questions were wrong and that my answers were fine, but whatever. So my dad looks, he's, "Oh my god, he marked you wrong for this but that's correct, and he didn't even know that," you know, went down there and gave it to him, and I was so embarrassed.

So it was pretty high-standard household of academics. So it was pretty tense growing up in that environment. Again, you have to think of who my parents were, you know. They were a little older when they had— My mom had a hard time conceiving, so she didn't have us until she was in her late thirties. My parents were both pre-the sixties' social revolution. I mean, they were very old-world values. They very much had the values of their immigrant parents.

MAESTREJUAN: Did you speak Italian in the house?

BERTOZZI: No, not at all.

MAESTREJUAN: Your dad didn't speak Italian?

BERTOZZI: He did with his family, but my mom didn't know any Italian, and she didn't like it when he would speak in languages she didn't understand. Also, my parents, his family came from Torino [Turin, Italy] area, and they spoke a Piedmontese dialect, which was different from the conventional Italian, so even Italians sometimes didn't understand my dad. But my dad could actually speak French, too, even though he never really learned it, just because the Piedmontese had a lot of French influences from near the border.

So, no, I just remember phrases that he would say to his mom. But it's too bad. Also, I think at that time, in the sixties, it was sort of less cool to be speaking other languages. It was more of a nationalistic time.

MAESTREJUAN: How would you describe the quality of your education and the schools, junior high, high school?

BERTOZZI: In retrospect, I thought it was good, although my mom had a lot of complaints about it, especially for my younger sister. My older sister and I were in these top classes. They had levels back then—they probably still do—so you got placed either in the top, the middle, or the bottom, and if you were in the top, I think it was great. You were challenged and teachers treated you well and so on. But if you were in the bottom or the middle, I think you got the worst teachers. The best teachers always got the best classes and so on. So my younger sister, who was never placed in these top classes, got, I think, a bad shake. She really wasn't taught to read. In third grade, she really still wasn't reading, whereas we got taught to read pretty early. Before we even went to school, we got taught to read kind of in preschool, and it just didn't happen for my younger sister.

So my mom has a lot of bitterness about the school system, mostly from my younger sister's experience. But I thought they did okay by me, especially in music. In high school, I spent more time doing music, probably, than anything else. We had this great music program. I played in the jazz combo and I accompanied three or four singing groups. I don't think out in California, I don't see a lot of that. I don't think they have the money to do that out here. It was a wealthy town where I grew up.

MAESTREJUAN: What musical instrument did you play?

BERTOZZI: I play the keyboard, piano.

MAESTREJUAN: So you clearly got the cold shoulder when you broached the subject of becoming a musician. When people would ask you what you wanted to be when you grew up, what would you say?

BERTOZZI: Back then?

MAESTREJUAN: Yes.

BERTOZZI: I don't really remember. I might have said, "Oh, maybe I'll be a doctor." I liked biology. I took biology in high school, it was a great class, I had a great teacher. And I might have said—I can imagine, I don't remember, but I can imagine myself saying—biology or medicine or something like that. It wasn't going to be math or physics. I didn't have the knack for it, and I couldn't compete with my older sister.

MAESTREJUAN: In the community you grew up in, what were they going to do, the neighborhood kids that you hung out with, if you hung out them?

BERTOZZI: Mixed. A lot of kids from my high school went to college. It was a pretty high frequency. Again, a lot of professors lived in Lexington, but some didn't. It was mixed. It's funny, because I have looked through my high school yearbook on occasion—just nostalgia—and I remembered some of the kids. There were groups of kids that were definitely college bound and wanted to do well in school, and then there were groups of kids that weren't, that were more kind of going to stick around town and maybe work in their dad's business or something after high school. There were a lot of family businesses around.

There were a lot of Irish and Italian kids from big Irish and Italian families who had a lot of kids in them and maybe couldn't afford to go. On the East Coast, it's different. Out here, you can go to a great school for cheap. On the East Coast, you really can't. It costs a lot of money to go to a good school, and if you don't have the money, then you go to a state school, but the state schools are not that great out there like they are out here.

So there were a lot of kids who thought they were going to put themselves through U Mass [University of Massachusetts] or UNH [University of New Hampshire] or U Vermont [University of Vermont] or something like that, and those were universities where you didn't have to do that well to get in there. So there were a lot of kids who would go to U Mass and then

drop out after a year or two and they didn't have a big debt, so they weren't that invested in it. But I do remember a lot of them going to college. I'd say over half of my high school went to college, and again, that's higher than the national percentage at that time. I don't know what it is now.

I certainly hung out with a very college-bound crowd. I mean, from my high school, for example, eleven kids in my class went to Harvard.

MAESTREJUAN: Wow.

BERTOZZI: We were kind of a local feeder public school. We were probably one of the highest-represented public schools at Harvard. And then there're private schools that are highly represented. But I remember a lot of kids from my class in high school going to Tufts [University] and Brandeis [University]. And a lot of them stayed in Massachusetts, went to school. We were pretty parochial and considered only the East Coast that much. California, I didn't even know where California was. I had no idea. Had never been anywhere. The first plane ride I ever took was to visit Princeton to see if I would want to go to college there. So I was like eighteen. It was the first time I had ever been on an airplane. It was a forty-five-minute flight. I was like, "Oh my god." Because my sister had gone to Princeton, so naturally I would want to go to Princeton. But I went to visit there and I hated it.

And then that was the first flight, and then the second flight I ever took was when I visited grad schools and I flew out to California to visit Berkeley and Stanford [University]. And now when I fly all over the place and there're all these little kids on all these flights. Was it always like that? I don't know. I mean, did little kids used to fly around?

MAESTREJUAN: I don't know, because I didn't fly, either, until I was older. But, yes, a lot of people, a lot of my friends, take their kids flying.

Okay. Just to bring this up, you had mentioned it before, what religious beliefs and practices did you participate in when you were growing up?

BERTOZZI: Well, my parents brought us to various Protestant churches. We're Protestant, I guess. But again, my dad, he would just go just to be with the family, but it was not like he was praying to God or anything, he didn't really believe in a higher power. So it was more of a social thing than a religious thing.

But we went to—I can remember—three different Protestant churches. One, actually, was the Unitarian [Universalism] church. It's kind of a funky, hip sort of church. And that didn't last long. It wasn't, I don't think, quite traditional enough for my mom's taste. And then finally they settled on a Congregational Protestant church. So, again, on the East Coast, there're all the

little flavors of Protestant, and they're all different. Out here, I don't know that there's so much subtlety.

And this church, this other one, was one we could walk to. But what was great about that church, and the reason I actually didn't mind going, was the organ. It had this spectacular organ with pipes up as far as you could see, with this enormous sound. And the guy who played the organ was a very well-known local musician, actually this was kind of just his weekend gig. He was a music teacher in one of the schools— local schools or something—and a composer, and conducted some orchestra. He was phenomenal, and he would just play these [Johann Sebastian] Bach and [Wolfgang Amadeus] Mozart things, and he'd always be playing something as people were walking in. I'd get there early just to hear this. Spectacular.

And, also, the Congregational church, the hallmark of that church is that the congregation participates, and mostly in the form of singing. So you'd have a list of hymns you were going to sing, maybe four or five of them, and every five minutes the whole congregation would stand up and sing, and really sing, you know, with this huge organ just belting out, and it was just really fun, you know. And we all stank. It was a pretty big congregation of people, but just trying to sing. And that was what was so good about it. There was a choir, and they were good.

As I got older, I became a teenager, and I got the gig of leading the little junior choir, the little kids' choir. So I would play and direct them, and then they'd go up there and perform. Every month or so the junior choir would come up and sing for the congregation and I would get to conduct them, so it was a big deal.

So that's what it was for me. It wasn't like a religious experience, it was more of a music experience. Again, out in California, it's a little different out here, and so when we first came out here, there was one year where my partner and I—Christmas Eve service was kind of the biggest service of the year where I grew up, and you'd get to sing all the Christmas carol hymns, right—so we said, "Oh, let's find a Christmas Eve service. I haven't been to church in years." I mean, I never went to church in college or anything like that. So, "Let's find a church and go to Christmas Eve service so we can sing some of these," you know.

So we found this church up the street. We were living in Noe Valley in San Francisco at that time. So it's a church with this little piano, sorry little congregation, and then it's time to sing. So the hymn starts, and I stand up and I'm ready to sing and everyone else is sitting down. I was like, "Oh my god," you know. And I sit back down again, all embarrassed, and then everyone starts singing in this tiny little voice, you know. [laughs] And I was, "Oh, no," because I was ready to get up there and— I haven't found a church yet out here where people do that. Maybe you need a different religion out here or something.

So you must have grown up Catholic. Is that right?

MAESTREJUAN: Yes.

BERTOZZI: Do people sing in a Mass, a Catholic Mass?

MAESTREJUAN: Well, it's changed. When I was going to school, when I was younger, it was post-Vatican II, and they brought in guitarists and folk singers and all that other kind of stuff, and it's gone back to more traditional hymns that have been in the church for hundreds of years, so it just depends.

BERTOZZI: This Unitarian church was the kind of hymns with a guitar kind of thing. It's a little weird. [laughs] There was no Father, Son, and Holy Ghost, or any of that stuff.

MAESTREJUAN: Yes, I think it depends on the church. Well, what religious beliefs and practices have you carried on?

BERTOZZI: None, really. To be honest, I never really had much, again, because [of] my dad, I look at him and, I think oh Dad's probably right. Don't tell Mom, but I think Dad might be right, because shit happens and how do you explain it. The logic of it was not there for me. I didn't have enough faith, I guess, to look past the logic problem. So, I have no—now—religious affiliation. I haven't been to church again since that one midnight service in San Francisco where I didn't get to sing. [laughs] Oh, well.

MAESTREJUAN: What about musical instruments? Do you still play the keyboard?

BERTOZZI: Yes, I mean recreationally, nothing serious. But I have a piano at home that I tinker with.

MAESTREJUAN: Well, then, to move forward a little bit, you had mentioned that you were going to go to Harvard on a soccer scholarship.

BERTOZZI: It wasn't a scholarship, because technically Harvard doesn't do athletic scholarships. But they sent a scout out to watch me play, and then I got in, and I was there to play, clearly. But I didn't. [laughs] I figured out pretty quickly that collegiate sports are pretty time-consuming. You have to travel a lot and practices are every afternoon, and all of a sudden you realize that there're no science majors on any of these teams because you can't handle it. You have labs in the afternoon. How are you supposed to do that? So logistically it was impossible to major in science at Harvard and play one of these sports seriously. And so you had to make a decision. Again, I just couldn't help but hear, "What will my parents think if I

major in English just so I can play soccer, when I don't really have a talent for English?" And, also it's not a viable profession, as my parents would have put it.

So, yes, for a while actually, after a few weeks into my freshman year, when things were getting ready and I had the schedule, I was like, "How am I going to do this?" I was getting my schedule of courses together and already I couldn't make half the practices just with my math and biology and everything I had to take. I was like, "What am I going to do?"

I decided I couldn't play soccer, and the coach was pissed. So I decided, well, I have to do something, because I couldn't imagine not being on some team, you know. I actually went out for the crew team because crew had their practices very early in the morning, so you could do an afternoon lab. You'd get up at four in the morning, get down on the river and row until eight, and then go to class. This was unbelievably hectic, because, first of all, it's a grueling sport, and even though you have your afternoons free, you're so wasted by eight in the morning that you can't really do anything for the rest of the day. Did you ever row?

MAESTREJUAN: I was on kind of a recreational team very briefly.

BERTOZZI: So you're tough. Did you row on an eight?

MAESTREJUAN: Yes.

BERTOZZI: That's what I rowed. And the other problem was that I didn't really have the body type to row. You need to be kind of tall and thin, and I had kind of the short and stocky soccer-player build. I didn't really have the right body. And so I weighed in as a heavyweight, but I was a foot shorter than all of the heavyweights, so the coach says to me, "If you lose fifteen pounds, you could row as a lightweight."

And I was how am I going to—I'd have to amputate a limb—to lose fifteen pounds. I couldn't do it. I tried, but your freshman year there's kind of a force in the other direction. [laughs] Could not lose fifteen pounds in my freshman year. So I had to row heavyweight, and I just stank, and I wasn't any good. There were three boats, and I was in the third boat.

Oh, what happened is I got mono [mononucleosis]. I got sick because I was pulling all these all-nighters to get my work done and get to the boathouse by four. So I wasn't sleeping and I got mono, and I was really sick, so then I couldn't row, and then that was it. I decided I should just quit. So that was it. I never did a sport.

I chose biology as a major at that point, and I switched to chemistry later.

MAESTREJUAN: What other opportunities besides going to Harvard—besides Princeton—did you have?

BERTOZZI: That was it. [laughs] Very parochial. Well, actually, I almost didn't look at Harvard because, again, my sister went to Princeton, therefore what other choice would there be for me but to go to Princeton? And I applied early admission to Princeton, got in, I was done.

And then I went, "So maybe I should go visit this place. My sister's there. I'll stay with her." So I went to visit and it was just awful. The people, the students, were snobs and they were just preppy and I felt really claustrophobic. It was really suburban, little golf-coursey. Have you ever been there? It's Ivory Tower in the truest sense of the word, you know. And just the students I really couldn't stand. And even the ones I was visiting with on the same trip, they were all from private schools and had this attitude, and I said, "Oh my god, I don't think I could go here." My sister loved it.

So kind of the day of the deadline, I was like, "Oh my god, I've got to apply to some other place. What am I going to do?" So I applied to Harvard because it was there, you know. And I—thank god—got in there.

So I said, "I hope this is better." I went to visit Harvard. Well, Harvard Square I'd been in and out of a million times, growing up, so I kind of already knew Harvard Square. And Harvard, it's definitely a snooty private school, but it's so diluted by the city that you don't have to necessarily notice that. You're living in the city, so that was a much better fit for me. I'm more of a city person. And thank god, because I think I would have died if I had gone to Princeton. It would have killed me.

MAESTREJUAN: Okay. Let me flip the tape over.

[END OF TAPE 1, SIDE 1]

MAESTREJUAN: Okay. Well, at what point did you decide on biology as a major, and why biology?

BERTOZZI: I liked it, you know, it was interesting. I had had this good high school teacher. I'd always thought of myself as interested in biology because of that experience in high school. And you've got to pick a major, and that seemed like a reasonable one to me. It was acceptable to my parents, and I was interested in it. And I did like it. Biology's fascinating. I took chemistry my freshman year as a requirement, didn't care for it. Freshman chemistry, I sort of gutted it out, but it was just a requirement.

And then what happened is in my second year I took organic chemistry, again, as just a requirement. I was all prepared to kind of hold my nose through it. And I loved it. I can't even describe the relationship I had with it. So that changed my thinking, and then the end of my sophomore year, my second year, I switched my major to chemistry. So, starting my junior year I was a chemistry major. But I still took a lot of biology classes because I liked it.

MAESTREJUAN: And at Harvard [University] at that time, where was the biological chemistry, or biochemistry? Was it in the biology department, did it have its own department, or was it in the chemistry department?

BERTOZZI: It was not in the chemistry department. I'm not sure. I guess it must have had its own department. There were courses that were biochemistry courses. Yes, there was a biochemistry department at Harvard. It's separate from biology. At least it was that way, I'm not sure now, actually, now that I think of it. Whereas at [University of California,] Berkeley, biochemistry is part of MCB [Department of Molecular and Cell Biology], which is everything. At Harvard I think it had a different identity.

Yes, organic chemistry was fantastic. The person who taught it had just moved from Caltech [California Institute of Technology] to Harvard. It was his first semester teaching at Harvard, and he was fabulous. And, also I just felt like I had this intrinsic understanding of it to the point where I just couldn't get enough. I was kind of a brainy kid, but I was never one of those kids that would rather stay home on Saturday night and study than go out and party. I was never that into academic stuff. I did it, I worked hard, and then I went out and played hard. And organic chemistry was kind of the first thing that I felt like I'd rather not go out because I couldn't tear myself away from this book, and I liked to do these problems.

Part of it was, organic chemistry's a very visual science. It's a very visual part of chemistry. And if you like to draw pictures and think about things in three dimensions and so on, then it usually clicks well with you. By contrast, I was never that proficient at math and physics, things that were more abstract, that you couldn't really draw a physical picture of and explain in three dimensions with objects, you know. So organic chemistry, I think, is unique in that aspect of chemistry, in that it is really the visual part and not so much the abstract part.

MAESTREJUAN: And how well did you do in physical chemistry?

BERTOZZI: I held my nose and I gutted it out. I took quantum mechanics, and thank god for grade inflation at Harvard. [laughs] Because at Berkeley I don't know if I would have passed that class, frankly, because I didn't take p-chem [physical chemistry] until my senior year, I put it off until the last possible minute. By that point I was heavily into a research project and I was kind of blowing off classes anyways because I was in the lab all the time.

And so physical chemistry, of all my chemistry courses, it's the one I never really did justice to, to be honest. I blew off a lot of it and I pulled some stunts in there. I didn't show up for one of the midterms at all, and on the final I kind of showed up an hour late because I was out studying in the hallway for an hour, and I left half the exam blank. So I didn't get much out of it. I'm sure I could have gotten more out of it if I'd actually paid attention to it. But there I was in my senior year, not really caring. And, again, fortunately, at Harvard you can kind of blow off a class and still get, like, a B-plus. It's totally grade-inflated, whereas, at Berkeley I would have had an F. I would have failed me if I had done that in my class, because we don't have grade inflation here.

MAESTREJUAN: Did you ever consider going to MIT [Massachusetts Institute of Technology]?

BERTOZZI: No. [laughs] How uncool would that have been? My dad was there. And plus, when I went to college, I wasn't convinced completely that I was going to be a science major. And if you go to MIT, there aren't a lot of options outside of science. Now there're more: Noam Chomsky's there, yes you can go into linguistics. I went to high school with his son, and elementary school and junior high school, all the way along, with Harry Chomsky. He was like my sister [Andrea Louise Bertozzi]: One of these brainiacs who had to skip two grades to be able to converse with his teachers and so on. And he went to MIT as an undergrad [undergraduate student]. No. He went to Harvard as an undergrad, went to MIT grad [graduate] school, but I don't think he stuck it out there. I think he left grad school early or something. And he lives out here in the Bay Area now, Harry. He works for some software company or something. Smart kid. But it's not about Harry, is it?

What was I saying? What did you ask me?

MAESTREJUAN: Just how well you were doing academically at Harvard.

BERTOZZI: Well, I did well. In the end, I graduated summa [cum laude], so I did well. But, again, it's a grade-inflated university, I worked hard, actually. I'd say I worked really hard. Like my sister, when she reminisces about college, it's all about the orchestra she played in, the band she played in, the trips to New York she took, and all that kind of stuff. And when I think of college, I think of all-nighters in the library, in the lab, studying all the time. I really studied a lot. Especially, my freshman first semester, I wasn't quite together, but after that I was. A lot of kids had this experience at Harvard. It's definitely a tough place, and grade inflation notwithstanding. Everyone who goes there is a type-A personality, and everyone wants to do well, and so there're a lot of people fighting over who gets the A versus the A-minus. You know what I mean.

I was lucky that I found something where I kind of had a knack for it, and it was a little

bit effortless for me, organic chemistry. But again, my older sister, when you're a math genius, you just can do it, right? And the kind of science I do is more about how many hours you put into it, because I'm an experimental scientist, and so you can have a great idea, but if you can't do it in the lab, it doesn't matter, it doesn't exist. And for my sister, if she has a great idea, that's the end of it, she's done. Write it up and have an idea.

MAESTREJUAN: Okay. You said you were still interested in biology. What was your relationship with biology at this point, as a chemistry major?

BERTOZZI: I still took a lot of biology classes. I took them as electives. Once I switched my major to chemistry, so I had to satisfy the chemistry requirements, which were some upper-level organic chem [chemistry] and p-chem. and labs and stuff, but there was enough space. I took neurobiology, I took photobiology, which was cool. I took, of course, biochemistry, and I took some seminar courses on general topics and cell biology. I probably would have been able to do a double major if I had bothered to do the paperwork, but I didn't really think about it.

I liked chemistry because it was a very small major at Harvard. There were maybe thirty majors per class or something.

MAESTREJUAN: Wow.

BERTOZZI: Whereas biology was huge, and all premeds [premedical studies students], you know. But Berkeley, it's the same. We have at Berkeley maybe fifty chem majors per class here, and then chemical engineers on top of that, maybe there're a hundred something total, and there're thousands of biology majors.

MAESTREJUAN: So in your labs, how is the competition among the students in your chemistry labs?

BERTOZZI: In upper-division chem labs, it didn't feel like there was much. It was very friendly, everyone's kind of together, you know. I never felt like people stink on each other in the lab or something. You know what I mean? I never had that experience. People did say things. I remember people saying, "Oh, premeds, they sabotage each other's labs," but I never saw that, ever. And especially in the upper-division classes. By that point everyone's just trying to stay alive and get through it. Who has the time to worry about someone else?

It was fun. We had groups that would get together and work on problem sets together. I had a group of chemistry friends I hung out with. I was in a lab for my senior year and the summer before that, and so I had a lot of grad student friends that I had made at lab, and we

hung out together and stuff. It was kind of a scene, you know.

MAESTREJUAN: At what point did you decide that this was something that you would want to go to graduate school or pursue this further, or just get a job? One thing I can remember: the chemistry majors had a good job.

BERTOZZI: In my family, we went to grad school. It was pretty much a foregone conclusion. In my family, getting a Ph.D. is like for other people graduating from high school. *That's* when your parents are proud. [laughs] Of course, my sister went to grad school, right, so I had to keep up with that.

But also, at the time I couldn't think of anything I would rather have done. It never occurred to me to just go get some job. And at Harvard, they train you very much like you're going to go to grad school, and so they never talk to you about getting a job. I didn't even know you could get a job out of college. I never heard of such a thing. That's what it's like out there. Out here, it's totally different, again. Our students seem very well aware of the fact that they can get a really good job as a BS [Bachelor of Science] chemist in a pharmaceutical company, because there are job fairs and they see that. But at Harvard, there're no real job fairs like that. It's very academic, you go to grad school.

So I worked for an assistant professor [Joe Grabowski] doing research. He was actually a physical chemist, so I worked kind of in a p-chem lab. It was, in retrospect, probably one of the best things that ever happened to me, but it actually wasn't my original intention because I had wanted to do organic chemistry, that's what I loved.

This is where the story's going to get interesting. This was the eighties, mideighties. The faculty had a very different face than it has now. There are a lot of people that have retired since then, and also they've had a lot of new faculty come in since then, so I don't want this statement to reflect on the present faculty, some of whom are very good friends of mine. But at the time Harvard was like [University of California,] Riverside's history department. It was a bastion of sexism and mistreatment of women. There were no women faculty, there was one who was hired around the time that I had started, and she was the butt of every joke. She was a brilliant physical chemist, and Harvard is a department that's dominated by organic chemists, and at the time she was one of maybe two or three physical chemists, and they had ten or fifteen organic chemists.

Berkeley, by contrast, has historically been a physical chemistry department, so in the old days, it was Harvard was organic department, Berkeley was the physical department, and that's what you did. It was a coastal kind of thing.

Now Berkeley in the sixties and seventies started hiring organic chemists. We have now a critical mass, but we're dominated by physical chemistry, and our Nobel Prizes are in physical chemistry. Harvard now has some physical chemists, but, still, all their Nobel Prizes are in

organic chemistry and so on, right. So you still feel that.

So those organic guys just ran that place, and of all the branches of chemistry, organic is the most well known for being kind of heavily male-dominated and very sexist. Not p-chem, actually, organic chem. So why that is, I don't know. It predates me, but it just is. So it was a very kind of macho scene. It wasn't even the faculty, because as an undergraduate at Harvard, you don't interact that much with faculty, you know. At least I didn't. It was just even the TAs [teaching assistants], the graduate students who were in charge of your sections and your labs, those were the people you interacted with most often, and some of them were awful. I felt like they were sniffing around me, you know. I mean, it was disgusting. One of them showed up at my dorm one night drunk, with half his clothes off, yelling. I mean, just crap like that.

And so nonetheless, I liked organic chemistry, I wanted to get into a lab and do organic chemistry, and I couldn't get into one. No one would take me, you know. And I had an A-plus, I had the top score out of four hundred students in that class, and I could not get into a lab. And, again, in retrospect, I think of if an undergrad from my class has the top score out of seven hundred students that I teach, I'm happy to have the student in my lab, who's usually a really bright student. But none of those guys would take me. So finally, out of desperation, I said, well, I guess I'm not going to be an organic chemist after all.

So I found a job in a biochem [biochemistry] lab, a different department. I was looking for something for the summer, and maybe for a thesis project after that. And then what happened was, I was taking an advanced physical organic chemistry course. So, physical organic chemistry is basically the study of organic reactions from a very mechanistic point of view. It's not really physics or anything. It's quantitative, but it's still organic chemistry. It's kind of upper-division organic. I loved it. It was a graduate course, but there were some undergrads in there, and so I was in there.

I was doing really well, and one day after class, the guy [Joe Grabowski] who was teaching that course, a physical chemist, actually—he would call himself an organic chemist—he was a guy who built instruments and stuff. He was an assistant professor. And back then, assistant professors never got tenure at Harvard, just categorically. And so because of that, it was very hard for them to get grad students to join their groups because they were—everyone knew—a transient. And so this guy had a hard time getting students to join his group to build these instruments and so on, so he started recruiting undergrads.

So he came up to me after class and he said, "You're doing pretty well in this class. What are you doing this summer?"

I said, "Oh, I'm going to do research in this biochem lab."

And he goes, "I think you should come do research with me."

And it was the first time a professor had ever talked to me at Harvard and knew my name and knew I was doing well, took an interest. So I went, "Oh, wow, okay." So I bailed on

the other job, and I went and joined this guy's lab for the summer.

My job was to build this instrument, which I didn't even understand what it was. It was a photoacoustic calorimeter. It was way above my level at that point, but this guy had faith in me. He said, "One of these things has been built before by this person who's at [University of] Colorado [at Boulder], and I have a copy of a Ph.D. thesis of the person who built that one, but I'm thinking of one that's a little modified in these ways, and so see if you can figure this out."

Okay. So I spent that whole summer writing software code to drive this instrument, and I'd understand the instrument. So back then if you wanted to make designs for an instrument, you did it on a drafting table with a drafting toolkit. You didn't have computer drafting programs. So I learned how to do drafting, which is a whole art because there're all these rules to it, and how do you indicate different specifications with what pen, and you have to set up twenty pens, and a different pen for each thing. So I taught myself how to do those with his help, and I designed this thing, and I had the machine shop building parts, and I would assemble them.

It's basically a laser-driven instrument where there're optics involved, and then you're collecting data from a piezoelectric microphone, which I built. And I just learned all this stuff, and it kind of reminded me of playing in my dad's basement with all his little gadgets. Some of the stuff was familiar to me, like oscilloscopes and digitizers. I knew what those things were.

And so I built this thing, and that became my thesis project, collected some data on it. It was actually a very sophisticated project for an undergrad to do, but this guy just had total faith in me. He just let me go. He said, "Oh, you'll figure it out." And there were no grad students around to sort of hover over me or anything, so he treated me like a grad student, and he treated me with respect, which none of the other ones really had, you know. And so that was great.

And then he was the one who was, like, "Oh, you should go to grad school." At Harvard they had these senior theses at Harvard that you write for certain departments to get honors, and chemistry actually didn't have a thesis requirement for honors, but this guy said, "I want you to write a thesis."

I said, "But I don't have to write a thesis. It's chemistry."

And he said, "You have to write one for me. I want you to write a thesis."

So I wrote this thesis on this whole project and everything, and it turns out he wanted to submit it for one of these undergraduate thesis prizes, which are highly coveted and so on. And he did, and I won this thing. It was a lot of money, you know. Well, at that time it was a lot of money.

And so, he promoted me that way, and he would talk me up to his organic colleagues. "Oh my god, I have this undergrad, she's amazing. She's going to go to grad school. I think she

should go to Berkeley," and so on. You know what I mean? No other female, I think, enjoyed that, at least none of my set. There were a couple of other women chemistry majors at the time, and one of them was in a lab, too, but she didn't get any attention. She's an inorganic chemist. The other one never worked in a lab in chemistry, maybe in some other department. I forget. It was usually men back then.

The grad students at Harvard, out of thirty incoming students every year into their graduate program, maybe two or three would be women, and they'd all quit by their second year because they were like, "You guys, screw it. Forget it." They're much better now.

MAESTREJUAN: What enabled you to overcome this animosity by the faculty, that you were a woman who was interested in organic chemistry?

BERTOZZI: Well, it wasn't so blatant. It's not like any one of those guys said to me, "Well, I don't have space for you because you're female." I mean, of course, they wouldn't have said that, because they'd go to jail or something. I don't know. They probably wouldn't have. It was just that none of them somehow had space for me, and then, like a week later, a friend of mine from my same class would say, "Oh, I got a job in Evan's lab." You know.

I'm like, "Gee, a week ago, he didn't have space for undergrads, and this week he has space for you, but no space for me." It was stuff like that, where in the end, with all these labs, I was just, like, "Gosh, why can't I get into one of these labs?" I couldn't have done any better in this class, you know. I was like, "How could I possibly have situated myself better?" I couldn't think of a way. I was literally the top scorer, and this was my one class where I was it. This class was my life, I loved it. And I was in there all office hours. I just couldn't get enough of it. But I just couldn't get into any of those labs, you know.

But now, again, in retrospect, I think this might have been a good thing, because knowing now what it's like in those big synthesis labs, with all those guys, it's a real testosterone fest. I'm not sure if I had worked in a lab like that, that I would have really wanted to go to grad school and do that, because a lot of women do get turned off by that. It makes them feel alienated and like they don't really belong, and they say, "God, is my whole life is going to be like looking at these Budweiser babes on the wall every day, and having these guys go out to the combats [unclear] on the strip clubs on the weekends and I'm not invited, and having my professor or my superiors, my boss, whatever, just look right through me over at some guy?" You know what I mean? I mean, that's what that field was like. It's better now, but again, backtrack twenty years and if you're female and you survive that— I mean, just look at the organic faculty across the nation. You would find less than a handful of women nationwide.

By contrast, bioorganic chemistry is much more representative of women. Even p-chem, inorganic, many more women. Material science. But organic synthesis, forget it.

MAESTREJUAN: And what do you think accounts for this?

BERTOZZI: It's like what accounts for the impoverishment of African Americans. It goes back so far, you'd have to trace it back to Germany, to the origins of organic chemistry as a discipline, back to the 1800s, 1700s. But I'm sure it can be traced. It would be interesting to do that. And also, organic chemistry does have its origin in Germany as a field, and it's very hierarchical.

The style in organic synthesis is to have big labs. The big organic synthesis labs have between forty and fifty people in them. And you're cranking out postdocs [postdoctoral fellows] and grad students every four years. A typical organic synthesis lab might take between four and six grad students a year, that's how they sustain this big lab. So one person in the course of his career can influence hundreds and hundreds and hundreds of grad students and postdocs. I mean, really, several hundreds. And so if that person creates an environment, it's infected now hundreds of people, right? And they create their lab like that, and they infect hundreds of people. You know what I mean? So it propagates very rapidly in a field where the labs are very big and can be traced back to a handful of people.

Whereas inorganic chemistry, that is a field that has tended to evolve more with smaller operations, more spread out, not so centralized to a few big players. But if you just go around, again, the country, and ask the organic synthetic faculty, "Oh, who did you work for?" they'd say, "I was a grad student in this lab, and a postdoc for that lab," and altogether there would be ten total labs that they all came from.

MAESTREJUAN: I think I'll pursue this a little bit more later, but at the time that you were deciding to go to graduate school, how aware were you that there was this kind of institutional characteristic.

BERTOZZI: I figured it out pretty quickly, just from having the TAs, just one after the next of these TAs when I was a grad student. As an undergrad, you get the feeling, okay, this is what these guys are like. This is sort of what it's like, this is the culture or whatever. I figured it out.

And I came to Berkeley. There were a lot of reasons why I came to Berkeley for grad school, but when I visited, I did the tour of the usual suspect-type places, and Berkeley was the place where I actually met a sizeable number of women students, and not only were they here, but they seemed very enfranchised. Like the way they talked about their research just, "So, what do you do?" "Oh, well, I'm working on this project." They just seemed like they owned their project, they were excited to talk about it, enthusiastic, they just had this confidence about them, as opposed to the few women at Harvard who had their head down and just trying to survive there, and never really got the feeling they were part of a group. They were just existing in parallel with the other forty guys that were in their group, and just trying to stay above water. But you never got the feeling they were really in with the group.

And here, it just seemed like there were all these women around. There weren't that many, actually. It was only about 10 percent at the time, but that actually was a lot. And in a big department, that's a critical mass. And just the way that they presented their research was just, wow, they're so confident, they're so in it, just like they're part of their group, and their whole group goes out to play ultimate Frisbee and so do they. They're all part of it together. So Berkeley just gave me that impression, and I think that was accurate.

MAESTREJUAN: And how concerned were you that you'd find yourself in another Harvard situation.

BERTOZZI: Well, there were women here in the organic labs, so, yes. You could see women in the synthesis labs, and also, again, Berkeley didn't grow up as a department that was organic, right? Organic chemistry is a newer thing for Berkeley's department, and so it didn't have generations of tradition going back to some old guy. You know what I mean? So you felt like you had a shot here. There were a lot of younger faculty who were more open, having women in their group.

And then I joined the lab of a brand-new assistant professor [Mark D. Bednarski]. I was one of his very first students, because this is what I had done as an undergrad, it worked for me there, and again it worked for me here. He treated me with respect. In fact, he probably treated me better than any other student in the lab. I wouldn't say he treated me differently, but I worked hard. He knew I was good, and I had a fancy fellowship and everything, and so he treated me with the respect due the work that I did for him, which was nice. He sent me to conferences. I'd good results, he'd send me to a meeting. So I had a lot of good experiences, wrote a lot of papers. Again, I could have worked for someone else here and would have done okay, but it would have been a different experience.

MAESTREJUAN: Well, what other programs were you looking at besides Berkeley?

BERTOZZI: The usual suspects: Caltech, Stanford [University], Yale [University], Columbia [University]. That was it. Nothing in Boston. I was finished with Boston. And, frankly, I was finished with the East Coast. I still looked at Yale and Columbia, anyway, because I figured I should

MAESTREJUAN: Why was that?

BERTOZZI: Because I had lived there forever and it was time to move. I took out the map and was like, all right. We've got Caltech, we've got Berkeley, we've got Stanford.

And I was so stupid. So when I planned the trip to go visit, I had never been anywhere, really, other than New Jersey. And I got this little packet from Berkeley: "Okay, well, you should fly into San Francisco Airport."

I'm like, "Berkeley's near San Francisco?" I had no idea. "Wow, that's a bonus," you know. [laughs] I had a little bit of a calling to the Bay Area, in part because I'm a lesbian, actually. Not that Boston's such a bad city, but San Francisco, especially in the eighties, was gay Mecca. I definitely had this feeling, "Oh, well, if I can end up near this place I've heard about, then that would be even cooler still." So that was part of it, too.

But really, if Berkeley's chemistry department—the people and their attitudes—had been in Columbia, I would have gone to New York. I visited these places and I was like, eh, Yale was like Harvard all over again, and Columbia was a bit like Harvard all over again, too. Actually, I thought I would probably end up going to Stanford, in part because when you're at Harvard, you think of Stanford as being in the mirror image, sort of. It's this fancy private school, and Berkeley's a state school, and when you're on the East Coast, you don't have any concept of what that means. And then I visited Stanford and I was like, hmm, it was a little bit Harvard, kind of, all over again, too.

And then I came to Berkeley, and within thirty minutes of being here, I was like, "That's it." I just knew it, just from the people and the way they behaved, the women particularly. I felt like I could survive here, like I'd probably be able to do science, people wouldn't get in my face about being lesbian, so I thought at the time, you know. It's never a perfect world, but you know what I mean. Better than it could have been.

MAESTREJUAN: Were there rotations in the chemistry department, or how did students choose labs?

BERTOZZI: No. Just choose. You talk to people, sit in on group meetings. We don't rotate, still don't. It's rare in chemistry, especially because we don't have training grants, no NIH [National Institutes of Health] to pay for that. Someone has to pay these students.

MAESTREJUAN: So you came in with your own fellowship?

BERTOZZI: Yes.

MAESTREJUAN: Okay. And how did you choose the [Mark D.] Bednarski lab?

BERTOZZI: He was this incredibly enthusiastic, energetic guy, and, again, all along I had really wanted to do organic chemistry, and I had this interest in biology, too, kind of on the side there. And his group, he was interested in applying organic chemistry to problems in biology, so it was a good fit for me.

MAESTREJUAN: You had done a lot of lab experience in more of a physical chemistry.

BERTOZZI: In p-chem [physical chemistry]

MAESTREJUAN: So how well were you able to hit the ground running?

BERTOZZI: I had no clue at all. I mean, I had to learn a lot. But in grad school, even if you do come in with the experience, you still have to learn a lot. You're so clueless. I was clueless, but a few months. And I knew on paper all about it. I mean, I really knew how to think about organic chemistry. I just had to learn what are the techniques for setting up these reactions, and so on.

But I had a very good intuitive sense of what should work and the way organic molecules behave and so on. I was slow at first. I was kind of a klutz, and I made some stupid mistakes. But, again, I look at my own students, and I think I was well within the range of stupidity. [laughs]

MAESTREJUAN: How was Bednarski as a mentor?

BERTOZZI: Interesting. He was only there for about three years. He got sick, actually. So this is another story. Okay. So he's an interesting guy. He was young— I now in retrospect realize—he had a lot of big ideas, but didn't have a very good practical sense of how do you set up a lab and get it to work. He, himself, had come from the organic chemistry tradition, and he had worked in these big labs. So he had been in a very famous natural products synthesis lab as a grad student, which had fifty people in it.

Then he went and postdoc'd [postdoctoral fellowship training] at Harvard. Actually, I had met him at Harvard when I was an undergrad there, so I knew who he was already. He postdoc'd with this famous guy, and there were fifty people, so he had never built a lab from the ground up. He'd always been in these big labs, everything running already, and I don't think he had a very good sense of what you can do with four clueless first-year grad students versus what you can do with fifty postdocs. So it was hard at first, because he didn't really define projects very clearly for those of us who joined his group. It was, "Oh, I think we want to build a mimic of the cell

surface," he'd say. "So go do that."

"Okay." [laughs] I had no idea. So my first year in grad school I had ten different projects all over the place, and I didn't know what I was doing. And every day he'd come in and say, "Oh, no, forget that one. I want you to work on this now." And then the next day, "No, forget that. I've got a better one." And it was this frenetic moving target.

So he lost a lot of students, actually, early on, because people just couldn't deal with it. A few of us stuck it out, and what happened is, we eventually settled in on a project that we felt we could make a thesis out of and just resisted all the weird inputs and distractions. So I had a couple of things that I thought I could develop and made a thesis out of that. It worked out for me, but it was not that easy. He was a strange guy in a lot of ways.

Then he got colon cancer, so in my third year of grad school he was ill, and it was pretty bad. I don't know. It was a combination of factors, but he decided that he needed to switch professions, basically. The stress of it all was not good for his health, and he wasn't that happy, I think. There are some big egos in the department, and he was getting stepped on by a lot of them because he was this young enthusiastic guy, and I think some people felt threatened by his enthusiasm or something, I don't know.

And then when his group started getting chaotic and he started losing a lot of students, people saw that as a weak point and started attacking him, you know. So, a little ugly.

Back then we had some things going on here where this professor would fail all of that professor's students in the qualifying exam, and then that one would fail— They had these little petty rivalries that were played out on the battlefield of these poor innocent students. Just weird stuff like that. So he didn't like that.

Also, this was during really tough California budget times, and so he didn't have a raise once in the three years he was here. He was getting paid some shit assistant professor's salary. He couldn't buy a house, he didn't see any prospect for ever owning a house, you know. And so I think all these things added up, and then he got sick, and he said, "That's it. I'm out."

So he quit and he went to med [medical] school, actually. He decided he wanted to be a doctor and work with cancer patients. So he went to Stanford [University School of Medicine]. So my last year of grad school was the end of his first year of med school, and he was still nominally my advisor—he was on leave— but I hadn't seen him in a few years, you know. I mean, I'd sort of seen him here and there, but he hadn't been actively advising me. I was just here doing my thing. There were maybe three of us that were far enough along that we convinced the chair of the department to just let us stay and finish our thing. And the money was there in the accounts, we'd just spend it out. And anyone who was younger than us had to find another group. So my last two years were weird in that I had this little group with no boss. We were in our own group.

MAESTREJUAN: In his old lab space?

BERTOZZI: Yes. We kept our space. Some of it was given to other people, but I kept my lab and my essential equipment and my domain, and I just had my little thing going. I had a couple of undergrads that were working with me, and I wrote papers. I wrote a lot of papers in that period, actually. And then I wrote my thesis, and I drove down to Palo Alto to his house for him to sign. [laughs]

In fact, it was bad. He had surgery and chemotherapy, the first round, so he was out for a year. Then he applied to med school and got in, and went to med school. And at the end of his first year of med school, they found a metastasis in his liver, which is really bad. This guy was thirty-three. It's very young for colon cancer. And so they did surgery and everything. He was pretty out of it. And his wife [Lynn] at that time was pregnant with their first child, and she was like, "What am I going to do?" And she was seven months pregnant or so when they found that metastasis, and so she all of a sudden realized, "Oh my god, this guy is not going to be able to help me with this pregnancy."

So my partner [Cynthia] was at that time working for the Health Care Financing Administration as kind of a state representative for Medicaid/MediCal, but she always had an interest in maternal/infant health and so on, and she had been working—just volunteering—as a labor coach at SF [San Francisco] General [Hospital] for women who come in and don't have a partner. They're young teenage moms often with no boyfriend anywhere and don't speak English. So she had been doing this, and Lynn, my boss's wife, knew that, so she asked if we would be willing to be her labor coaches. So we did Lamaze classes with her, and we were there for their daughter's birth, and it was really exciting.

And then I haven't really seen them much since then, because then I graduated and I went off to postdoc. He actually is still alive and doing well, I understand, but I haven't seen him in a while. But kind of a weird experience.

And, again, at the time, I was, "Oh, poor me, oh my god, what a disaster," blah, blah, blah. But now, again, I look back and I think it was a really good experience because I wrote grants, I got his grant renewed so we could keep working, I wrote papers, I argued with editors about getting papers accepted, and things that a lot of grad students might not get exposed to. And it's probably good that they don't most of the time, but I thought that was a good experience for me. It forced me to take it up a notch.

And then when I postdoc'd, I worked in a much more normal lab, where I had a normal boss, and it was a very well-established lab, and so I got to see what a real lab was like instead of this crazy lab that I had been in as a grad student. And although it was really good for me, sometimes I'd miss the crazy lab, the kind of everyday—now what obstacle will be in your way that you'd have to overcome—sort of thing. But it was good to be in the sane lab for a couple of years.

MAESTREJUAN: Most graduate students fret a lot about taking the next step and knowing how important pedigree is, what labs you work in, and the relationship with your mentorship.

BERTOZZI: I know. I hate that.

MAESTREJUAN: And also the politics of publication. You want a good postdoc because you want a good job. You need to publish in the right journals.

BERTOZZI: I can't stand that.

MAESTREJUAN: So how aware were you that there is this: You have to do the certain right steps in order to get the right postdoc.

BERTOZZI: I didn't care at all at the time. I really didn't give it a thought. So in grad school, as I was finishing up, I was like, "Okay, I know I want a postdoc." I had a sense that I might want to be an academic person, I was feeling that I'd be good at that and I would enjoy it. And so when it came time to choose postdocs, I talked to my various professors around here who I knew from committees and so on. And I said I'd been reading the literature, and there was a story coming out at that time.

I had been a carbohydrate chemist, so my Ph.D. thesis was in synthesis of carbohydrate analogs for various biological applications, but really mostly what I did was synthesis. Okay. And the story had come out in the early nineties that carbohydrates are important in inflammation, and there was a family of receptors that had been discovered that bind to carbohydrates and mediate the attachment of white blood cells, which normally would flow in your bloodstream, to the sides of the blood vessels. And that's the very first step in the cascade of events that leads to inflammation, and that can be a good thing if it's inflammation against an infection or something, or it can be a bad thing if it's an inflammation against an autoimmune reaction, that you get arthritis or something. And so the fact that sugars were playing a big role in this early part of the inflammation cascade was really exciting to people who were chemists who work on carbohydrates, and so on.

And so I had been following *Science, Cell, Nature,* and everything, and I had been reading these things, and I thought, oh, I'd really love to work in a lab that studies these interactions between blood cells and the blood vessel walls, and really delve into the biology of this, and bring, maybe, my chemistry sensibilities to bear on this somehow.

So I looked around the literature, and there were a couple of labs that were clearly at the

frontier of this, and one of them was at UCSF [University of California, San Francisco], and that was Steve [Steven D.] Rosen's lab. Steve is well known in his circle of cell biologists who study leukocyte adhesion, but no chemist would have ever heard of him.

So I went around to these guys here, my various professors, and I said, "I'm thinking of postdoc'ing for this guy Steve Rosen."

And they're like, "Who?" Oh, no, no." And so the advice I got was that was career suicide, that rather what I should do is—since I had done graduate work for a guy who basically left the field of chemistry and therefore I didn't have the backup of some big overlord who could help me behind the scenes, whatever these guys are supposed to do, which I had no idea—they said, because I didn't have that it was imperative that I go postdoc for a, b, c, or d. And "These are the people who will get you the academic job you want. You have to work for one of them. And for you, especially, because you don't have a pedigree coming out of your graduate work, your advisor is gone."

I was like, "Okay." And so I thought, okay, well, let me read about a, b, c, and d, and I knew what those guys did, and it just didn't flip my switch at all. It's like, yes, it's interesting work, I'm glad someone else does it. I couldn't see myself getting excited to go work in one of those labs, that was the problem. Whereas this other thing, these leukocyte interactions, I was like, oh, that's just incredibly cool.

And so finally one day, I was like, "Screw it. Flush the toilet of my career, that's fine. I'm going to go postdoc for this guy because it's what I'm interested in doing. And if that means I'm dead to the world of chemistry, so be it." Because that's what they told me: That basically you might as well be dead. You will have died.

And so I did that. And, again, at the time, I didn't really give any thought to my long-term career. I just really wanted to work in this area.

MAESTREJUAN: And what was it specifically about this?

BERTOZZI: Yes, so this guy had discovered one of the receptors that binds to the endothelium, and he knew—and the community knew—that this receptor was binding some kind of carbohydrate, but nobody knew what the structure of that carbohydrate was or how it's regulated or what it's doing on the endothelium, how it got there, and so on. And so that's where I thought I could contribute something, because I knew how to think about the structure of this thing.

So I sold myself to this guy [Steven D. Rosen]. I sent him a letter, "I'm interested in your lab as a postdoc."

And he wrote back, and he's like, "Oh, well, hmm. I don't really get applications

from chemists, usually. I get cell biologists." He said, "But I'm intrigued, so why don't you come on over."

So I read all of his papers and all of his paper citations, and I was like, "I'm going to go over there, and I've got to be able to talk biology or this guy's going to laugh me out the door, because I don't know how to clone a gene. I don't know how to do tissue culture." I had never done techniques of biology. So I said, "I'd better go in there and at least sound like I have a clue."

So actually I was taking a graduate course in immunology here at the time, because I kind of had a feeling I was going to be interested in this stuff. And so fortunately, in this course, we had read a lot of papers, *Cell* papers, so I could speak the language of lymphocytes and so on.

And I went over there and I gave a talk to this guy, and I just gave him the hard sell. I was like, "You've taken this problem down to the point where you really need a molecular understanding, and you need someone who understands carbohydrates" and I started drawing structures.

And I really liked the people in his lab, they were really a nice group. I clicked with them and had a good time. And so I talked my way into this guy's lab, but then when I got there, I think all of a sudden they realized how clueless I was. [laughs] Like in group meetings, I was the lab idiot, you know. They were very, very nice to me, very patient, got me up to speed. But in group meetings they would be talking about some experiment, but then they'd say, "Oh, sorry," and they'd slow down and they'd look at me and talk baby talk, like, "All living things are made of cells," you know, and explain it to me. "Oh, okay." [laughs] It took me maybe six months, and then I felt like I had caught up. But it was fun. It was really a good experience, too.

Again, at the time I was advised against doing that because it was too far away from chemistry and it was too far away from familiarity and so on, and the name wasn't name recognition kind of person to the chemists. And then, of course, two and a half or whatever years later—not even, actually, it might have even only been a year and a half—but whenever it was, I came out, interviewed for jobs, for academic jobs, and then guess what. From labs a, b, c, and d, the usual suspects, there were five postdocs from each of those labs all looking for the same jobs, all interviewing, all looking the same. And I came out and I looked totally different, you know, and I had a story that was totally different from those guys, and I really stood out by comparison. And I was like, "God, I'm so glad I didn't go to one of those labs and end up looking like just everybody else and doing the same old thing." And I had just a different interest.

Then after that, shortly thereafter, it really became en vogue for chemists to go postdoc totally into some biology lab. And now, I advise all my students to do this, and so do all these other guys here, and all their students are going off to postdoc: Someone from Bob [Robert G.] Bergman's group goes to Keith [R.] Yamamoto's group, and that's considered cool. But it

wasn't that cool when I did it.

And there was a guy, he also did that, the one guy before me who did it was Kevan [M.] Shokat, and he was sort of my idol when I was in grad school. He was my TA and he was like superstar student and he had gone to postdoc for this immunologist, Chris [Christopher C.] Goodnow, at Stanford, which was the transgenic mice and all this. For a chemist, "Oh my god, mice," you know. So he had done this thing, and he, I think, got the same advice I got, which was, "Are you nuts? Just go postdoc for a, b, or c." And so I had talked to him at one point after he had been in that new lab for a year and he came back here to visit some people, and I said, "How's it going?"

"Oh, I'm really glad I did this," he said. "It wouldn't have been half the learning curve if I'd been in some sort of standard chemistry lab." And so, I held onto that, and I was like, no matter what everybody says, that guy did that, too, and I'm going to do the same thing. So I'm really glad Kevan did that, because maybe I wouldn't have had the balls to do it if he hadn't done it, I don't know.

MAESTREJUAN: Let me pop in a new tape.

[END OF TAPE 1, SIDE 2]

MAESTREJUAN: I was looking at your *Journal of the American Chemical Society* articles, and as somebody, a lay person coming outside the field—

BERTOZZI: Why did you look at those?

MAESTREJUAN: Well, I wanted to get a sense of what you did as a graduate student.

BERTOZZI: So you looked at really old JACS [*Journal of the American Chemical Society]* papers, like grad [graduate] student days.

MAESTREJUAN: Yes. And of course, then I read some of your postdoc [postdoctoral fellowship] work, and to somebody like me who's not versed in any of this, it doesn't seem that unnatural a selection to go from looking at these analogs that bind to antibodies to target pathogens, to looking at the synthetic ligands or selectins. So what is it about these fields that there are these boundaries that say, okay, that you can't go here if you want to be a chemist, you can't go there if you want to be considered a biochemist or molecular biologist? How do these boundaries get constructed?

BERTOZZI: It's totally artificial. It's like the boundaries between the North End in Boston and South Boston. Italian people settled there and Irish people settled there, and anybody who crosses the street, they killed. So I don't know. In carbohydrates, maybe it's easier to lose the boundaries. I don't know if it's really fair to say that.

Well, okay, first of all I should say that Steve [Steven D.] Rosen's group was very much a cell biology group. They would identify genes, knock them out in the mouse, look for phenotypes, look for how cells distribute in the body, run inflammatory models. There's no chemistry in that group. So I brought chemistry to that group, and now you see some chemistry papers come out. And so it's not like I went to that group because there was an interest in chemistry of carbohydrates. That was what I brought to that group. That's how I sold myself to that group, and so just me being in that group erased a boundary that maybe existed before that.

But in carbohydrates, those boundaries don't hold up very tightly anyway. So there're three biopolymers, let's say. There're nucleic acids, there're proteins, and there're polysaccharides. And the first two, nucleic acids and proteins, have this binary relationship with each other and they're encoded in the genome. So, a gene, DNA, encodes a specific RNA, and that RNA encodes a specific protein, and you can get all the way through that cycle just from the gene, which means that you can express the protein starting from the gene in cells, and you can make changes to the protein by making mutations in the gene and express the protein in cells. You don't have to do any chemistry to change the protein a hundred different ways, and to grow up the protein and to purify the protein. You don't need to know a lick of chemistry.

And so it breaks down when you get to carbohydrates, because they're not primary gene products. So you can't express a carbohydrate. It doesn't work that way. They're the products of many different enzymes working in the secretory pathway, and so on. And it's not that you can't really reconstitute that and manipulate that with the ease that you can just do molecular biology and genetics.

And so how do you manipulate polysaccharides? You have to make them, you know. So that's why chemistry is really an important part of glycobiology. It always has been, much more so than people think. I shouldn't say that, because molecular biology wouldn't exist without chemistry, because how do you do PCR [polymerase chain reaction] without the primer? How do you make the primer if you don't have a synthesizer? And where did that come from? It came from [H.] Gobind Khorana at MIT [Massachusetts Institute of Technology]. All of this does have a chemical origin.

But now you can function as a molecular biologist without knowing any synthetic chemistry, god knows, right. I mean, there're thousands of them. But it's hard to function as a glycobiologist without some chemistry. Either you do it yourself or you collaborate with someone who can do it with you. And so I brought that into Steve's [Steven D. Rosen's] lab, but I think Steve was certainly cognizant of the notion that without chemistry, you just can't get any molecular information with polysaccharides. You can't PCR-amplify them, right? You want

more, you have to make more. So that's maybe part of it, I think.

So, yes. When I tell the story, if I say, "Oh, here's what I did as a grad student," it looks very logical. It's hard to imagine that at the time anyone would have advised me against that because it was too far afield. But, again, the context of the time was such that, first of all, no one here really knew what glycobiology was. There wasn't anybody in this university, really, working in that area, and certainly not in the chemistry department. So they had no clue—anything—about that. Leukocyte, what is that? They'd never even heard about it. It's like somebody's Polish aunt or something. So I wouldn't have gotten any glycobiology advice from my colleagues here.

But, also, you're right, there's such high value placed on the pedigree, that I think sometimes people overlook their own scientific interests just to get this elusive pedigree. And I see it. I can't stand it. My own students will come to me saying, "Okay, well, I think I should start thinking about postdocs. I'm starting my fourth year," and whatever, "and people have said if I go postdoc for so-and-so, then I'll get a good academic job."

I hate that, you know. I'm like, "Are you interested in doing that work? That's the only reason to go postdoc for this person, if you're interested in that work. If they also happen to be very influential, bonus, okay, but that's not why you go to that lab." It just absolute baffles me that people do this. But, of course, they do it more often than not, and I hate it. I really hate it.

MAESTREJUAN: It's clearly prevalent, because we've both been talking about it, and why is it that this is the standard?

BERTOZZI: Because it's human nature or something, you know what I mean? How do you get into a certain club? Well, you have to know the right people and so on. It's part of humanity somehow. It starts in junior high school. You're either in the cool clique or you're not. You know? That just is played out on a different field at this level. So there's a clique of people, and if you're in a certain clique, you have more connections, indirectly, to academia, or certain companies. Companies, pharmaceutical companies, only hire medicinal chemists who came from *this* lab. I'm not kidding, it's so inbred.

But the worst thing about it is now, in my own career, I have enough of a stature where there are people who will come postdoc for me because I'm me, and they don't even care what I work on. And I can't stand it. I'm like, "What are you doing here? Do you even know what we do?"

"Well, no, but I've heard that you can help me get a job." [laughs] It just absolutely baffles me. But, you're right, it's totally entrenched. Really, I don't even know what I'm doing here, frankly, because I don't have that pedigree. I have it at the university level, right, so maybe that's enough. I don't know. Harvard [University], [University of California,] Berkeley, UCSF

[University of California, San Francisco], that's a pedigree of universities, but I never really worked in a lab of someone who is—I don't know—considered a powerful, behind-the-scenes kind of person who would be making phone calls behind my back to help me, whatever even happens. I don't even know what happens at that level.

Like the Pew [Scholars Program in the Biomedical Sciences] scholar, I always felt like, "What am I doing with this group of people?" Because every single one of them had this pedigree that, "Oh, I've done a postdoc for one of these five people," Howard Hughes [Medical Institute] labs. You know what I mean? And I was there, this chemist who worked on sugars. Glycobiology's a pretty small field. So maybe that's it. Maybe I was the sugar quota, I don't know.

But definitely when I took this job, and since I've been a grad student here, I've felt very comfortable. When I came back to Berkeley, it was like I knew how everything worked, and I didn't really figure out this whole value of the pedigree thing until things like the Pew [Scholars Program in the Biomedical Sciences] scholar, started participating in that kind of stuff. I was like, "Oh my god. All these people postdoc'd for the same person." [laughs] And I was an outsider, you know. Also, I had come from chemistry, and Pew [Scholars Program in the Biomedical Sciences] doesn't have a lot of chemists. A few.

MAESTREJUAN: Not many.

BERTOZZI: One every year is how they seem to do it.

I tell my students you can be successful without a pedigree, and you just really have to be following your own interests. It's really important because it shows. When you give your talk, it shows. And when someone comes here and they're the tenth postdoc out of some lab where we interview—every year we interview three people from the same lab—and they all sound the same, they really do. They get here and they go, "Well, I'm doing this."

It's like, "That's what that lab has been doing for twenty years, and now you say you're going to do this, and how did you get interested in this?"

"Well, I worked in this lab."

And I was like, "What are your interests? So that's your lab's interests, but what are your interests?" And it's really hard to pin it down, and a lot of them start to look like their advisor. Maybe they're trying to emulate their advisor, I don't know. Once in a while someone really distinguishes themselves.

MAESTREJUAN: What do you think the impact is of this entrenchment of a pedigree, and graduate students who just buy into this as well, on scientific discovery?

BERTOZZI: In biology they really buy into it a lot, way more than chemistry, actually. Chemistry they buy into it, no doubt, but there're enough examples in chemistry of people who have come from not the usual background that have been successful in academia, that I think there's value that's placed on being on the outside a little bit—you know what I mean?—more so than in biology. I see it a lot more in biology. Like, I've been on a couple of search committees in MCB [Department of Molecular and Cell Biology], and I'm sitting there like, "Oh my god."

They're like, "Well, we're going to interview these five people. Well, the first one worked for so-and-so.. Well, they worked for so-and-so and so-and-so." [laughs] Not that it doesn't play a role in chemistry, but it's not usually the first thing you discuss. It's more like, what are they going to work on, what's their idea, what's their proposal?

MAESTREJUAN: And so what do you think the difference is, then, between the field of chemistry versus the field of biology in terms of scientific progress and rates of discovery?

BERTOZZI: I don't know, because we'd have to do a controlled experiment. You'd have to find a planet where it's not like that and then compare, which you can't do. I don't know. Okay, on the one hand, these people who have a pedigree usually you have it for a reason. They're brilliant, and good managers and sustain big labs and fund lots of people and have, probably, a good sense of what's at the cutting edge and what's hot. They can always position themselves to be right there. And I could see how that can be a thrill for a young person to see what that's like, to work in that environment.

In my lab, I feel like, hopefully, it's fun for some of these students to work with me, but even funner [sic] is that they're with each other. So one of these things these pedigree labs do is they attract a lot of really bright people and put them together. The fact that there is a boss with a name is almost irrelevant. Really, there's an environment with a lot of smart people. Like the Manhattan Project. You put all these people together and just see what happens. And, in fact, those big labs would, I think, be wise to let those people have a little bit of free reign and see what creativity comes out of it.

So to be fair, I think a lot of people coming out of those big established labs probably have been very independent and a lot of their work was self-driven, although their boss will forever get the credit for it. And I benefit from that, too. I think that obviously these labs do really good things. What I don't like is when I see somebody choose to go to a lab like that simply because the name of that person is carrying some weight in politics—you know what I mean?—and not because the research is what really drives them.

I've asked people here, "Well, why did you choose that lab?"

"Well, I want an academic job, and this person has a strong track record of placing

people in academia." And that might be true, but I hate to hear that as the first thing. Like, "That's the first reason you joined that lab? You didn't even care what you worked on?"

What I really respect is somebody who says, "I really have an interest in this, so I looked around who are the labs that are doing this kind of stuff where I could do this in that environment, and I found these five people. So I went and met with them all, and this is the one where I clicked." And maybe it happens to be some big-shot with a pedigree. Great. But if it didn't, you should still go there. You know what I mean? And then when they get out, it shows. They present their work, they give their job talk, you really know instantly whether this was, they followed their heart—you know what I mean?—and they really did what they wanted to do, or whether they were just getting on a bandwagon and just checking off a list of things to do to get an academic job.

MAESTREJUAN: In the Rosen lab, what would have happened, do you think—and, again, this is a counterfactual question—if you hadn't been able to sell yourself to the Rosen lab?

BERTOZZI: Well, I actually interviewed at four labs for a postdoc, so I had two other labs that I'd looked at, too.

MAESTREJUAN: Who were they?

BERTOZZI: One was an HIV [human immunodeficiency virus] guy at U Penn Med School [University of Pennsylvania Medical School]. And, again, back in the late eighties, early nineties, everybody wanted to work on that and make a difference. A lot of my friends have died of AIDS [Acquired Immunodeficiency Syndrome], so I had definitely a personal investment in HIV research. I did a little bit of very tangential work with HIV as a grad student: I collaborated with the guy. So, actually, that was very serious. I went to visit that lab and actually didn't think I could click in there. The guy was a real micromanager, it turns out. Every morning he would sit down and say, "This is what you're going to do today," and have a list. And I went, "Whoa." Couldn't do that.

Then the other lab was at Johns Hopkins [University], and it was a lab of a guy who had discovered a form of glycosylation that was very unusual, because it takes place in the cytosol and nucleus of the cell. All other forms of glycosylation occur in the secretory pathway: the ER [endoplasmic reticulum] and the Golgi [apparatus]. So because of that, most sugars on proteins end up outside the cell or on secreted proteins, but this one form that takes place in the cytosol, of course, those proteins stay in the cytosol, and a lot of them are involved in gene expression. And so there was this idea that glycosylation of this unusual form might be somehow involved in signaling and controlling levels of gene expression. And it's actually, to this day, still kind of mysterious what that form of glycosylation is doing. But it had just been discovered at that time, and I was like, "Whoa. That is so cool."

So I interviewed with that guy, too. That was a good lab, I really liked that, actually. I could have done that. It was a toss-up. But there was a rumor going around that that guy had been offered a chaired position at University of Alabama in Birmingham. He was originally from Alabama, and he, in fact, then left a year later and went to Birmingham. So it was like, "Whew, dodged a bullet." Because I did not want to go to Birmingham.

And my partner at the time had an opportunity. She was, again, working for the federal government, but as a California state representative, and she had a chance to go to Baltimore to their federal office. So we had it all worked out, I'd go to Johns Hopkins, she'd go to Baltimore. But then I found out about this Alabama thing, and she was like, "I'm not going to Alabama."

So I said, "Oh," so I decided to play it safe and I went to Steve's lab instead.

MAESTREJUAN: And how well did you, as a chemist, integrate into a cell biologist lab?

BERTOZZI: Apart from my cluelessness for about six months, and, again, I had to work hard to pick it up, but it was pretty seamless, because I did know my carbohydrates. I knew I needed to learn that, and I was there to teach them. And also they had some great personalities in that lab, and so I made a lot of really good friends really fast, friends-for-life-type friends, you know.

UCSF is a very unusual place, in a way. Nothing like it on the planet as far as I know, and I really enjoyed that. It's transformed me. I'm really glad I spent time there. It's really different from a chemistry department. There're women everywhere. They're crawling out of the woodwork. I'd never seen that before. And the whole way people talk to you is different. It's biology, it's not chemistry. When you talk, they are quiet and listen. I was like, "Whoa. You don't have to talk over people."

And the egos are of a different nature. So it's funky. UCSF is like this totally funky, cool, place. It's a med [medical] school, and that helps. It's got young people around who are all trying to save the world, and it's a hospital, people walking around with IV [intravenous] poles. You're working, really, in a place that's real. It's not so academic like a chemistry department at a basic science campus like Berkeley. It's disease. You're around disease, and you're getting tissue samples from patients to analyze. It's very cool, actually. I really loved it there, to be perfectly honest.

And I had an offer. I got offered a job as an assistant professor there, and I thought about it, and I was really sad. I didn't take it mostly because there really wasn't any chemistry there, and I thought I'd be lonely without chemistry. I wanted to have some chemistry in my life, teach chemistry. But just in terms of people and the atmosphere and the kind of collaborative nature of the place, I really miss that. It's not quite like that here. But you can't have it all. Actually, you can. Because I have a dream appointment. I mean, I am on a faculty nominally at UCSF, in [Department of] Pharmacology. I'm on their website. I have a faculty

appointment there, I can take students from there, but I'm not there every day with all those people.

MAESTREJUAN: You had mentioned before that, intuitively, organic chemistry came fairly easily to you, but you did have to learn the hands to do [?], when you got to grad school. Well, what about learning the techniques of molecular biology or cell biology?

BERTOZZI: Yes. It was hard.

MAESTREJUAN: How well did your hands work?

BERTOZZI: I got it. I'll never be the world's greatest experimentalist, I've decided. My hands are pretty good, I can do experiments, but I've seen people in my own lab that blow me away. They're really good. I wasn't the most patient experimentalist, and I used to be the cowboy at times, trying to do a lot of things quickly. But I was good enough to do experiments that I was confident I could repeat. [laughs] I would say I was maybe in the upper twenty-fifth percentile as an experimentalist, but I wasn't going to win any awards. I did know how to do it to get the answers.

MAESTREJUAN: And is it easier to train a molecular biologist to do organic synthesis, or is it easier to teach a chemist to do molecular biology?

BERTOZZI: Hmm. Okay, the dogma—and it's incorrect, by the way—is that it's easier to train a chemist to do biology than the reverse, okay. So I've now done the experiment both ways, and actually I don't think that's true. I don't see any difference, really. I think it depends. If someone works hard enough, they can learn anything, is how I see it.

I've had cell biologists come in here who really want to do some chemistry, and they worked really hard, and they became really good synthetic chemists who I'd put up against any chemist any day of the week. And I've also had some come in and be dilettantes about it, and they'll never be able to design their own chemical experiments, although they could repeat experiments other people have written out for them, you know. So being able to follow a recipe and follow an experimental protocol is one thing, but being able to troubleshoot and figure out what went wrong, fix it, is another thing. And I think anyone can do that latter thing, but they just have to really be committed and work hard at it, understand it.

I think chemists pretty much underestimate the complexity of biology. A lot of chemists say, "Oh, yeah, I'm going to come postdoc in your lab. I want to come postdoc with you for a year to learn biology."

And I'll be, like, "You're going to be here for five years, then, because you're not going to learn it in a year." They don't know that, actually. They think "Another job, another microbiologist." So I think, yes, chemists really need to understand the complexity of all the different experimental approaches, and what are the caveats and so on. There's a lot of lore in biology that you just can't read about, you just have to get in there and kind of experience it.

Also, I've also noticed, compared to chemistry, biologists have to function more as a community. Chemists can often choose problems where the lab becomes internally the world's expert and self-sufficient, and biologists, you need to have other people. You know what I mean? There needs to be a consensus for how things work. Otherwise, you could screw it up. I found that in Steve's lab. Like, if you need a knock-out mouse, and you characterized the phenotype, you like to get there first, but you also like it when other people independently find the same thing coming from a different direction, and it converges on a model that's consistent with what everyone's seeing.

And you need to know what everyone else is seeing, so you need to go to these meetings all the time, always be talking to people. And Steve was always on the phone with somebody finding out, "Well, have you guys seen this in your lab? Because there's this weird thing. And is it because that antibody doesn't work in Western blots, or is it really that it's really a different structure in the mouse than in the rat?" and blah, blah. You always had to be talking with people.

And in chemistry, you could just be in your own little world. It didn't matter what other people were doing. You had your own thing. This is what you did, you know. It's so different.

So I think that's what chemists underestimate, that you can't just dabble for six months and be an expert in nuclear transport. You have to know what that whole field has been doing for the last twenty years, which papers have been debunked, because half the literature's wrong twenty years later, right? In chemistry that's not true. It's a very mature, very well-developed field. The organic literature hasn't changed. If it was published twenty years ago, it's still true now.

But you learn that with experience. I think my students sense that, even if they're chemists. I think what biologists underestimate is the years of cumulative knowledge you need to make intelligent decisions about doing organic chemistry, and that you can't come in and learn it. Like, you could be an expert in genetics— *Drosophila* genetics—and then you could probably learn about biogenesis of the Golgi compartment, because you speak the same language about genes, and you know about regulatory pathways, and it's kind of a kinase is a kinase, whether it's here or there.

And in chemistry, to understand why a reaction goes the way it does, you have to be able to go back and understand the difference between the pK_a of all of these different functional groups in water versus DMSO [dimethyl sulfoxide], and you probably learned that a long time ago, you know. You have to go back and accumulate that.

MAESTREJUAN: You were a postdoc in Rosen's lab for about two years.

BERTOZZI: Two and a half.

MAESTREJUAN: And were you able to learn biology?

BERTOZZI: No, I probably should have stayed longer. I'd intended to stay longer. So, in chemistry, a postdoc is usually two years, three is long, except it has to be a special circumstance, you have to explain it to people why you were there for three. Did somebody die in your family? You have to explain it.

In biology, five is not uncommon, or longer. Some of them spend longer as a postdoc than a grad student, and that would never happen in chemistry. So when I was in Steve's lab, I said "I'll be here probably for four-plus years."

And then what happened is, jobs became available. I had a friend at Stanford [University] on the faculty. I'd only been a student for about a year at that time, and this guy called me, he says, "We're going to be looking for sort of a bioorganic chemist, and that's your area, and we really need to hire somebody this year, so we're not going to have another search for another five or whatever years," after they'd hire that person—basically that's the way they work at Stanford—and he said, "You should apply."

I said, "I'm not ready. Are you kidding? I just got here. I didn't even publish anything yet, and I need to be here. I don't know everything yet."

He said, "Yes, but it's a window of opportunity. You should take it."

I was like, "Oh, shit." And also I wanted to stay in the Bay Area for personal reasons, so I figured you don't get that many shots at a job in the Bay Area. If there's one, you've got to take it.

So I talked to Steve, and I was like, "There's this job at Stanford, and I know I've only been here a year." And in biology, to apply for a job after a year? Are you insane?

He was like, "What? Are you insane?"

I was like, "Yes, but in chemistry it's not that weird. It's actually pretty normal," and so on. "And I think I have a shot at this job."

He's like, "Well, all right." He never thought I'd get the job. He was like, "All right, whatever."

So I applied for that job, and then it snowballed because I needed to get some letters, right, from my professors, so I came over to Berkeley and asked these guys, "I need some letters, and I'm applying for this job."

"Oh, if you're applying to Stanford, why don't you just apply here, too? You might as well send your package to us."

"All right."

And then at UCSF they were hiring in Pharmacology. I had a friend who's a former Berkeley guy who's on the faculty, he said, "Oh, if you're applying to Berkeley and Stanford." So it snowballed. So I just applied to all three, is what happened, and knowing all the while that I probably could have used more time as a postdoc. But the jobs became available, and you've got to do it.

As it was, I deferred my start date by six months just to get a little more out of my postdoc. But I wanted to defer it a year, actually, at first, but Berkeley was like, "No, we can't wait a year. We really need you now."

So I was like, "Hmm, what about six months?"

MAESTREJUAN: Well, I'd have to say that it's unique that a Pew [Scholars Program in the Biomedical Sciences] scholar would say, "Oh, I wasn't a postdoc long enough." It's usually the other way. Most people would see that as an advantage, to have all these job opportunities. What is the disadvantage for not being able to be a postdoc for as long as one—

BERTOZZI: Just learning more. I wanted to learn more biology. It was a new field for me, and I had aspirations in my own research to combine these things together, and I felt very comfortable with my abilities in chemistry, but I felt like an amateur biologist. I was like, "How am I really going to realize all these things when I'm just learning now basic stuff that first-year grad students know?" And so that was where I felt insecure.

But I had to make a decision. Once you get offers, the decision is made for you, really, because you can't turn down those jobs. They just don't come around often enough to forsake them, you know. And I had these three offers, and I was, like, "All right, this is it, then. I'm going to take one of these jobs."

So I took the Berkeley job, and I had it in my head, I said, "All right, if I take this job, there're two strikes against me with respect to my research plans." First of all, I'm an amateur and I know it. And although I can think about biology, I'm not going to be able to take my students in the lab and show them how to do everything. I can show them some basic stuff that I've learned yesterday, but I'm not going to know every little trick in the book to fix things, and

so on, A.

And, B, I'm going to be in this chemistry environment where I'm surrounded by other chemists, but no biologists. They're down the hill and across the street and so on, but it's not like I can send my student down the hall to get help where I can't supply it. So I'm going to have to compensate for that somehow.

And so the first thing I did when I came here is I looked to hire a postdoc who was a cell biologist, and I said, "I've got to get someone in this lab, either a technician or a postdoc, who has the expertise that I lack, who can fill in my deficiencies and help get my students up to speed and help them troubleshoot," and so on. And the other thing I did is I networked my students with those people I did know who were biologists, for example, all my friends in Steve Rosen's lab. And so my first year here, on occasion, I would actually send my student over to Steve's lab, and one of my friends over there would help them do something that we just couldn't get to work over here. It was incredibly helpful. It's not that far, you know. So, yes, I had to fill in the gaps.

MAESTREJUAN: And how well were you able to attract a postdoc.

BERTOZZI: I got lucky. Again, it's all who you know. So remember the undergrad who couldn't write [William Kobertz]? He was my undergrad [undergraduate student]. Well, then he was a grad student at MIT at the time, okay, and I was starting my job here. I called him, and I said, "If you know anybody." So I was calling everyone I know. I said, "If you know anybody who's got the balls to come postdoc for a new assistant professor, who's like a real expert with molecular and cell biology, who doesn't mind coming to a chemistry building where nobody knows even what a PCR machine is, please give him my name." [laughs] I was half joking, of course, because where would this person come from?

And he goes, "You know, I think I know a guy." So his friend, Kevin [J. Yarema], who was a grad student in the lab where he was [Johns Hopkins University Whiting School of Engineering], who was several years ahead of him and was finishing up, and he was a very unusual guy, this guy Kevin. He's Canadian, and he was like this ace cell biologist who had made hundreds and thousands of stable cell lines and cloned all these genes, and done all these things, created artificial chromosomes and stuff, but was an off-the-wall guy, who was thinking maybe of starting a company and was really smart but wasn't looking for the pedigree to get his job, and just wanted to do something fun and different.

He said, "This guy may be exactly what you need. He's a real whiz in the lab," and so on.

I said, "Hmm." Well, it turns out this guy once a year would make a pilgrimage to his home town in British Columbia, and he would drive from Massachusetts all the way across Canada, pretty much.

And I said, “Well, the next time he comes out, tell him to stop by.” I was still at UCSF at the time, in San Francisco, it was kind of on the way, with respect to Massachusetts. So he did. This guy stopped by and I took him out to lunch, and I said, “I’m going to be setting up my lab next December, and it sounds like you’re looking for something next spring, and how would you like to come out? It would be really fun work with the team,” and blah, blah, blah. And I just gave this guy the sell.

And he was like, “All right.” So his name was Kevin Yarema,. He’s on a lot of my first papers here. He came in here and he set up our cell culture lab and he trained all my students how to keep cells going and grow them, and do flow cytometry and microscopy, and he just—I’m in the upper quartiles in experimentalists, but no higher, really—was in the upper 1 percent. It was unreal. They guy could have a thousand tubes at once, both hands were pipetting, and ten experiments were going, reams of data. Unbelievable. He was a machine. The guy was a machine. He was so perfect. So I lucked out.

MAESTREJUAN: And where is he now?

BERTOZZI: He’s a professor at Johns Hopkins. So he’s now assistant professor in the biomedical engineering department. And he married one of my grad students. It was really cute. So I feel like I paid back.

MAESTREJUAN: It’s a very tight community. Because you were in the Rosen lab for such a short—relatively short—period of time, when it came time to establish your own lab and separate whatever work you did there, how were you able to divide and take with you?

BERTOZZI: Some of this is easy in chemistry. Yes, so this is much easier in chemistry than in biology. Well, first of all, I’m a chemist. So automatically I have a different take on things than Steve. And I had a lot of chemical interests that really had nothing to do with what Steve’s lab did. So most of my research program at Berkeley had no relationship to what I did as a postdoc.

There’s only one project that did, it was a bit of a spinoff. And that was more like what biologists typically do. So they postdoc for *n* years with somebody, develop some facet within the same system, and then take it with them. But you can always see where they came from, because there is a direct link. And sometimes they end up competing with their former advisor. But certainly they end up in the same circle as their former advisor, for the most part.

And in chemistry, that’s very rare. It’s discouraged, in fact. And if you apply for a job with proposals that look like what your old advisor did, and it’s too close, you won’t get a job. They want to see what are you going to do that’s different and so on, which is what makes it so

hard for these five postdocs every year that come out of x lab. You know what I mean?

But this was not a problem for me. I came out wanting to do synthesis of things, and chemically alter things, and this is nothing like what Steve does. And my former advisor who had been here was gone, so I didn't have that conflict to worry about. You know what I mean? Not that that necessarily would have been a conflict, because I have diverged quite a bit from those days. So I never had that issue.

So the one project I took that definitely had a relationship to what I did as a postdoc was in the area of sulfation. So part of my lab, even now, still works on enzymes involved in sulfation pathways as drug targets. These are enzymes I became cognizant of while a postdoc, because it turns out these polysaccharides I had been studying in Steve's lab were sulfated, and that was an important part of their structure for their receptor binding. So it became obvious that the enzymes that are putting these sulfate groups on could be targets for intervention, like drugs for anti-inflammatory, basically diseases that are inflammation. And so I took the medicinal chemistry aspect of that with me, like how do you develop drugs against these enzyme targets, whereas Steve's lab would be more interested in knocking out the genes and looking for phenotypes and figuring out which gene is induced by what signaling pathway and so on.

But the system was related. In fact, we had always talked about, when I was in his lab, "Oh, yes, we should start a company or something on this." We had this discovery where you see patents and so on, and I was like, yes, I could see the path towards getting the chemistry running to tackle those targets from a pharmaceutical point of view, and we were half joking at the time. Steve and I are good friends, and we talk a lot, and as the years ticked by and I was here and I became tenured and so on, I had some kind of stable situation here, we revisited that idea, and then we did form a company about two years ago. So now we have a pharmaceutical company [Thios Pharmaceuticals, Inc.} that we're both cofounders of.

MAESTREJUAN: Thios [Pharmaceuticals, Inc.].

BERTOZZI: Yes, Thios, which focuses on sulfation. Thios is Greek for sulfur. You have to be a chemist to know that. No, you don't. Just kidding.

So there was one project, but that was only about 25 percent of my lab, and the rest works on other stuff, which has no relationship. So I never had that problem. But I know biologists talk about this a lot. It's an issue for them.

So Kevin, my former postdoc, my great postdoc who's now professor, he's more the biologist type, so he was working for about four and a half years as postdoc. He took this position at Johns Hopkins, and he continues to work on stuff that's now spun out of what he worked on in my lab. So he has done a much more traditionally biological thing: Postdoc for somebody, develop something, take it with you, and take it in a new direction, but you can trace the history of it.

By contrast, I've had chemists go through the lab who have their academic positions, and what they're working on is very different from what they did in my lab. You know what I mean?

MAESTREJUAN: You were offered three positions. Were they all within chemistry departments?

BERTOZZI: Stanford and Berkeley, yes, and UCSF didn't have a chemistry department. Now they have a chemical biology graduate program, but they didn't back then. Molecular pharmacology was the department. They wanted to build chemistry, and since then they have. They brought Kevan [M. Shokat] in and some other people, but at the time they didn't have anything and their labs were not set up for it. So they're like, "Oh, this could be your lab," and there was one little four-foot fume hood in there.

It's like, "What?" I have twenty-eight hoods here, and that's what you need, you know. And they just didn't have it. They didn't have Mission Bay, and Mission Bay was so far in the future, you couldn't even conceive of it in '94 or '[9]5, whenever I interviewed. And now, they moved in there this past year. Have you been to Mission Bay, the new campus?

MAESTREJUAN: No.

BERTOZZI: It's gorgeous. So they have this new campus near the Pac [Pacific] Bell Park [now SBC Park], near the water here, and it's all brand-new buildings set up for chemistry, and they're hiring chemists, and they saw that in the future, but it was too far away, you know. They were like, in '94, like, "Oh, yes, you can work in this other lab with this one hood initially, but then you'd move to Mission Bay."

I was like, "Yes, in 2002. That's seven years from now. Forget it." [laughs] So that was a problem at UCSF.

But Stanford and Berkeley, it was like the same job. It was a chemistry department, basically.

MAESTREJUAN: And how attractive would you have been—again, a counterfactual—to a more biological department than a more traditional chemistry department?

BERTOZZI: Probably not that attractive, I think. I think most biologists would have looked at me like, "Weird." They wouldn't have really got it. Even here, my colleagues here, I have a

lot of collaborations with people. I'm in MCB, but I don't sit amongst MCB people, so I still feel separated. And I do have collaborations and I go to seminars and everything, but I still think a lot of them are not quite sure what I'm doing. It's a little off to them. I think certainly they understand the big picture. It's not that complicated. It would be hard for me to recruit grad students out of a biology department because you've got to do all this chemistry, and it's not exactly what most of them signed up for. Although, I do have biology students in my lab, but they're a minority. I have, I think, twenty grad students, and three of them are from biology.

MAESTREJUAN: And why do they come? Do you know?

BERTOZZI: Because I'm fabulous and interesting. [laughs] No. Because we do enough biology. They're the biochemical end of biology. Some of them are like, "Yes, I want to do some chemistry." They've heard it's cool. And, also, some of them are savvy. They feel like that will distinguish them from the thousands of biologists of the universe that crawl out every time you lift a stone up.

MAESTREJUAN: When you left to go to Rosen's lab, your colleagues here in the chemistry department at Berkeley thought you were going off the deep end. So when you came back to the chemistry department after having this exploration and excursion into biology, how well did—

BERTOZZI: They were very enthusiastic here because, of course, they're like, "Well, yes, we all advised her to do that, of course." [laughs] Like selective memory.

But, no, I think they appreciated it when I came back. First of all, I wasn't stupid. When I interviewed here, I emphasized chemistry. The proposals that I emphasized were those that were more chemical because those were the ones I knew they'd understand. And there were proposals which I knew they'd have no appreciation of and be interested in, and I didn't talk about those.

At UCSF, by contrast, I talked more about my ideas that were more biological, and the more chemical stuff I downplayed it a bit, I knew they'd be bored with that. So, I tried to tell them something that they'd be interested in, and there's certainly enough to go around.

Here, they were very enthusiastic. Part of the reason I came here is that when I interviewed, I had a good day. They seemed engaged, they asked questions that were good, they talked about their stuff and seemed interested in interacting with me about it. And it was on a Friday. I interviewed on a Thursday-Friday, and they called me Monday and made me the offer on Monday morning. They were so right there.

Whereas, at Stanford it was not quite that great. I interviewed there first, actually, and

it's a traditional department. They don't have as much appreciation of biology as Berkeley had, and some of them were sleeping. [laughs] I could tell it was a bit out there for them. It wasn't so out there for Berkeley, but it was out there for Stanford. And at the end, they were like, "Okay, that was interesting, and, uh, we'll be in touch."

So I left, I drove back, and I was like, "Oh, I didn't get that job," you know. "Well, that's life."

And then what happens, of course—and this probably happens in biology, too, in academic circuits—is nobody really knows what they think of all the applicants until one person commits. So Berkeley committed to make me an offer, and then it gets around that you have this offer, and all of a sudden everyone's really interested in you. All of a sudden, Stanford's, "Oh, we're going to make you an offer," which they probably wouldn't have if Berkeley hadn't, because I don't think they actually knew what to think that day.

And at that point, UCSF hadn't even interviewed me. They were interviewing other people. They were interviewing the usual suspects from big G protein labs, right? They were definitely looking at pedigrees, it was clear. And I had been going to their job talks of these people they were interviewing, because I was there. And they knew I had applied, because they encouraged me to, but they hadn't actually invited me to interview. I was like, "All right. Maybe it's too chemistry, too much chemistry or something."

And I was waiting at the elevator with a bunch of them after one of these job talks, and they were feeling a little uncomfortable because there I was, and they knew that it was clear they were interviewing other people. "Oh, Carolyn, how's it going?"

I said, "Oh, it's going pretty good."

"Well, we're going to get to you. We're going to invite you for an interview." I'm like,

"Oh, that's great."

"So, are you interviewing elsewhere?"

I said, "Well, yes, I have been." I said, "I have an offer at Berkeley. I have to decide soon."

"Really?"

All of a sudden that day they scheduled an interview. But it's funny. People really don't know what to think, I think, until they see what other people think. And then all of a sudden. So God bless Berkeley for making me an offer.

So, when you interview for a job, if you feel like they're enthusiastic about you, you're more likely to go there.

MAESTREJUAN: Okay. Well, one last question—we're probably at a good point to stop—is, how was Rosen as a mentor?

BERTOZZI: He was good. Again, he couldn't have been more opposite from my graduate advisor, in good ways and bad ways. So what I liked about my graduate advisor was that he had this enthusiasm was endless, and he never slept, and he was always pumped up to talk to you for hours about anything, and he thought everything was interesting. He would read very broadly. So he was a chemist, but he would read *Science*, and *Nature*, and *Cell*, and so on, and wanted to talk about stuff.

And Steve was very focused and very scholarly. That's what I liked about him. He had read every paper ever on this topic. And he was very diligent in looking at people's experiments and criticizing them. He wanted to see the data and so on. Whereas my graduate advisor was too scattered around to think about details.

And Steve, he read the literature and he would take notes on it in a notebook, his notebook of literature notes. He was very scholarly. He was organized. And he had EndNote database with it, and I was like, "Oh, he's really organized." And he had just been in the field a long time. You could tell he really knew that field, every paper ever published in that field.

But, by contrast, he wasn't so broad like my graduate advisor [Mark D. Bednarski] had been. So if I found some paper on a totally different topic, and I was like, "Oh, that's really interesting," it was hard to get Steve jazzed up to talk about it because it wasn't about this thing that he studied, it was tangential to that. So I think Steve showed me what it meant to have depth in an area, which I had never seen before, and that was really good for me to see that, because I think I could have easily become someone who is more like a dilettante, like my graduate advisor, who didn't have a lot of depth. But he had a lot of breadth. And he had an energy about him, which was fun, you know, and Steve was much more subdued.

Like the joke in Steve's lab was that you could never tell if he was really excited about something because his demeanor went between a very small scale. The volume was at five, and maybe he'd go up to six, or four, but that was it. He never was really depressed, and you never really got a rise out of him, ever. The best result ever, and he'd be, like, "Oh, huh, that's a fortunate result."

Whereas my graduate advisor, any little positive thing and he'd be like, "Oh, my god, that's amazing!" And he'd jump around, tell everybody that, and he'd drag you down the hall to talk to some other student and show them your data, and you felt really good about yourself.

So they were just so different. I don't know. I really liked Steve. Steve was a very classy, very elegant man, always did the right thing, always treated people correctly, with respect. Even when people in his lab were screwing up, he always did the humane thing. He

had one postdoc who was really screwing up bad and had a drug problem, and Steve was getting this guy counseling, got him into rehab [rehabilitation], really went the extra mile as a human being, which I had never seen that, either. I had seen a lot of people just get summarily booted out of labs and out on the street on their own.

But, Steve was such a good human being. It was more important to him to be a human being than to be a scientist and get the paper in *Cell.* And that was really, I think, cool. He was a good role model, I thought, and that's underscored by the fact that we have a relationship that lasted a long time and will last forever. We're now forever linked, you know. We have this company and one of his students came and postdoc'd with me and so on.

Whereas my graduate advisor was this shooting star, and I haven't seen him now. I left a message on his machine seven years ago, he hasn't called me back yet, you know. [laughs] And maybe he will some day, I don't know. But he's got his own life and his own thing, and I'm just a speck somewhere on his radar screen.

But Steve is always thinking of me. He'll e-mail me, "I saw this paper I thought you might be interested in." And I haven't worked for him for almost eight years.

MAESTREJUAN: Okay. Well, I think we're at a good point to stop, and we'll pick it up again tomorrow.

BERTOZZI: Okay.

MAESTREJUAN: Thanks.

[END OF TAPE 2, SIDE 1]

[END OF INTERVIEW]

INTERVIEWEE: **Carolyn R. Bertozzi**

INTERVIEWER: **Andrea R. Maestrejuan**

LOCATION: **University of California at Berkeley**

DATE: **18 August 2003**

MAESTREJUAN: It's August 18th . I'm Andrea Maestrejuan with Carolyn [Ruth] Bertozzi, in her office in the chemistry department at UC [University of California.] Berkeley, to conduct the second and final session for Pew Scholars Program in the Biomedical Sciences Oral History and Archives Project.

I'd like to start off with a couple of questions from yesterday that I had from listening to the tapes this morning. You had mentioned a high school biology class that you said was important. From that point, after taking this class, you were interested in biology. And then also in your first-year organic chemistry you had a fabulous teacher. And I just wanted to ask what made these teachers particularly good about capturing your interest.

BERTOZZI: The biology teacher, she was just good, had a really entertaining lecture style, was funny, and she explained it well. It was an AP [advanced placement] biology course, so it was a pretty sophisticated textbook, and the kids were selected to be pretty motivated kids, so you had a smaller class. So it was a combination of having the material presented in a really interesting way and having a book that was a challenging book that had a lot of really interesting tidbits in it. I can't really remember because it was a long time ago, but it did make an impact on me.

I remember that teacher. She was just one of these teachers that you always got the feeling she was talking really to you—you know what I mean?—and not just sort of lecturing at you kind of aimlessly. And she was funny. She had a sense of humor.

MAESTREJUAN: You've received a few teaching awards across the years. What do you think makes for a good instructor in science? How should we teach science to undergrads [undergraduate students]? I'm going to assume that's where your—

BERTOZZI: Yes, the awards were primarily for undergraduate teaching. I don't know. People here have different styles, and I know there's been a lot of really innovative curriculum development here, particularly in our freshman chemistry course, but I've never taught that course. I cannot claim any credit for any particularly innovative curriculum development. There are certainly a lot of people who have a lot more well-developed philosophies

of teaching than I have. I've never had much of a philosophy in that way. For me, it's more just a matter of getting up there and trying to keep the audience engaged and get them excited and entertain them for an hour.

Most of the recognition I've gotten is probably for teaching organic chemistry to sophomores, and it's mostly health sciences majors and premeds [premedical students]. It's a pretty big class. I taught this class for about four years, between 1996 and 2000, and every time I taught it, there was on the order of maybe seven hundred students in the class. It's a big class. And none of them are chemistry majors, so we have a separate organic chemistry for the bio [biology] majors and premeds than we do the chem [chemistry] majors and chemical engineers, and I taught the health sciences organic chem because that was my interest.

It was a tough class, because none of them are really interested in chemistry. They're taking it because they have to, and most of them are terrified because it has such a horrible reputation as being a weeder course, and if they don't get a good grade, they're never going to get into med school. There's a lot of fear in that course. But it's easy for me to get up and get excited about that course because that's the course I took as a sophomore that inspired me to change my major to chemistry. It was that same course. I started as a bio major, so I felt like I had a pretty good idea of what someone who has an interest in health sciences would: What would appeal to them about organic chemistry, and what are the things about organic chemistry that would hold their interest. And so those were the things that I would tend to emphasize when I taught the course.

But it was easy, because every time I taught that course I had a flashback. You know what I mean? I felt like, "Oh, yeah, I remember when I first learned this. It was so unbelievably cool," and how interesting that was to me. But it's not like I did anything special in that course. I used the textbook that had been used forever, and I basically generally followed the outline of the textbook and got on the board with my chalk. I didn't really do anything that special. Nowadays, people get up there, they have PowerPoint and animation and there're all these teaching techniques, and I've never been very good at that kind of stuff. I'm much more of a piece of chalk and an eraser on a blackboard, and I don't get really high tech. But I have some demos [demonstrations] that I would do in the class. I used to throw things at the audience. That helped. [laughs]

MAESTREJUAN: Because they were sleeping?

BERTOZZI: No, no, no. Just because it was a big class and I had a model of a compound. I said, "Okay, look at how this thing," and nobody could really see it because they're all way up there and I'm way down here. So I would say, "Here, pass it around." I would throw it into the audience and, "Whoa," you know, they'd start passing this thing around. I would get three or four of these models going and just toss them into the audience. And I spent a lot of time up in the aisles when I'm teaching, like kind of Oprah Winfrey sort of thing. And students seem to like that, because it's a big class.

But I think the reason, more than anything, that I might have been recognized for teaching that course is that they came in with such trepidation and such low expectations, and in the end they actually discovered it was far more interesting than they thought it might be and didn't have such a bad time after all. And, in fact, it wasn't such a weeder course, and I wasn't out to get them. So I think in the end they were just thankful that it wasn't the hell experience that they anticipated, that they're like, "She's a great teacher," you know what I mean. I think that's part of it, the psychology of that class.

MAESTREJUAN: We talked a little bit off tape yesterday about perceptions of undergraduates in terms of what science expects of them or what a profession in science expects of them, particularly in terms of writing skills. So there's this perception that those who can write go into the liberal arts and those who can't go into the sciences. And what do you think accounts for that, especially when, really, the medium of exchange for scientists are either verbal presentations at conferences and symposium, or publishing articles?

BERTOZZI: That's a good question. I really don't know where the misconception comes from that somehow people in the humanities write and speak and people in the sciences derive equations or something. I don't know what they think we do. I don't know. But I remember that I thought that way, too, when I was a kid, and I don't remember why.

It might be that when you're a kid in elementary school, there're math and English, basically. Those are the two things that you learn. You learn to read English and grammar and spelling and alphabet and all that, and then you learn to add and subtract and divide and multiply. For your first twelve years of life, there're pretty much math and English. There's not much else. And then later things branch out a bit, so math turns out to be all these different sciences, come from that. And writing and grammar turns out to be history and social studies. You know what I mean?

But that doesn't really happen until you're in junior high school and high school, so there're many years of your life—formative years—when there're really two things: there're reading and arithmetic. And that might just cling to us, engrained in our hippocampus or something, so that no matter what your actual experience is, you can't help somehow feeling that if you're not good at writing, the other thing is math. And math is what you use as a simplification for the sciences.

Even in college I don't think that our science courses demanded that much written material from us. At least mine didn't. There were lab reports, but that wasn't really any serious writing. So all the serious writing I did as an undergraduate student was in the context of literature courses, political science courses, history. I went to a liberal arts college where there was a lot of that, so we had a lot of requirements in three literature courses and two history courses, you know, because Harvard [University] is very much a liberal arts kind of place and it's not a science-heavy university.

Whereas at Berkeley, if you're a chemistry major at Berkeley, you, first of all, take a lot more chemistry courses than were required of me when I was an undergraduate, A, and, B, you take a lot fewer humanities courses and the writing expectation is very low by comparison. So I remember as a college student every semester I had to write three twenty-page papers and four ten-page papers. I was always writing papers for courses and there was a lot of writing. So every semester I was writing a couple hundred pages in some context. A Berkeley undergraduate has nothing even close to that. They might every semester write five pages of something at the most. And so Berkeley you can get away with not having very developed writing skills and graduate and have a degree in chemistry. Probably the same is true for physics and engineering. And then what, I don't know. It's not easy in the world if you don't have good writing skills, no matter what you end up doing.

MAESTREJUAN: There are articles and editorials in *Science* and *Nature* about getting young people interested in the sciences. You have the example of Berkeley and, to a certain extent, the example of MIT [Massachusetts Institute of Technology] and Harvard. If you were to model a kind of a good education for somebody who wanted to pursue further scientific career options or opportunities, how would you model it?

BERTOZZI: Well, I think it was a tremendous advantage for me to have some writing skills. That didn't really become evident until I started writing a lot of papers in graduate school, and then it became even more evident when I was writing grant proposals and so on as a professor. Not that my writing skills are so superior, but they're probably above average for someone who spent their life as a scientist.

But I have students who have come from small liberal arts colleges. I have graduate students from Bryn Mawr [College] and from Carleton College. I have the student who came from Williams College, who I mentioned yesterday, and in general these students have excellent writing skills. Those liberal arts colleges have a lot of writing courses and a lot of writing demands, and because the class sizes are so small there, they can assign a lot of writing.

So the problem at Berkeley is how do you assign a twenty-page paper to each of the two thousand freshmen in your English course? You can't grade all that. You just don't have the manpower to crank out that much paperwork. So the reality of a large institution is that the writing assignments have to be downscaled. And when you're at Bryn Mawr and the course has five people in it, those students can do a lot of writing and you can spend the time really reading what they wrote and giving them a lot of good feedback and so on.

So those students came in here with no—like, the Bryn Mawr student, for example—graduate courses as an undergraduate because there are no grad [graduate] students there, and so they came in probably with less of a formal course training in chemistry than I came in with. I was able to take graduate courses when I was an undergrad and get kind of a head start on my graduate work. And my students from Bryn Mawr, Carleton, and so on, don't have that benefit.

But what they do have are these great writing skills and great presentation skills, and they've had a lot of one-on-one mentorship from their professors. In the end, I think that really helps them because I think you can fill in the gaps of missing chemistry courses when you're in graduate school. You're surrounded by 100 percent chemistry, you're going to fill in those holes pretty easily. But you can't fill in very easily the gap of having undeveloped writing skills, because you're just not surrounded by people who are going to help you fill that gap in. So if you have to come to Berkeley with any deficiency—although it seems counterintuitive—you might as well come with a deficiency in chemistry and have good writing skills, because you'll be able to make up that deficiency because your surroundings will support that. You know what I mean?

So again, I have a postdoc [postdoctoral fellow] now who's applying for faculty jobs and she did her undergraduate work at Bryn Mawr, and then she was a grad student at Yale [University], and so she's a postdoc in my lab, and she's an excellent writer. She just wrote an application for the Burroughs Wellcome Foundation [Burroughs Wellcome Fund Career Awards in Biomedical Sciences]. They have this career scholar award or something for postdoc s—advanced postdocs— some money that you then take with you as you start your academic job. It's good money. And she wrote this brilliant proposal, and I'm just thinking, gosh, it really is such an asset to her that she can formulate ideas in this way, just excellent the way it's written. And that just puts her way ahead of the pack and it distinguishes her, no matter what the ideas even are, just the fact that she can express them the way she does.

So, yes, I mean, it would be great if we could get our students here a little more training in writing, but, again, it's a problem of volume. I don't know how to do it. We don't have enough faculty to teach that many students how to write a really good twenty-page paper. We have TAs [teaching assistants] that can just turn the crank on these things and check them for typos, but that's about it. And, frankly, I don't really feel like I learned to write in a formal setting. No one ever sat down, said, "Here's how you write. First you do this, and then you do that, and that's the secret of writing." It wasn't like that. It was more, you know, I read enough books that were well written, and when you read good writing, it helps you learn how to be a good writer.

[tape recorder off]

Sorry. To follow that up, when I have writer's block, which happens, and I just can't get it out, sometimes I go home and read a lot of fiction, good fiction, well-written stuff, because that helps loosen it up for me. And, again, the more I read stuff I think is well written, it helps me. Not science, just whatever. So maybe the undergraduates could benefit from having more reading assignments where they're reading really well-written stuff, but they should be reading those books with an eye for why are they well written, and really take an analytical view of what's the difference between good writing and bad writing and how do you incorporate elements of good writing into your own writing.

But it takes practice. I mean, you just have to write a lot of stuff and find your style. So

probably a lot of these people that have underdeveloped writing skills now, if they had a job that forced them to produce a lot of written material, I'm sure they'd get better pretty quick just by necessity, which I did. When I go back and look at the papers I wrote as a grad student, I'm embarrassed. They're horrible. The very first paper I ever published I now go back and read and I'm thinking, "Oh, my god, what was I thinking?" At the time it seemed okay, but I feel like I've improved things since then.

MAESTREJUAN: In terms of mentoring graduate students, I wanted to ask, it seems to me that you were fairly self-educated as a graduate student, that you ended up writing your dissertation without much direct supervision, at least, that's typical for most graduate students. And when you got to the [Steven D.] Rosen lab, you were teaching them as much as they were teaching you.

BERTOZZI: [laughs] They were teaching me a lot.

MAESTREJUAN: So how do you approach mentoring your own students—graduate students and postdocs—to balance the need to be self-reliant and teach oneself how to write grants, that you did as a graduate student, but also have an active role in their education?

BERTOZZI: Well, I have a pretty big group now, and I travel a lot for work, and so because of those two things, I don't have as much time as I used to have to interact directly with people. So nowadays, I think the students who join my lab, they realize that they have to be pretty independent and self-sufficient to do well because I'm not going to see them every day. I might see them once a week. There might be some weeks I don't see them at all. They can come find me. The more aggressive they are about finding me, tracking me down, the more time that they'll get from me, but if they don't come find me, I don't have the time to go hunt them down.

So having said that, I think I tend to select a fairly independent group of students all around, and they help each other and they have their own little subgroups that are self-educating, so not all of the burden of their training is on me. The more senior students and postdocs pick up a lot of it by necessity.

But even still, there're some formal things I do with my students and postdocs on a regular basis. So, for example, we have mini meetings every Friday. I have about thirty, between thirty and thirty-five people in the group, and so I break them down into these groups of six or so, like five groups of six or so, and they come in here every hour, a different subgroup, all day Friday. Maybe half of them will present their data, their recent experiments, things they did over the last week or two, and show their data, and we have an overhead projector here, and we'll talk about it and we hash it out and I ask them questions. And that's their opportunity to talk about nuts and bolts, problems, experiments that aren't working, get suggestions from the peanut gallery, and just have a discussion. But it's only an hour for all six

of them, and maybe only half of them will present each time. So that's one forum in which I can get some feedback from the people that are most connected to their research project, other people in the group, and that they get to show me what they've done and I get to give them my twenty minutes of my undivided attention.

But then a lot of them will come in, some of them I'll see several times a week. They'll just come in here, especially at night where it's quieter and I have more time to talk with people. The ones that are more night owls have a better time finding me. So they'll come in and we might hang around for an hour just shooting the breeze or talking about something or bouncing some idea around. They make appointments with me. I just scheduled for this Monday, ten o'clock, with a student who really wants an hour of my time, where I'm not answering a phone and there aren't a million people coming in. So I tell them, if you really want to talk with me, no problem, just put it on my calendar. It's an appointment, come in, and I won't talk to anyone else but you. I won't answer my phone, and so on.

So there're those kinds of interactions, and those are interactions that deal more with what's wrong with this experiment, or what direction should we be taking, where should the project be going.

Then the other thing I do is for all my second-year students, I have them come in and do practice qualifying exams. So a qualifying exam is an oral exam where the student has to defend their research and their general knowledge of chemistry to a committee of four faculty. And they all have to do this in their second year. So starting now—we just started this a few weeks ago—they'll come in, and every Sunday, five o'clock, five p.m., they come in here for several hours. And each week a different one gets up at the board and the rest of us sit around the table, we just grill them.

So that's my chance to really get them trained in the fundamental principles, improve their board skills and how they present their research, how they present themselves as a professional. And I give them advice on just how to take command of the literature of your project, so when someone asks you a question, how do you respond to it. You respond with saying, "Well, so-and-so back in 1982 did this experiment, published in that journal." You have to show that you know how your research fits into the context of the history of the science, and who are the other players, and what universities are they at, and what have they done, and what are the experiments they do, and what are they doing next, and how do you fit into that. So it's an opportunity for me to really train them how to be a scientist and present yourself that way, but under the auspices of a practice qualifying exam.

And it's good for me because we do this every single week until they all have finished their qualifying exams, which might happen in April. So it goes from like August to April. And I get pizza and everything. It's a thing, like a weekly thing. And I ask them questions I don't even know the answer to, and we dig around in books and try and figure it out.

So that second year for me with my students, that's how I bond with them. They don't know this. They think I'm just helping them practice for their qualifying exam. But what I'm

really trying to do is get to really see who they are and how they think, and get to know them really well in that context. And I feel like that relationship lasts. It would be nice if I could do it in their first year sometime. I don't really start that until the summer before their second year, but it's just I don't have the time, really, to do that with my first-year students.

But it's funny, some of these students they come right in here and they demand your attention and they really want to talk, and I can get to know them really quickly and they really get a lot out of me. Others, they don't want me in their face, they don't want me in their business, they'll talk to me when they're good and ready, you know. And they probably get less out of me. But that's their choice. Maybe they don't want any more. And they can still be successful, of course. It's just a personality thing.

MAESTREJUAN: How [good], then, are your experimental skills if you aren't spending as much time in the lab.

BERTOZZI: Well, the last experiment I did was in February of 1996 or something. I haven't been in the lab in a long time. So I'm of limited utility with respect to daily technical trials and tribulations of research. Okay, organic synthesis is a very mature field of research. It hasn't really changed much since I was in the lab. So because of that, it's easy for me to give good advice when they have a synthetic problem, because nothing's changed and I know everything.

But biology has changed a lot, actually. The kits that you buy, the way that you clone, there're all these kits and techniques that these students use now that didn't even exist even seven or eight years ago. And so I just don't have the intuitive feel for those techniques, I haven't done them myself. All I can say is, "I don't know. You're going to have to figure that out yourself. I have no idea. Talk to someone else who knows."

So if they really get stuck and I really can't help them, then what we do is we try and figure out, okay, who in the Bay Area knows how to do this, and let's just track them down and call them. I'll help them find somebody who can help them, but it's not going to be me.

MAESTREJUAN: Where is your usefulness?

BERTOZZI: My role is bigger picture. So if they can't get their PCR reaction to work, or if their ligation isn't going, they're going to have to figure that out themselves. That's a detail, that's life, I can't help you. Go figure it out. Try a hundred conditions, talk to people, be resourceful, and so on.

But if it's where do we go from here, this system doesn't work the way we thought, should we even pursue this project anymore, is it time to bail out and do something else, that's where they need me to give them some feedback. Just big picture, like why I think this is interesting,

why I think that's not interesting, and how I might see a future for one line of pursuit and I don't see a future for another. There are some projects you work on that you can see that they could expand into a lot more projects, and I consider that a divergent system. And there are other problems you might solve or work on that really converge to an endpoint. And I don't like that, myself. That's more of a convergent line. I like projects where I can see what you see there: If you do this experiment or this series of experiments and you discover this, then that's going to spin off into this, this, this, this, and this.

And I try and have my students think of it that way. So if you pursue that, you know, if that works, you can see that application, that application, that application, you can try it on that other system in that different organism, and so on. I consider that a really productive project. Whereas if you're trying to solve a problem where when you get the answer it's over and there's nowhere to go from there, then that's less appealing to me, personally.

So that's the kind of advice I give them. But they have to be very independent. I will let them go out there and dangle from a rope. I can see it, I might say this person's going off a cliff and there's a rope around their neck. And I'll say this is what I think, you know, but if they feel like, "No, I really want to do this," I'm going to let them do it. In the end, at some point, hopefully, they'll come crawling back up, but that's part of the whole deal. I certainly went dangling off cliffs when I was a grad student, and it's the only way to really learn.

But I try not to let them just totally waste their graduate career. At some point I've had to occasionally sit down and have that really difficult talk where I just say, "You know what? You really have to just drop this project now because you only have n years left. This isn't going to get you anywhere. There's something more interesting you could be working on, and here's what it is, and just do this."

But most of these students are pretty savvy. They see when things aren't going well and they look at other students whose things are going well. Some of them will take my advice, some won't. Some of them have better ideas than I have, and I'm glad for it. Some of them are working on projects that had nothing to do with me, they just had this idea, they wanted to pursue it, they convinced me it was interesting. I found a way to fund it, and off they went. And that's really exciting because you can see this nugget of talent. You know they're going to be really great. And I've had several like that. I've been really lucky.

MAESTREJUAN: Well, is it a matter of luck?

BERTOZZI: Well, it's Berkeley. We attract really good people, so I think with Berkeley you're more likely to get these great students than some other place. So it's not totally luck. I mean, we have a number-one ranking and students know that. And I think they know that they're going to get a certain amount of freedom if they join my lab, and that could be good or bad, depending on how they look at it.

For example, we have a project on tuberculosis. We're studying sulfation pathways in tuberculosis. I didn't know a thing about tuberculosis, and what happened was we were studying sulfation pathways in humans that are involved in inflammation that had been ticking along. And I had a student come and rotate in the group who asked me one night, "Well, okay, that's great, but what's known about sulfation in prokaryotes?" And I said, "Well, nothing, really. I don't know anything about it, and I haven't seen much. It's just no one's really looked much at those pathways and what role they might play in bacteria." So enter the genome sequencing project, so all these microbes—this is 1999—were getting sequenced, and out had popped the tuberculosis genome and it had been sequenced. This student had taken a gene sequence that we had been working on—it was a human gene involved in inflammation—and done a BLAST [Basic Local Alignment Sequence Tool] analysis, which is a computational analysis of all these microbial genomes to see if there was anything similar, and out popped a whole family of open reading frames from various mycobacteria that were very distant relatives of this human gene. We were like, "Well, that's weird. What are these genes doing in mycobacteria?"

So the student was like, "I really think that we should work on this. I really want to pursue this."

I'm like, "Great!" But I was thinking, "Mycobacteria, I don't even know what that is." [laughs]

So we bought a book, and we were like, "Okay, who around here works on mycobacteria? We need to talk to some people."

It turns out Lee [W.] Riley. So we went knocking on his door, "Hi, we're in the chemistry department and we found these genes and we have all these ideas. We think we should figure out what they do and knock them out and everything, but we don't know anything about mycobacteria, and rumor has it you do. And what do you think of that?" [laughs] And so Joseph [D.] Mougous, my student, convinced one of Lee Riley's postdocs that this might be a really interesting collaboration, and he got those guys on board to help us learn the genetics, like how do you knock out genes in TB [tubercle bacillus], which is not easy. It's much harder than *E.* [*Escherichia] coli*, for example. And they grow very slowly, and you can't do the same kinds of selections with *E. coli.* And then knocking out the gene is one thing, but the only way to really analyze a phenotype in a meaningful way in mycobacteria is to infect a mouse and see what happens.

You need a special facility for this because TB is a human pathogen, and you need to put a space suit on and so on, and you need to work with mice in a special facility. It was clear we couldn't do this without Lee or without somebody like Lee. So we just talked Lee into it. And this student was really entrepreneurial, because no one in my lab was anywhere close to this, and I didn't know a thing about it. And this student just went out there and just talked to people and pounded the pavement and read things and talked to other faculty and just networked. He knows everybody.

And now he's just starting his fifth year of grad school and he's famous on this campus,

everyone knows this guy because he's been Mr. Everywhere, you know. So not only did he knock out these genes and characterize the phenotype in a mouse, which turned out to be really interesting, but he decided he wanted to get the proteins purified and isolated and crystallize them and do crystal structures. He wanted to learn mass spec [spectrometry] and then probe all their metabolic products and see what was missing when you knock the genes out. And the guy's got like six or seven projects he's multitasking. He's got a team of undergraduates working with him. He's directing this postdoc in Lee's lab.

MAESTREJUAN: Wow.

BERTOZZI: He spun off projects to two new students in my lab and a postdoc in my lab, and—this is the best thing—he, together with the help of a postdoc, but really he did the bulk of it, he wrote an NIH [National Institutes of Health] grant, an RO 1. Because at the time this project was spinning out of control and I was like, "I can't support this. There're mouse costs." And I have some unrestricted money from Hughes [Howard Hughes Medical Institute], but it only goes so far. And I said to him, "We need to get some real money if we're really going to do this, and all these other projects are spinning out of this."

And he was like, "All right, well, I'll just write an NIH grant."

And I was like, "Okay, you know, but we'll see. But all right, let's give it a go. It's a good experience." So I gave him some copies of NIH grants, I said, "This is how you do it," and we talked about how it could be organized. Then I said, "Go write a draft and see what happens."

So he wrote a draft of this thing and gave it to me, and I kind of fixed it up a bit, but the meat of it was there. And the thing got funded. It got a really good score. We brought in Lee as a collaborator, and now we're funding that postdoc in Lee's lab and paying for everything.

So now, you know, we're publishing papers in *Tuberculosis* and our lab is getting a little bit of recognition for TB. Again, this had nothing to do with me. If it had not been for this student, this wouldn't have been on my radar screen. So this one student comes through your lab and it's like they leave this trail of stuff behind them, this whole research area.

It's fascinating to me because I've really enjoyed learning about it. We went to this Keystone meeting [Keystone Symposia] on TB this past winter and I was like, "Wow." I learned all this stuff about the genetics and the epidemiology and the immunopathology and so on. So it's just given me this whole new dimension in my life, just because of this one student.

And every student I could tell a story like that, maybe not quite as dramatic, but every student has had their impact so that when you look at my lab, it's not like, "Oh, here's Carolyn's lab and it reflects Carolyn's interests and Carolyn's ideas and Carolyn." That's just such a minor part of it. For the first year or two, yes, that was true, my lab reflected my interests, my ideas.

But after that it just became this conglomerate of all the students and postdocs who have passaged through and made their mark. So our research program as it is defined now is probably as much or more a reflection of the interests of the students and postdocs who have been through the lab than my own personal interests. You know what I mean? So if I had different students, if I'd had just different people come through, my lab would look different as a result of that. I mean, no question.

So what do I do? It's a good question. I just sit here and direct traffic. [laughs] I'm the overseer. I strategize how we're going to get money to pay for all this stuff, so I do a lot of strategizing for how to get grants funded and how to get papers published and how to sell the work that we're doing from different angles and so on. I go out on the road and I tell the story and I get input from people at different universities and I bring it back here and I file-dump it on my students so that we have new ideas for our own projects and so on.

So I'm sort of like FedEx. You know what I mean? FedEx just carries things around, and it's like St. Louis is the hub and everything comes in and then gets sent out again. That's like what I do. So, information gets dumped into me and then I pass it out again, but all the traffic is my students and postdocs. It's hard to explain that. That's what's so interesting about labs, it really is like this big city, and there're all these little microcosms and they all have this little life of their own, and you're just trying to kind of keep it all organized and functional.

MAESTREJUAN: There are anthropologists of science who look at labs as communities and study them like any other—

BERTOZZI: They're self-organizing and they also—What is it? What's the recent popular term?—have emerging properties. You know what I mean? There's all this stuff that happens which is more than just the sum of the parts or something. It's really interesting, isn't it?

MAESTREJUAN: I want to talk more about your research program, your current research program, as it has evolved from the material I had available, which is the Pew [Scholars Program in the Biomedical Sciences]—

BERTOZZI: The original Pew [Scholars Program in the Biomedical Sciences] application?

MAESTREJUAN: —application, [in] which I could see the links between your work as a postdoc and your Pew [Scholars Program in the Biomedical Sciences] application.

BERTOZZI: What project did I send in to Pew [Scholars Program in the Biomedical Sciences]?

MAESTREJUAN: Sulfotransferases.

BERTOZZI: Oh, yes, yes, right. Sorry. I should know that.

MAESTREJUAN: That's okay. You were using more the language of cell biology and things, but you have now won a lot of prestigious awards, the MacArthur Award [MacArthur Fellow], and extended that area into looking at the cell-surface proteins and taking the Staudinger reaction and tinkering with it, which I was kind of struck by when we were talking about what you did in your dad's basement, tinkering with things, and chemistry as a very established field and yet you're taking it in new directions with your experience in biology.

But I guess at least one avenue to open this up is, many Pew [Scholars Program in the Biomedical Sciences] scholars will have a *Cell*, *Science*, *Nature*, paper as a graduate student and maybe as a postdoc, and then it takes them a while to achieve that level again when they're an independent PI [principal investigator]. And for you, it seems to be a little bit different. You have had three *Science* publications in consecutive years, so that if you use one standard by which we measure success, you have now made it to the top journals and have had several papers in *PNAS* [*Proceedings of the National Academy of Sciences of the United States of America],* a good, solid second-tier journal.

BERTOZZI: *PNAS* is a second tier? Oh, damn. [laughs] It's funny, because how you rank these journals really depends on if you're a biologist, actually. If you're a chemist or a physicist, it's very different.

MAESTREJUAN: Right.

BERTOZZI: Because *Science,* for example, *Science* for a physicist is like *People* magazine. It's like there's nothing important in there. And for a chemist, *Science,* it's nice, but it's not necessarily the most serious journal, you know.

MAESTREJUAN: What would be the best?

BERTOZZI: Well, again, it depends. *Science* is great because of the PR [public relation], the press, the pizzazz, but there's no detail in a *Science* paper. It's not long enough to have any substantive experimental information. You can't really criticize a *Science* paper, you don't have the information.

So the *Journal of the American Chemical Society* [*JACS]* is the flagship journal for chemists where you would publish a paper that is fully elaborated with all the experimental details. That has value. It's not quite the right comparison. I would say that a *JACS* paper for a chemist would have the kind of detail and quality as a *Cell* paper for a biologist, except it's much harder to get a paper published in *Cell* because the submission to publication ratio is so high. Whereas *JACS,* there're fewer submissions and more publications, so it's really not as hard to get a *JACS* paper as a *Cell* paper, just statistically. But conceptually it's the same kind of thing.

MAESTREJUAN: When it comes to making decisions about where you're going to publish, why choose *Science* at all as a chemist? And what did it mean for you, then, as a chemist, to get an article—report—in *Science?*

BERTOZZI: Why submit things to *Science?* So if it's short, if you have a short story to tell that you can fit into an article that's that short. Some of my stories I couldn't fit into a *Science* paper if I tried. You know, like, *War and Peace,* you just couldn't condense it into four single-spaced pages in *Science.*

So it has to be a short story, A, B, if it kind of impinges on the biological sciences, material sciences, or environmental sciences, then you have a shot at *Science* because they want things for a broad readership. So if it's a story that's really a very chemical story that only chemists would really appreciate, chances are *Science* won't be interested in it. They want something that has broader appeal, so you have to have a sense of how broad is the appeal of the importance of what you've done, which is very subjective.

But you go to *Science,* obviously, to get the readership and the PR. You know what I mean? A lot more people read *Science* than read *JACS.* So the impact factor, the value, which I hate. But of all the papers—I have to tell you—from my group that I've taken pride in with respect to our accomplishment as reflected in that paper, it's not actually any of our *Science* papers. I would have to say the one paper that I'm most proud of because I think of it as a really important discovery, an important achievement, a heroic experimental effort that took such a combination of skills that very few students could have pulled it off, was this one, actually, which I'm just fixing up for *JBC* [*Journal of Biological Chemistry]*. Now, *JBC* is a huge journal with hundreds of thousands of pages every year and a lot of really long, gory articles that are too hard for anyone to read. It's not considered a journal that you skim through on the airplane, right? It's a journal that you pick up papers as they come up in your SciFinder searches. And so *JBC* is a well-respected journal, but it's definitely a kind of nuts and bolts. It's not considered a flashy, high-profile, make-you-famous kind of journal.

And yet, to be honest, I think that this paper will have more impact long term. It's a more fundamentally important discovery than the snazzy stuff I've published in *Science.* In chemistry, *Science* is really for snazzy stuff. You know, it has a kind of sex appeal and it's kind of flashy and it's something kind of cool that might be really important, but maybe not. I mean, maybe it's

just kind of cool.

And so, yes, we've published papers in *Science* and I've sent things to *Science* because I thought that the biological community could really take advantage of this chemical tool. So we had a tool, we thought this could really help a biologist do things that they couldn't do any other way. We should try and get this into *Science* because they'll see it. That's when I would go to *Science.* This is a paper that we could hardly even fit it in these twelve journal pages, just to really explain a story in all of its glory, and it really is just an unbelievably interesting story. But it's a glycobiology story that you probably wouldn't care about unless you were a glycobiologist. So it doesn't really belong in *Science.*

MAESTREJUAN: Why don't you tell us about this story, because it hasn't been published yet.

BERTOZZI: Well, It's just in press. It's a galley.

MAESTREJUAN: Let me flip the tape over.

[END OF TAPE 3, SIDE 1]

MAESTREJUAN: Well, this article is obviously about sulfotransferases. So there's clearly a thread.

BERTOZZI: This is the culmination of the project that started with the Pew [Scholars Program in the Biomedical Sciences] funding, so it is appropriate. And again, this did come from the work that I did as a postdoc [postdoctoral fellow] in Steve [Steven D.] Rosen's group. So Steve for many years had been interested in lymphocyte recirculation through lymph nodes, and this is part of the normal immune response.

So lymphocytes are your T-cells and your B-cells, and their job is to patrol your body and look for foreign invaders like bacteria and viruses. And when they encounter those foreign invaders, they have to communicate with each other, and then that stimulates an immune response. But statistically, the right T-cell and the right B-cell would never find each other if they were just flying around your body, because there's just so much volume to cover, and so the job of the lymph node is to collect them and concentrate them in this organ so that they are much more likely to encounter each other.

And so we have this thing called immunosurveillance, where your T-cells and B-cells exit the bloodstream, go through the lymph nodes, sort of sample each other, and then go back to the lymphatics and into the blood again, and they just do this continually. They recirculate. And

lymph nodes, you have hundreds of lymph nodes throughout your body, under here and in your armpit. Hundreds.

So it's an interesting topological problem because the blood system is a closed system, and yet these T-cells and B-cells have found a way to exit out of the bloodstream and enter the lymph node tissue, so they've crossed over this barrier, which is made up of endothelial cells that line the blood vessels. So Steve, for his career, has been really interested in how that happens.

So back in the 1980s, late eighties, it was discovered that there's a protein, on the lymphocytes, called L-selectin, and it's binding to ligands that are on the endothelial cells, but only in these lymph nodes. And those ligands turned out to be sulfated polysaccharides, but that wasn't known until later in the nineties, and that was work that I contributed to as a postdoctoral fellow.

So at the time that I went to Steve's lab, it was known that, yes, there were some carbohydrates. They were binding to this receptor L-selectin, and this was important in lymphocyte recirculation. They knew that they were sulfated because of some metabolic radiolabelling experiments, so they put hot [radioactive] sulfate into lymph node organ culture, and this radiolabelled sulfate ended up in these glycoproteins. But they didn't know what the structure was. So I had been following the story in the literature at the time. "They need me to come into the lab and help them figure out the structure." So I talked my way into a postdoctoral position.

While I was in Steve's lab, we discovered exactly what is the structure of this polysaccharide, exactly what were the sugars and how were they linked together and where were the sulfates, and the other thing we discovered is that the sulfates were absolutely critical for the binding of this receptor. So without the sulfate there, the binding was really weak, but with the sulfate there, it was really strong.

So the sulfate was a switch, and I thought that was really profound, because sulfate as a chemical group is kind of similar to phosphate, and inside your cell you have a lot of phosphorylation pathways. And you've probably talked to other Pew [Scholars Program in the Biomedical Sciences] scholars who work on kinases and phosphatases and signaling pathways. This is a huge area of biology, and every biologist knows that phosphorylation of proteins can change their properties and lead to a signal transduction event.

And I thought it was really interesting that here was another example of biological regulation, but instead of phosphate, it was sulfate, instead of proteins, it was sugars. So this is early nineties, okay. Now, if you dug around the literature at that point, you could actually find a few examples out there of other receptor-ligand interactions outside the cell that were governed by sulfation of a sugar. So, you know, those of us who were working in Steve's lab started wondering, well, maybe there's actually a paradigm here. Maybe one can think of sulfation of sugars more broadly as a way to regulate their function, as we think of phosphorylation of proteins. And maybe there're, in fact, whole families of enzymes that put sulfate onto sugars and

modulate them and activate them or deactivate them, just as there's a family called the kinases that put phosphate on proteins.

And at the time there was only one such enzyme—they're called sulfotransferases—that was known in humans, and this was, again, before the human genome became publicly available in its entirety. But there are a few bits and pieces of the genome around at that point. You could get EST [expressed sequence tag] databases and so on. So what we did is we took this one known gene and did a BLAST [Basic Local Alignment Sequence Tool] analysis, and out popped a whole bunch of ESTs that looked like relatives of that enzyme from the human genome, and that led to the discovery of a family of sulfotransferases.

So we, at the time, in Steve's lab and with some collaborators, we called those the GST family of sulfotransferases [Gal/GalNAc/GlcNAc 6-0- sulfotransferase]. I think, now there're seven of them. And other people had discovered other sulfotransferases, so by the year 2000, there were about fifty sulfotransferases from the human genome, as opposed to one, which was the case five years earlier.

So you really started to get the sense that there's a super family, and that there's all this sulfation going on, and it could be very broadly involved in biological regulation, and that's what I wanted to study on the faculty at [University of California,] Berkeley. So that's what Pew [Scholars Program in the Biomedical Sciences] funded.

So when I came to Berkeley, I wanted to pursue this GST family of sulfotransferases in more detail and from more of a chemistry perspective, and so there were a couple of different lines of inquiry that we pursued. One was a very practical line of inquiry: So it turns out that one of these GSTs not only sulfated these polysaccharides in the lymph node and was important for recirculation in the lymph node, but it also sulfated polysaccharides at sites of chronic inflammation. And it turns out that a chronically inflamed tissue—like the joint of someone with arthritis— it starts to look like a lymph node. So the tissue starts to reorganize itself and gets remodeled, and the T-cells and the B-cells form zones and germinal centers, and all these genes get induced that are normally lymph node genes, including the sulfotransferases that were induced in these inflamed tissues, and the sulfated sugars were getting expressed on these blood vessels. And all of a sudden, you know, you'd get recruitment of leukocytes, all kinds of white blood cells into this tissue which was not a lymph node, and that would cause damage of the tissue, and that's the pathology of inflammation.

So, you know, one of the fundamental goals in the pharmaceutical industry is to keep those leukocytes out of the tissue, to keep them from attaching to the blood vessel walls and creeping through the blood vessels. And since the sulfated polysaccharide was really important for the cell-cell binding event, you know, it was clear if you blocked sulfation, you might block the whole cascade of events, and that was sort of validated with a knockout mouse in which that sulfotransferase was deleted.

So in my lab, one of our first projects was to try and figure out how do you develop drugs that target sulfotransferases, really a very medicinal chemistry approach. So we worked on

that.

The other thing we worked on, which was this, and this took about five years to really come to fruition, so this is a long project, with one heroic graduate student, starting from day one and now starting his sixth year, with his first paper. I mean, this is really heroic. He was interested in what is the difference.

Okay. So, again, we now know there're fifty sulfotransferases, and it turns out they come in subcategories. So five of them are GlcNAc-6-0-sulfotransferases. So they'll put sulfate onto a sugar called N-acetyl glucosamine at the 6-hydroxyl group. And why are there five of them? Why do we need five? And that's like saying if you look at the kinase superfamily, you know, there're hundreds and hundreds of kinases in the human genome, eight hundred or so. Several hundred of those are tyrosine kinases. They all put phosphate on tyrosine.

So what's the difference between them all? Well, they target different tyrosines within different protein substrates, so there's a context in which they'll recognize their particular tyrosine of interest and phosphorylate that protein. And so we were wondering where does specificity come from within these GlcNAc-6-0- sulfotransferases: Why does this one put sulfate on the GlcNAc residue in this particular polysaccharide but not in any other, where this other one will find a GlcNAc in this other polysaccharide, where does that come from?

So this student spent a couple of years probing the in-vitro substrate specificity of these enzymes. So he synthesized a bunch of polysaccharides—that's not easy— and cloned and expressed these enzymes and developed in-vitro assays. That wasn't easy. And what he found in vitro is that all these enzymes behave identically. There's just no difference between them, and yet in vivo, they are able to find different glycoproteins to sulfate on different GlcNAc residues. So there was obviously some information in coding their specificity in the cell that wasn't outside of the cell, and so we're like, okay. So it was clear we had to study them inside the cell.

Okay. So now we had to develop a way to look at their activities, their substrate specificities all in a cell, and these are enzymes of the Golgi compartment, so they are membrane associated within the Golgi stacks.

So the student made somewhere over a hundred stable cell lines that were engineered to express different members of the sulfotransferases family together with different enzymes that built different kinds of polysaccharides and he developed antibodies to probe the sulfated polysaccharide products on the cell surface by flow cytometry and microscopy. The guy's a chemist, you know, and he had to learn all this cell biology.

What he discovered after all of this was that what gives these different enzymes specificity for different targets has nothing really to do with the way their catalytic domain binds the substrate, which you might have suspected. It's the simplest explanation. Instead, it has to do with their differential distribution in the Golgi compartment. So some of them are really early in the Golgi, and some of them are really late in the Golgi, and some of them are distributed throughout the entire Golgi. And so those enzymes that are really early in the Golgi

have access to different types of structures than those enzymes that are really late in the Golgi, and so there's kind of a temporal and spatial contribution to the substrate specificity that has not much to do with the actual catalytic domain of the enzymes. And that was a really fundamentally new discovery that explains how the system works and what the real difference is between these enzymes and why when you knock out this one, that one doesn't compensate. He's not in the right place.

And he made a lot of chimeric enzymes where he would take the localization domain of one and put it on the catalytic domain of the other and have them swapping places in the Golgi compartment. It was just a brilliant piece of work, you know, and to pull this off, it required a really detailed understanding of the glycobiology, the biosynthetic pathways, the structures of the polysaccharides, how to do the genetics, and he did a lot of really glorious pictures in here, and so deconvolution fluorescence, microscopy. And, you know, no one in my lab knew how to do that at the time. He had to figure all this out on his own, just by hanging around. He's got these figures with T panels, you know, A, B, C, D, E, F, G, H, I, J, K. Just really nice, and heavy-duty quantitation, you know, because you're always open to artifacts.

So when we put this paper together—it took a while to get this thing all together—and now he has this model for how these biosynthetic pathways take place and how enzymes located in different places will sulfate in different ways and so on. And I just know it's a brilliant piece of work, and no one else might ever really know that, because it's just a complicated system that two people in the world might read this paper. But I know what it is. Yes, it's not a *Science* paper, because who could have fit it in a journal like *Science.* But it's a really nice piece of biochemistry.

MAESTREJUAN: Well, again, I'll bring this up from yesterday, about pedigrees and the politics of publication and worrying about who you work with. And science, particularly in the biomedical area, moves at a dramatic pace, and how do you encourage students to do these kinds of projects and do this heroic effort?

BERTOZZI: It's hard for him, because especially chemists—synthetic chemistry— you tend to publish at a much quicker rate than if you're a cell biologist. And it's not uncommon for a synthetic chemist to publish ten, fifteen, twenty, even, papers in the course of a Ph.D., where it's very unusual for a cell biologist to do that. They might have two or three papers, and it's great, you know.

So it was hard for Chris [Christopher L. de Graffenried], because his classmates were pounding out all these little communications, and he's slogging away and finally had this one monstrous paper. So I had to do a lot of cheerleading. I had to say, "But, Chris, it's not quantity, it's quality," and, of course, in reality, it's both, right? But we don't say that to our students. And I had to do like, "Chris, you know, this is such an important piece of work. This is one of those landmark papers that's going to go down in history. People are going to cite this paper for a long time."

In fact, I was reading an article—and I cannot remember where—it was really interesting, on impact factor and kind of what a joke it is because it turns out that, yes, there're impact factors and there're numbers and you assign them to journals, but they change as a function of time, post publication of that paper. So impact factor has to do with the number of citations, and the number of citations for *Science* papers, it turns out, drops precipitously, so the impact factor a year after the publication is much higher than the impact factor five years or ten years after the paper.

By contrast, *JBC* [*Journal of Biological Chemistry]* has the opposite trend, so the impact factor starts out maybe a little low on the scale but it increases with time. So ten years or even five years after the publication date, the impact factor of a *JBC* paper is higher than that of a *Science* paper, and that's a statistical fact. So, of course, I relayed this story to Chris, and I said that, "Chris, five years from now, nobody will remember what was published in *Science* five years ago. Half that stuff is probably retracted anyway." There're a lot of booboos in *Science* and *Nature*. That's flashy quick stuff, and some of it might have a long-term impact, but a lot of it won't, because it was hot today and was gone tomorrow. I said, "But this paper will last. This is a paper that people are going to cite for a long time," and that's important, you know. What else can I say?

MAESTREJUAN: Right. And where is he? What's he doing now?

BERTOZZI: He's doing to go postdoctorate with Graham Warren, who is a cell biologist at Yale [University]. So Chris has now become fascinated with the Golgi compartment, and he has, as he phrases it to me, so glycobiology is really at some level the study of the function of the Golgi compartment, because the Golgi compartment is basically a very fancy assembly line that organizes enzymes so that you can post-translationally modify proteins. That's fundamentally what it does. Not just glycosylation, but fold them and get them in the membrane and so on.

But glycosylation's a big part, so you have three hundred—Yes, in the human genome three hundred—well, two-hundred-and-fifty glycosyltransferases and about fifty sulfotransferases and all of them are in the Golgi compartment, all of them, all right. That's a lot, you know, to pack into this one space. So that is the primary function of the Golgi, and yet most glycobiologists don't think that much about the Golgi compartment and its architecture and its biogenesis and its dynamics. They really don't. They think about what's the product? It's the sugar, and they study that.

And then likewise, you have this whole Golgi community, and it's this really tight little Golgi-like aficionados. They're a lot of high-tech electron microscopists and so on, and most of them don't know a thing about glycobiology. So they study the structure of the Golgi, but don't really know, don't really think about what's its primary function, because it's hard to think about sugars, you know.

So Chris says, “I’m going to be the guy, you know.” Yes. He takes like the function of the Golgi, understands the structure of the Golgi, and kind of puts them together. And so in my lab, you know, he has spent five years being *the* world’s expert on how glycosylation takes place in the Golgi compartment. Now he’s going to go work for Graham, and Graham Warren is one of these aficionados of the most fancy microscopy technique you could think of to pick apart all the aspects of the Golgi and cut it and see how it heals and look how it grows from scratch and so on. And I think it was a really good choice.

So Chris has a vision for his scientific interest, and so it took me like five years, but after five years, I really feel like here’s a guy who is not caught up in whether his paper was in *Science, Nature,* or *Cell*—and is not caught up in, “Well, what’s everyone else interested in, and that’s what I should do, too, so I can get a job.” That’s not it for him. It’s all about the Golgi compartment, you know. He reads a Golgi paper, and he’s up all night thinking about it, and he wants to talk about it with me at eight A.M. the next morning, and that’s what makes him a great scientist, you know what I mean?

So now I can only hope, as he goes out into the world and applies for jobs, that I can write a letter that conveys that sentiment so that the people who are evaluating his job applications will hopefully read that letter and that will be a letter unlike any letter that they are used to seeing. You know what I mean? And I can honestly say that about this guy. It’s not just, “Oh, yes, he’s a good student, you know, and the forty students I’ve worked with, he ranks in the top percentile.”

[Referring to visitor in room.] That’s another superstar. That’s not this guy [Christopher L. de Graffenried]. Different guy. That one is going to postdoc at Harvard Med[ical] School for Hidde [L.] Ploegh. Do you know Hidde? He’s a viral antigen-processing guy. Biologist. This guy went to Carleton [College], by the way, and he’s a really good at microscopy.

MAESTREJUAN: Oh, really? Well, good. So what’s the impact of this paper on the direction of where your lab’s going?

BERTOZZI: Oh, huge.

MAESTREJUAN: Are you going to be like a new Golgi fanatic as well?

BERTOZZI: Well, I’m a Golgi amateur. It really takes a long time, I think, to become one of those Golgi people, because, again, it’s microscopy, it’s all about microscopy, and I don’t have that sort of background. If I had Chris forever in my lab, I could do it, because he has the intellect, he has the drive, and he has the passion for it. But when he goes, which is going to happen this year, I don’t really have anybody behind him who I think can carry that torch.

There're other torches they'll carry in different directions, but I don't see anyone doing exactly this.

But I'll tell you what did happen, which spun out a whole new project. So again, there we were like mucking around in the Golgi compartment, and it's funny, I had actually never really thought of this. I had been working with sugars for a long time, and I knew that glycosyltransferases put them together, and I knew that these are membrane-associated Golgi enzymes, but I had never really made the leap to how the organization of these enzymes in a physical sense might encode a biosynthetic pathway. I just never really thought of it that way, and this problem opened my eyes to that.

And there's another big problem in glycobiology, which is that we have kind of a dearth of chemical tools that we can use to study processes, and one of the most useful chemical tools as a biologist you can have is an inhibitor of the enzyme that you want to study. So if you're a kinase person, it's really great that you can buy staurosporine and it inhibits protein kinase C or you can just buy some little toxin inhibits your G protein. You know, these are tools you buy from Calbiochem [Co.], and you could see whether, "Okay, does the process involve protein kinase C or does it involve this G protein?" And there's nothing really like that for the glycobiologists, and the reason is that these enzymes, the glycosyltransferases, which are kind of what you'd like to hit because they're biosynthesizing these things, they're just really hard to block with small molecules. They don't lend themselves to small molecule inhibitor design, and it has to do with aspects of their structures. And I won't go into the details.

So there has been no way to perturb glycosyltransferases with small molecules—switch them on and off—and I should say there has been no way to do it in the conventional enzyme inhibitor sense, where you target the catalytic domain with an inhibitor.

So when the story started coming together, a bunch of us were like, well, gosh, there's this whole other dimension of glycosyltransferase function. Yes, their catalytic domains are catalyzing reactions, but their ability to do that is really dependent on their proper positioning in the Golgi compartment. So what if you muck with that? What if you targeted their Golgi localization, not their catalytic activity?

So it's like you're talking to me and I want to inhibit you from doing that, there're two ways I could do that. Right? I could stuff a ball in your mouth, and that's the conventional inhibitor. Or I could stick you in another room, right? So we started thinking about, "Well, is there some way we could just relocate these enzymes in the wrong place, and then they'd basically be inactive?" So we figured out a way to do that, and so I have to draw it, but then it won't get tape-recorded.

MAESTREJUAN: Yes, that's a problem with recording.

BERTOZZI: Anyway, so we figured out a way to do it, and basically what we'd do is there're two domains. All these enzymes have the same domain architecture. They have a catalytic domain and a localization domain. And these things are part of one polypeptide, and so localization domain puts them in the membrane, catalytic domain catalyzes reaction. So what we do is we separate those two domains. Now they're two separate proteins. And localization domain goes to the Golgi compartment, but catalytic domain isn't attached anymore. It just gets spat out of the cell, okay, so that's inactive.

So then what we also do is we fuse to each domain a little small molecule binding protein that doesn't really interfere with the domains because it's pretty small. And there's a small molecule that's a drug that we feed the cells, and the drug binds to both things at the same time and glues them together. So, basically, in the absence of the small molecule, the catalytic domain flies out of the cell, no activity. In the presence of the molecule, it gets glued together to the localization domain. Now it's in the right place, and it catalyzes the reaction. So that small molecules flips the enzyme on and off, but not by attacking the catalytic domain, by affecting the localization.

And although that is kind of a separate problem from this one, this project really inspired that, and so that is what Jen [Jennifer J.] Kohler has been working on, and she's now in the academic job market. She's the one from Bryn Mawr [College], who's a great writer. And two new graduate students—just finished their first year— have projects in that area, too, and we just submitted a big NIH [National Institutes of Health] grant to get some funding for that. So that you could say that that is a spinoff of this project, because it was inspired by this one.

So when Chris leaves, our interest in the Golgi compartment will probably be in that venue, but unfortunately Chris is going to be a tough act to follow, because the cell biology in this project was really significant. It was complicated and it was difficult. This guy's a chemistry student, and most of my students are chemistry students, and they're not up for it, most of them. They want to do synthesis. That's why they came here. And Chris was very open-minded, didn't care what his technique was, he just wanted to solve a real interesting problem, and found his calling in the Golgi compartment. And I think that was a lucky find for me.

MAESTREJUAN: Yes. Well, you have written a review article on glycobiology and the state of glycobiology a couple of years ago. Where do you see your future research interests heading? So where do you think you're going to be five to ten years from now?

BERTOZZI: Gosh, I don't know. I think it's going to depend on who ends up in my lab, and what they want to do, because the stuff we're doing now, I don't think I could have predicted five years earlier. So, likewise, I hope that we continue to make important discoveries that move the field of glycobiology forward, provide new chemical tools, make some new fundamental discoveries.

I like having a balance of real fundamental work, like how do things work, and also developing cool tools that you can use to do things, you know. It's nice to have a balance of kind of snazzy, sexy stuff that you put in a *PNAS* [*Proceedings of the National Academy of Sciences of the United States of America]* and *Science,* and also some real kind of fundamental stuff where you can really develop a full story and quantitate the heck out of it, and do really scholarly work that nobody might ever read, but you feel proud. You know you did it. You know what I mean?

MAESTREJUAN: Yes.

BERTOZZI: But exactly what systems, I, five years from now, probably will hopefully still be working in TB [tubercle bacillus], although exactly what we're doing will depend, again, on the people that come through here. It's so dependent on the people. I hope I get good people. I hope I continue to get good people who have these great ideas and are bold and want to go out and do things that are new and not afraid to bring new techniques into the group.

MAESTREJUAN: Well, again, to use one of these tired old criteria for one of your papers with [Steven D.] Rosen in *Current Opinion in Cell Biology* [Rosen, S. D., Bertozzi, C. R., 1994. The Selectins and their Ligands. *Current Opinion in Cell Biology* 6:663-73], was considered a hot paper by scientists.

BERTOZZI: That was over a year ago.

MAESTREJUAN: Right.

BERTOZZI: Because it was the selectins and they were hot, yes.

MAESTREJUAN: Yes, they were hot, and it kind of put all the information anybody needed to know in one place. How well did this initial selectin project fill your expectations?

BERTOZZI: Oh, it was way more than my expectations. So, L-selectin was the receptor on the lymphocyte that was involved in recirculation. That receptor binds to this sulfated polysaccharide that these enzymes sulfate. So all of that is part of this story.

Yes, the great thing about the selectins is that they turned out to be far more complicated than anybody anticipated, and that was a bummer, actually, for the pharmaceutical companies, because, again, back in late eighties, early nineties, all these companies got really excited. And

part of the reason this was so hot is because people were like, “Oh, my god, this is a new inflammation target, and the inhibitors of the selectins are going to be broad-spectrum anti-inflammatory agents,” and every company had a big selectin program at that point. And this was pivotal for the field of glycobiology, because until then, sugars were considered the Special Olympics of biology, you know, and not that interesting and kind of weird and of no significance in medicine and pharmaceuticals.

So then out pops this family of receptors that are the very first stages of leukocyte adhesion at sites of inflammation. They bond to sugars. And all of a sudden, immunologists had to learn about sugars and people in the pharmaceutical industry had to learn about sugars, and they were, “Oh, my god, oh, no. I never read that chapter.” So glycobiologists became really important, because we held the key to understanding these things, and companies wanted to hire carbohydrate chemists for the first time ever, which was great. And it just brought a lot of attention to the field.

Glycobiology meetings before that—I went to a couple as a grad [graduate] student, like Keystone [Symposia] meetings and stuff—they were small. It was a hundred people and kind of like fringe-element. And then after the selectins, a few years later, these meetings were oversubscribed and they were huge and you couldn’t get in and it was a big deal.

But at the time, people vastly oversimplified what they thought the ligands for the selectins were, and pharmaceutical companies tried to develop drugs based on these simplified view of these ligands, and all those programs failed. So by the midnineties, no big company had a selectin program. They gave up. It just wasn’t flying. And companies, they can’t wait forever to get a hit on something.

So it’s a bummer, because, again, you used to have these meetings that were the whole meeting was the selectins. There was a whole Keystone meeting on the selectins. Now you go to some glycobiology meeting and there’s one little poster on selectins. No one even works on it. It’s just people were frustrated, gave up. But there’s going to be a renaissance, and I’ll tell you why.

MAESTREJUAN: And we heard it here first.

BERTOZZI: No, it’s true. And because ten years later, now we do understand the true complexity of these ligands, we didn’t back then, and they’re much more complicated. I won’t even go into all the complexities. But sulfation was a part of it. That wasn’t even known in the early days. That came out in ’95, ’96, after all these programs had bailed out.

So now we have an idea what the real ligands are, we’ve identified the enzymes involved in the biosynthesis of these ligands, and those enzymes are now attracting attention as drug targets. And enzymes are probably going to be easier to inhibit than the actual selectins themselves, which are receptors, because enzymes are in the cell and they catalyze reactions,

they have hydrophobic binding pockets, and you can target them with drugs.

So it was that recognition that spawned the second-generation companies like Thios Pharmaceuticals [Inc.], right. So there're UC [University of California] patents on these sulfotransferases, and this is some of the intellectual property on which we based that company. So Steve [D. Rosen] and I and another former postdoc [Stefan Hemmerich] from Steve's group formed Thios around sulfation as a kind of niche for drug discovery, including this enzyme and some others, too. And we were able to raise money for that company, which wouldn't have been the case earlier in the nineties when people were really bumming on the selectins. So we did all right, despite the economy and so on.

MAESTREJUAN: Okay. I'm going to be jumping around a little bit here, but I'll pursue this. Why start a company?

BERTOZZI: Because you know in your heart that you have a really interesting target for a disease, a really big disease category, and you've been working on it, slaving away in your academic lab for all these years, and you want it to come to fruition. And you start every paragraph of every paper in every grant with, "These enzymes are important in inflammation, and inhibiting these enzymes could be a way of blocking inflammation," and you want to realize that. And you can't do that in academia. You have to do it in a company. You need the resources, you need the personnel, you need the infrastructure and the right commercial motivation.

So that's why we did it. We had been kicking around the idea since I was a postdoc in his lab, all of us. We're like, "Oh, we should start a sulfate company," and none of us were in a position to do it. I was a postdoc. The other founder, Stefan Hemmerich, was a postdoc. Steve had a big collaboration with Genentech [Inc.] at the time, was kind of tied, and couldn't really do things on his own.

And then, you know, years later, I got tenure here, so I was a little more secure. Stefan had been at Roche in Palo Alto [LLC] [Roche Holding Company] for about six years, so he had now a pretty good idea of the drug discovery process. Steve broke off with Genentech, and the time was right.

So we finally said, "Let's just do it." And we did it, and we hired Stefan out of Roche to come and be the first employee of Thios, and then we started hiring from other pharmaceutical companies to get experienced people in medicinal chemistry, high throughput screening, target validation, crystallography, and now we have a fully integrated company. It's a small start-up company. We have about thirty people.

We raised our first round of venture capital financing, and we closed that deal in April of 2002. So we've now been operating for about a year and a half, and we've raised 15 million dollars in that first round. We did all right.

MAESTREJUAN: Yes, okay.

BERTOZZI: And it was fun for me because it was something different. I had no idea. I'd never started a company before. I thought it would be a learning experience, and I thought it would be really fun to create.

And one of the things I liked about my lab is come in, empty space, clueless first-year students, and create out of nothing, something. And starting a company is the same thing. You go in, and it's nothing, and you raise money, and just from nothing you create this entity. And now you're employing people and you have these ideas and you're putting together business deals and so on. It's really, really fun, actually, but a lot of work.

MAESTREJUAN: And why stay in academia?

BERTOZZI: Well, I had actually the opportunity to move to this company, so I had an offer to go there as the head of research, the chief scientific officer, and I thought about it really seriously. And there were mornings when I woke up and I was like, "I'm going to do it, I'm going to do." But then, I look at my little students, and I couldn't. It's such a privilege to work with someone like Chris [Christopher L. de Graffenried] and Howard [C. Hang], and Joseph [D. Mougous], and Jen [Jennifer J. Kohler], and all these people.

And I don't think I could duplicate that in industry. There're smart people that you hire there, but you have a different mission, and you don't get to see them develop and find themselves the way that you get to see these students do that. You know what I mean? To have like some kid come in out of some undergraduate place, doesn't know anything, knows a little chemistry, a little biology, but not much else, and then comes out of here with his eyes burning passion about the Golgi compartment, that's so precious. So that would be hard to give that up.

And Joseph [D. Mougous] would come in and be all about tuberculosis. And when he came in, it was nothing, it was blank, and now this guy has a purpose and this is what it is. And I feel like I got to see it and I got to catalyze it, and then I get to follow them around afterwards and see what they do.

My first student ever, Ph.D. student, to graduate, she just started on the faculty at UT Austin [University of Texas at Austin], and she has her own website. I don't have kids of my own, so this is the only way I get to feel that feeling of pride. Plus, I come and go as I please. Nobody tells me what to do. I don't have to report to people. I don't have to make milestone slides and answer to investors. I do at Thios, but I don't here, and I think that would drive me nuts, if I had to do that for my vocation and my avocation.

MAESTREJUAN: Yes. Well, one can argue that there are these constructs we have in place called patents that can maintain a barrier between academia and industry, and the University of California is one of the pioneers in this area, whereas fifty years before, universities had policies that said you can't patent anything. And now, everybody has a material transfer office or technology transfer office at all their universities.

One very famous way is Berkeley had an agreement with Novartis [Pharma AG] that the technology would be here and through a patent would be licensed for commercialization with the biotech company, and those would be separated. Why have you chosen to blend the two? Because you do own patents and you could just license that to Thios and not have anything more to do with it. Why choose to be involved on both ends of the spectrum?

BERTOZZI: Well, maybe I don't know the rules that well, but at Berkeley anything I discover at Berkeley belongs to UC.

MAESTREJUAN: Right.

BERTOZZI: So any of my scientific discoveries from my lab, that's a UC patent, and then Thios can license that patent from UC, and they can pay for the patent preparation costs in exchange for the first right, for an exclusive right license. But I don't really have a lot of flexibility in how I do things. That's my only mechanism.

And also being a [Howard] Hughes [Medical Institute] Fellow investigator imposes certain limitations on what I can do. I can't take money from Thios to do research here, where Thios, in exchange for that money, gets some special right to the patent. Thios has to compete for my patents with everyone else. The only advantage they get is they can have the first right to compete for an exclusive license if they pay for the patent preparation cost. That's the best that they can do.

So, it's actually been really simple for me here, just because I really don't have any other option. I can't license things directly to Thios without going through UC. I can't. I'm not allowed to do that.

And I think even if I'm at Thios let's say—I consult for them a certain number of days a year, right—if I consult over at Thios, and I come up with some idea at Thios, even then, it's blurry whether Thios can really own that idea, because that idea would have to be completely uncoupled from Berkeley. But the truth is that the science at Thios is a spinoff of what we've done at Berkeley, what Steve did at UCSF, and so on. And they've licensed several of my patents, or are negotiating a license, and they've hired my former students, and they work there. You know what I mean?

So I try and keep it clean. If we make a development at Berkeley that I think is of interest to Thios, I don't tell Thios about it. I can't. I have to first file disclosure with UC, and only then after disclosure's been filed, UC can disclose that disclosure to Thios and so on. I have to be really careful about that. But it hasn't been that hard, because Thios is a drug-discovery enterprise, and in our lab we're really doing basic research. We're not doing drug discovery. We can't. We're not set up for that. It takes too much.

MAESTREJUAN: Well, in this whole area, the controversy is this conflict of interest.

BERTOZZI: I don't see it as a conflict. I see it as a synergy, because, basically, if we make discoveries here, we'd like that to have some impact outside of the thesis collecting dust on my shelf, right? So the way to have impact is to start a company and try and realize the commercial potential of these discoveries. And I just have to make sure that I never exploit a student. I have to make sure that I'm not having students work on a project for Thios. That can't ever happen. Students work on their work, they publish their work, they write their thesis. If there's something I think Thios is interested in, we file disclosure on it before we publish it. The student is a co-inventor, so if there're royalties to be made, the student gets a piece of the action. So it's good for the student, and it's good for Thios.

Now, Thios would really like it if they didn't have to negotiate with UC, if these could be Thios patents and not UC patents. But that's life. That's the way it's going to be. Nothing I can do about it.

MAESTREJUAN: Right, right. And then to follow is that funding happens in different ways for contemporary biomedical research. We haven't talked about your funding, where most of your funding comes from. I know you're Howard Hughes, but NIH is publicly funded.

And commercialization means privatization of a certain aspect of certain ideas, and part of this conflict of interest is taxpayers funding research in one institution that they'll have to pay for in another sector? One way to regulate that is just to have ethical standards by which scientists regulate what gets worked on where. But in the absence of ethical behavior—and there're always problems with that—how do we regulate how standards are upheld?

BERTOZZI: I don't know. You know, when I was a grad student, I heard stories about people—professors—having their students work on projects that were really for some company, and having even the students' notebooks getting photocopied in the middle of the night and copies sent to the company, which you're not supposed to do that.

You know, I've never been in a position where I've worried about that. For us, if I think something is going to be of interest to Thios, I patent it. It's that simple, you know what I

mean? And then Thios can decide how interesting it is to them. They can either license it or not. They can decide, "No, we'll get around that. It's not that important."

If I don't patent it, that's no good for Thios. That's no good for anybody. Because if I don't patent it, that means anyone can practice it. And if no company can get the intellectual property protection on it, it might not be worth it for them to pursue it, because they have no exclusive benefit. Someone else could compete with them, and why should they get involved if they don't have IP [intellectual property] rights? You know what I mean?

So in a way, if you don't file a patent that someone can license and practice and get exclusive rights to, then there's a chance that no one will ever practice your invention, and I don't think that's really that good either. I guess it depends on the invention. You have to really think carefully about what is this invention.

There're some things I never patented because I didn't want to ever limit anybody's access to it, like research reagents. You know what I mean? I made the mistake of patenting one early on, and then Molecular Probes [Inc.] licensed that patent, and they sell that reagent in their catalog now, but they charge an exorbitant price for it. No one else can sell that reagent, because Molecular Probes has the exclusive right to market it as a research reagent. So no one can afford it from them, and I feel, "Oh, that stinks."

Now, if I hadn't patented it, Molecular Probes still might have chosen to sell it in their catalog, but so could Sigma[-Aldrich Co.] and so could someone else, and there could be a little bit of competition, and the price might be a little more reasonable.

On the other hand, if I hadn't filed a patent, Molecular Probes might have said, "Well, the market's too small, and why should we even bother investing in this reagent unless we can get exclusive rights to it? Otherwise, we have to share the market with other people." It's already a small market.

So you have to think about how's your reagent going to be used, is it good or bad if you patent it, and make a decision based on that. But, again, whether you patent it or not, you always should be driven by optimizing the commercialization potential so that you can get it out into the community. That's how I see it.

So now there are other reagents since then that I have not filed patents on with the hope that anybody could use it, sell it freely, and that it wouldn't get locked up to one company who then overcharges for it or just decides not to sell it at all, but just sits on the patent without practicing it. But other things I have patented because I know that if Thios, for example, cannot get secure intellectual property rights to it, it's not going to be worth it for them to pursue it because of the risk of competition. And I do want someone to pursue it, and Thios is the only game in town, because this is the company that's doing sulfation. So if it's a patent having to do with a new high throughput assay for sulfate enzymes, a new enzyme that we discovered from some genome mining or something, target we validated in some way, then I will file a patent on it, yes, or at least a disclosure.

MAESTREJUAN: And I think you have thirteen patents or patent applications pending, and I didn't look at them specifically at the [United States] Patent Office database, but I'm going to assume that you're listed as one of the inventors and the assignee is the University of California.

BERTOZZI: Yes, with the exception of a few of them. A few of them are LBL [Lawrence Berkeley National Laboratory] patents, actually, and that only means that the funding came from LBL.

MAESTREJUAN: How much in royalties do you see, and where do those royalties go?

BERTOZZI: Nothing. Only a few of these patents have actually been licensed. Some of them are just sitting there, and they shop them around, and they would love it for someone to come in and express an interest in a license. But some of them are too new, I think, to really have caught the eye of potential commercial enterprises. But, yes, those that have been licensed, I haven't seen any royalties yet, because it's too soon. They are patents having to do with a drug-discovery program where there wouldn't be any royalties to see until ten years from now when there's a drug on market that was developed using that assay or using that against that target or something.

So I don't expect to see anything for a long time, if ever, because even then, once royalties start coming in, the royalties, first they get used to reimburse the university or LBL for the costs of executing and maintaining the patent because the patent costs money to maintain. When all the expenses have been satisfied, then whatever is left, then you divide it up with all the inventors, and it's me and all my students, so I don't think there's ever going to be a lot of money in any of these inventions. But if there is, it might as well be me and my students.

I get like a few hundred bucks a year from my contact lens patent. We have a contact lens material that we developed, but that royalty is not royalty from the market, because that material is actually still in the clinical trials. It's not even commercial yet. It's a royalty that just came from an upfront cash payment that was part of the licensing agreement for the company that licensed it.

MAESTREJUAN: Let me pop in a new tape.

[END OF TAPE 3, SIDE 2]

MAESTREJUAN: How much pressure do you feel from the university [University of California, Berkeley] or from the [Lawrence Berkeley] National Lab to pursue patent rights.

BERTOZZI: Oh, they encourage us. Every year we get a little memo from [University of California] Office of Tech [Technology] Transfer, and they say, "If you have a discovery that you think might even remotely someday be commercializable, please file a disclosure." They remind you every year to don't overlook that.

And I think that's really important, because universities can make a lot of revenue from a patent like that. Look at University of Wisconsin. I mean, oh, my god. They've had a couple of hugely lucrative patents that have allowed them to build new buildings for biochemistry and the med [medical] school, and it just contributes to the overall infrastructure. It's revenue to the university, and public universities desperately need this.

And to the extent that there could be some intellectual property that comes out of a department of the magnitude of the vitamin B12 [vitamin D] patent from Wisconsin, or stem cell patents, or something like that, or at [University of] Minnesota, pharmaceutical chemistry department [Department of Medicinal Chemistry] has a patent on an HIV [human immunodeficiency virus] drug, and this is huge. It would be great if we had something like that. We could fund all of our students. So, if for no other reason.

And also it just brings notoriety to the university. It feeds the economy because companies can be launched based on this intellectual property, and that's great. So I think it's great. I think it's really nice that UC [University of California] has a relatively friendly policy towards licensing intellectual property and helping faculty who want to start up companies, being kind of liberal about our time in that regard. I wouldn't say UC has the most liberal policy, because it's a pain negotiating with UC. By contrast, we've licensed some patents at Thios [Pharmaceuticals, Inc.] out of Stanford [University]. It's smooth sailing. It's so much easier. They are much more amenable to open negotiations. UC is really tough.

MAESTREJUAN: One thing I'm always struck [by] when I talk about patents is because I am familiar with the history of patents and why industrial societies developed patent systems, it's to gain exclusive rights as an incentive to continue to innovate in societies. And then the opposite but important other half of that is to disseminate technological information. So in order to get those exclusive rights, you have to show your ideas out to the public and that's what patents are for.

But in the sciences it's interesting because there seems to be a little redundancy now. You know, there's a whole—we talked about it before—politics of publication and what publications mean to careers in science, which is also the whole point: To put technological and scientific information out to the community that's going to use it and take it forward. Why not just put all your material in patents, or all your material in articles? Because on that aspect of patents, it's putting information out to the public where it's needed.

BERTOZZI: Okay. So one thing that's true about the patent system is that you can patent pretty much anything and there's no peer review and there's no quality control. So the patent literature is just full of garbage. The literature is full of some garbage, but not nearly as much. So a lot of patent procedures are very incomplete, intentionally so, often, so that no one actually could repeat it. So actually, patents don't necessarily disseminate all the critical information. A lot of it is misleading or incorrect intentionally, again, to thwart anyone from duplicating or competing in that area. And, of course, there's no way to control it because there's no peer review.

So I think of patents as simply legal documents, and I don't put any scientific stock in them. If they're from industry I might have a little bit higher esteem for them, but from academia, I've seen so much garbage in patents. It violates the second law of thermodynamics. It's impossible. And some patent agent doesn't know that. They're just like, "Okay, well, I punch in some key words. No conflicts pop up. Okay, I'll allow that claim." They don't really know. And then the burden, if you're trying to file a conflicting patent with something you know to be garbage, then the burden's on you to prove that that patent is garbage and you have to challenge that patent and so on. In theory, in principle, the literature has been peer reviewed by qualified individuals who pass judgment and catch incorrect things and make whatever, and just basically exercise some degree of skepticism so that it holds you to a higher standard. So, in theory, that's a big difference to me. Of course, in practice it's a little bit gray.

I also think of the literature, the scientific literature, as a didactic medium. So literature is there to educate you. So when I write a paper, I write a paper to educate the person. I give them the background and the references and I explain things and I show illustrative cartoons of things they might not have known, backup. You know what I mean? So that when they go from beginning to end, they should have learned something new.

With a patent, that's not the point of a patent. Patents are not written to educate you, they're written, again, as legal protection and often they are intentionally written to confuse you, again, to thwart you, to put up barriers, and not to invite you in. So a paper should invite you in to a new little world, and that's a totally different purpose. That's how I see it. And so for someone whose career ambition is to have a kind of scholarly position in academia, they need to demonstrate in the literature that they can educate the public, they can create knowledge, and then teach it to you. A patent just doesn't serve that purpose.

So do we need patents at all? Well, do we need lawyers? [laughs] If we need lawyers, I guess we need patents, and vice versa. So it's, to me, just totally different. I have no pride in any of the patents that we've constructed. And we never wrote any of them, anyways. We just wrote disclosures, and the lawyers crafted this impenetrable legalese that has nothing to do with science. So I pay very little attention to how our patents are written. I don't care as long as the basic claims are in there and we get them.

MAESTREJUAN: Just to wrap this area up, it seems courageous in this day and age to start a biotech [biotechnology] company after the great boom and the huge bust, of which the Bay Area certainly is reeling from the effects. And not just the small biotech companies need a hit fairly quickly in order to survive, but also that Big Pharma [pharmaceutical] is here and the pharmaceutical companies are merging at dramatic rates because they know that the only way they can survive is to have huge R&D [research and development] budgets. So what are your expectations?

BERTOZZI: What were we thinking? [laughs]

MAESTREJUAN: Yes, what are your expectations for this company?

BERTOZZI: Well, first of all, when we started our company, things hadn't really crashed yet, okay, so we were still under the illusion that the economy was going to continue doing really well. So we fund our company at the beginning of 2001, end of 2000, and at that time the dot coms were just starting to fizzle out and go under. But everyone saw that as an opportunity for biotech, because usually when some industry crashes, biotech is the fallback. When high tech crashes, biotech. Then Silicon Valley, biotech. Then Internet, we've got biotech.

What we didn't anticipate was September 11th . We started raising money right around September 11th . Our first appointment with a VC [venture capitalist] down in Palo Alto was on September 11th, and when that happened, we were, "Oh my god. What are we going to do?"

Fortunately, things were really starting to teeter. You could see that something was going to happen, and we managed to keep pounding the pavement, and before things really took a nosedive we had done our deal. So we did all right. We had a pretty good valuation, we raised a good chunk of money, fifteen million is pretty good for an early-stage company. And if we had waited six months we would not have been able to raise fifteen million. We'd have been lucky to get six, because people weren't investing at that level and risk of ours. It was small money and horrible valuations and it wouldn't even be worth your time. So we barely got in under the wire.

So that was just Round A, and we have to raise Round B and C and so on, right? We'll be raising money for several years. So we originally had this fifteen million dollars and we had this growth plan that brought us out to thirty-five or forty employees in a year, and then we'd raise Round B. And when the economy really tanked, we realized that we were going to have to scale back on our growth plan and try and stretch out our Round A money as far as possible so we didn't have to raise Round B for a long time, and we're just hoping the economy picks up.

So we're actually now going to start raising Round B in September, October, November. We're hoping to close the deal by February or March, so I'm hoping that in the next six months. There is some life coming back to the economy. There's a little more optimism now

than there was six months ago, so hopefully we managed to ride out the worst year as a funded company. But there's no doubt that when we raise money in the next round, we're not going to have this huge valuation like Round B companies used to have two years ago. We're probably going to have a flat round, maybe even a down round, but we're prepared for that.

But our company [Thios Pharmaceuticals, Inc., we're doing well. We have some really exciting stuff. We have an end-licensed compound that we brought in as part of a deal with a big pharmaceutical company, so that gets us a clinical candidate really fast. We'll probably be in the clinic within a year, and I think that will look good for us and so on. So I think if anyone has a shot, we have a shot, but a couple of years ago you could just spout cool ideas and raise fifty million bucks, and now you actually have to show something just to get ten. So we'll gut it out, and I'll do the best I can. I'm the one who has to give all these presentations to these investors, so it's on me to tell a convincing story and get them excited and have them believe that what we've got is really something novel and very promising and high likelihood of success. Are you sold? Do you believe?

MAESTREJUAN: Totally. As a co-founder of this company, how interested would you be if a Big Pharma company came along and said, "Okay, well, here's—

BERTOZZI: "Here's the deal, we're going to buy you out?"

MAESTREJUAN: Yes.

BERTOZZI: It wouldn't be my decision. I mean, it would be the investors' decision. I'm not on the board of directors. Hughes [Howard Hughes Medical Institute] prevents me from doing that. Steve [D. Rosen] is on the board, and then our investors are on the board, and our investors are the majority of the board. So if the investors felt that the deal was better than the prospects for making it on our own, then they would sell our company.

I don't want that to happen, because a big company buys you for one program usually and then dumps all the rest of it. And we have all these really interesting programs. We have inflammation programs, cancer, even some infectious disease stuff. And a big company might buy us for our most advanced clinical program and dump all the rest, and I'd feel like, "Oh, there's so much potential there and it won't be realized now." That's life, I'm prepared. On paper I'm prepared. We'll see. I mean, if it happened, I'd be really crushed. We might have to spin out Thios-II or something. I mean, financially I'd make out really well, but emotionally it would be hard.

MAESTREJUAN: Well, when you're back here within the walls of the ivory tower and you're doing basic research in your lab, how important is it that there is some kind of clinical application

to the basic science that you do?

BERTOZZI: To me?

MAESTREJUAN: And the decisions you make on a daily basis of whether to pursue a project or not.

BERTOZZI: It's not that important to me as long as it's interesting in and of itself. If it has a clinical—some long-term clinical—relevance, that helps my funding: It makes it much easier to write grants, whereas if it doesn't have any obvious practical application anywhere, then it's really hard to sell it to people.

Personally, if something's interesting and I can fund it, I'm into it. It doesn't matter if it's going to cure disease. I have some projects in nanoscience— nanotechnology—and the applications there are not really clear to anyone yet, but I think everyone's excited about the idea that you can make little machines on the nanometer scale and they might be able to do things that machines on a larger or smaller scale couldn't do. What exactly they can do for you, we're not all really sure, but it just seems like it's going to be important. And I'm into that. So I have students working on modifying carbon nanotubes with interesting polymers to be able manipulate them. There's no clinical application to that that I can see, but when the transistor was first built, it was like, "Oh, yeah, it would be cool if you could— " No one really knew that there would be satellites and cable TV. So sometimes technologies create their own need and it's just the creation of the technology came from someone's imagination without an application driving them. I think that's okay. It's a valid way of doing science.

MAESTREJUAN: Another joint venture between private science and public science that had a lot of naysayers originally but has really exceeded everybody's expectation is the Human Genome Project. What has been the impact on your work as a result?

BERTOZZI: Well, it's been really useful. So for us, just having access to human genome information—or just genome information in general, not just human—has fast-forwarded projects like the sulfotransferase project and this tuberculosis project. So instead of spending years just trying to clone some gene, you've got them all there at your disposal, and it's just a matter of finding what you want. So it just completely obviated the whole chore of cloning things. They're all cloned. All the information is there. It just really accelerated, and it just opened up projects in the lab that wouldn't have been anywhere without it. So for us it's been really, just, helpful. It's kind of like having a freeway connecting you from A to B instead of having to take a million backroads. You're still going from A to B, and B hasn't changed, you still know where you want to go, but you just get there really fast. That's what I think of the genome as. So that's helpful.

MAESTREJUAN: Well, it's introduced a new kind of language to science, which was in the midst of a new language. Biochemistry was transforming itself, cell biology, chemistry, and now we're talking about genomics and proteomics and glycomics.

BERTOZZI: Glycomics. [laughs] That's a San Diego term, they invented that down there.

MAESTREJUAN: So what does all this new terminology mean to you?

BERTOZZI: Okay. Well, people throw those words around, of course. I don't know. The actual definition of glycomics I really don't know. I'm not sure we really needed that word. Okay, I teach courses, people ask me stuff like that, and what I tell my students is that usually people use that kind of omics jargon when they're talking about science—it's the same old science—but it's at the level of a system rather than an individual molecule, that's all. So if you're taking a genomic approach to studying cancer, then maybe what you're doing is looking at changes in expression of all the genes, not just one gene, but all of them at the same time. And a proteomics analysis of something is looking at differences in all the proteins of that cell or tissue, not just one protein. Just in the past you might study interleukin-2, okay. It goes up at sites of inflammation, but a proteomics approach would look at all the proteins.

So there is nothing conceptually different with respect to looking at all the proteins versus one protein. The difference is that you need, to look at all the proteins, a very high throughput parallel technology to do it. So omics to me is about doing systemwide analysis and often using high throughput tools just to cover that much information in a short period of time. So glycomics, you could say that glycomics is science that somehow seeks to analyze all of the polysaccharide structures of a cell or tissue all at once, and maybe changes in those polysaccharides as the cell changes its state. So you can have a glycomics approach to studying cancer, a glycomics analysis of inflammation. That's how I think of it, but I didn't coin any of those terms.

MAESTREJUAN: Right. Well, you have described yourself as interested in carbohydrate chemistry. What's your relationship to glycomics, in whatever form?

BERTOZZI: Well, I don't really feel the need to use that term to describe my research, because I think there are other terms that describe it, but the truth of the matter is that the NIH [National Institutes of Health] has been convinced that it should be funding glycomics, so I'm more than happy to put that term in my grant proposals.

But in terms of systemwide analysis, we do have some projects in the lab that have that flavor to them. So, for example, I have a student—the student who just poked his head in

here most recently, with a shaved head—Howard [Hang], and he's interested in developing chemical tools that would allow you to probe all the proteins that are modified with a certain type of sugar. And so as an example, there's a class of glycoproteins called O-linked glycoproteins, and so what they all share in common is that there's a polysaccharide linked to the oxygen, the O, of serine or threonine, okay. And it's really hard to predict which proteins are going to have these sugars on their serines or threonines because there's no consensus sequence for it. Do you know what I mean by that? Yes. So because of that, you can't just look at the sequence of a protein and say, "Oh, that serine will have one of these sugars on it," because there is no sequence that would tell you that.

So how do you know which proteins have that sugar on it? Well, you can isolate each protein one at a time and pick them apart and look for these sugars, but that would be very slow. And so that's not very omics, right? But omics would mean figure out a way to look at all of them at once very quickly, just high throughput, the whole system. So he developed a tool for that.

So it turns out the one commonality among all these O-linked sugars is that they have as the residue that's hooked directly to the protein N-acetyl-galactosamine, it's called GalNAc for short. And it turns out that if you feed cells modified forms of that sugar GalNAc that have a functional group called an azide—N3—which is going to get us to the Staudinger ligation in a minute. So the azide is just three little nitrogens, and it's pretty small, and you can attach it to GalNAc. So now you have GalNAc with this little azide sticking up, and you feed that to cells and the cells will eat it and metabolize it. And they don't know that there's an azide on it and they'll actually put it into all these O-linked glycoproteins at that core position, in place of the regular GalNAc, which you've deprived them of. And so now there's this azide hanging out in their GalNAc, and it just comes along for the ride, it's inert.

But the azide has a unique chemical property, which is that it can react with these reagents that we developed in the Staudinger ligation. So anytime you have an azide, it's like a little Trojan horse and you can basically tag it with a probe. And so now what you can do—if you can imagine—is you feed the cells this GalNAc with the azide, all the O-linked glycoproteins get the GalNAc with the azide, and they're just hanging around, you break open the cells, take all the proteins, all of them at once, and you mix them together with this phosphine reagent.

Now the phosphine swim around, and it's only going to react with the azide and it's going to attach itself to all the proteins that have these O-linked sugars, but no other protein. Now all you do is you separate out all the proteins and then you probe which are the ones with the tag, and those are the ones that had the O-linked glycoprotein. So that could be construed as a glycomics. We don't call it that, but it's a tool for systemwide analysis of proteins modified with O-linked sugars. Howard calls it glycoproteomics.

MAESTREJUAN: Glycoproteomics, okay.

BERTOZZI: And, you know, that's his little word, so I know I have to use that word. But other people might say, "Oh, yes, it's glycomics." But the guys in San Diego, they don't really have a very clean definition for it. It's a marketing tool.

MAESTREJUAN: Well, to start moving in that area, a couple of things I wanted to talk about [are that] here at [University of California,] Berkeley you wear several different hats in several different departments. You have two different appointments at the National Lab [Lawrence Berkeley National Laboratory] in material sciences and physical biosciences. Chemistry department, molecular biology, you mentioned your tiny pharmacology mention at UCSF [University of California, San Francisco].

BERTOZZI: Where am I? That's a good question. [laughs] I don't know.

MAESTREJUAN: I know that your office is in the chemistry department, and you clearly identify yourself as a chemist, but what does it mean to have all these different hats?

BERTOZZI: A lot of committee meetings. What it means is I'm 100 percent in [Department of] Chemistry, so I teach 100 percent in chemistry. I'm zero percent in [Department of] Molecular and Cell Biology, so I don't teach there, but my face appears in their little catalog, which makes it easier for me to recruit students from that department, which is really helpful to my research program. I'm in the Material Sciences Division at LBL [Lawrence Berkeley National Laboratory], which means I get a little lab space up there and I get money through that division.

The physical biosciences division hasn't really been anything for me. I thought I'd get money. So they asked me if I would be affiliated with their program, but I don't really get money through physical biosciences. I get a little bit of money, but it's a long story, it doesn't really count, so I'm not really sure what I'm getting out of that, but I'm there for whatever it's worth. I think it looks good to have my name kind of affiliated with the group somehow, because I'm a biologist.

What else am I? Oh. So the reason I have an appointment at UCSF is that Howard Hughes [Medical Institute] has a rule that you have to be affiliated with a medical school to be a Hughes investigator. So [University of California,] Berkeley doesn't have a formal medical school, so all of us Hughes investigators at Berkeley have been given courtesy appointments at UCSF just on the books. What that means in practice is I could get a student from UCSF to join my group if I wanted to, or if they wanted to, but the truth is that they have a small graduate program and they have four hundred faculty there, so statistically why would I ever get a student from UCSF?

Although the other thing I get is there're special little funding pots for faculty at UCSF.

Some very wealthy donor will donate some bunch of money to the med [medical] school to fund prostate cancer research and then anyone affiliated with UCSF can apply for this money. So I actually have money through UCSF to work on prostate cancer, and I wouldn't have had that if I wasn't a UCSF faculty member.

MAESTREJUAN: Well, what difference does it make if you're working in your office here or up in the National Lab, which is just up the hill from here, in the way you approach your science.

BERTOZZI: I don't know, because I've never really sat up there. I pretty much have always sat here. I have a lieutenant up there that I hired. She's great. Her name is Jie Song and she was a postdoc [postdoctoral fellow] in my lab for a couple of years, and then I hired her as an "über-postdoc," sort of a staff scientist, and she oversees the whole lab up there. She's independent a little bit, but she still works on my grants.

I used to have three or four postdocs up there, but I'm converting that lab. So we have this thing called The Molecular Foundry, which is a new nanoscience institute [Department of Energy Nanoscale Science Research Center] that's under construction at LBL, and I'm the director of the Biological Nanostructures Facility, so you can put that on the list of things. What that means is, I design the labs, which are sitting here on a blueprint, and I'm going to hire staff to fill up that institute.

The vision of that institute is to do nanoscience but to bring to bear on that, biology, chemistry, physics, theory, everything. And I'm in charge of the biology group, so I'm going to hire about thirty or so people to fill this institute. And I've already hired Jie as my lead lieutenant, main person. So my lab at LBL right now I'm using as temporary space for The Molecular Foundry, so I'm hiring people into the Foundry but they're working in my lab at LBL and eventually they'll move to that building, but it won't be finished until 2006. So that's what's going on up there.

So they have full-time staff at LBL who work up there, and it's nice and quiet and you have a beautiful view. It's not really well equipped for chemistry and biology. It's much better equipped for physics, engineering, that kind of stuff, just historically. We're trying to fix that so that it's a little better for chemistry and then I could take an office up there. I think I'm supposed to have an office in The Molecular Foundry.

But the problem is, I like to be near my students. The students like to be on campus because that's where all their student stuff is, and my students are my bread and butter. They are the heart and soul of my lab and sustain me, so it would be hard for me to be physically separated from my students because then if I'm having a nervous breakdown, I don't have anyone to talk to. I need to have my students so I can vent and rant and rave and come back.

MAESTREJUAN: In your Pew [Scholars Program in the Biomedical Sciences] proposal you stressed the interdisciplinary nature of your work.

BERTOZZI: Did I?

MAESTREJUAN: Yes, you did.

BERTOZZI: It was one of the very first things I ever wrote here.

MAESTREJUAN: Basically as a justification of why you should be funded, because you are one of the few who are doing interdisciplinary work. And clearly by just what we've been talking about, you have tried to approach this as interdisciplinary, but also the structure, though, within the university that you have all these different appointments. There's no one centralized place for you. How well do you think you've been able to achieve this goal of interdisciplinary research?

BERTOZZI: I'm the most interdisciplinary person on this campus, I mean in the sense that just the composition of my lab would underscore that because I have postdocs who are from backgrounds in immunology, synthetic chemistry, I have grad [graduate] students from biology, from chemistry, I have a physical chemistry student, I've had physics postdocs come here and work for me. I've published in biomaterials journals all the way to *Science*, and everything in between.

So I think that I have achieved that, and too much, in a way. Like my eyes are bigger than my stomach, or whatever. You know what I mean? It's so broad that I am losing it. You know what I mean? I don't have the expertise to cover it all, and so we're getting out into areas where I feel like I can't ever really command the area. I don't have the time to develop that much knowledge in all these different areas and then worry I'd go out and give a seminar on that topic and be exposed as a fraud. You know what I mean? [laughs]

So I've actually reached a point where I do feel like I need to somehow get a little more focused, I've got to herd some of these sheep back in a little bit. I think we're just incredibly broad right now. It's been good for me. I've learned a lot, but being in charge of a nanoscience facility and running a lab in chemistry and biology and having projects in prostate cancer and tuberculosis and inflammation, and doing the microscopy and the synthesis and all the animal work, it's just a little overwhelming sometimes, and it costs a fortune. I spend a lot of time writing grants.

MAESTREJUAN: Then to go on there: How well have you been able to attract funding

when, again, the NIH [National Institutes of Health] has a million study sections and not every chemist applies to the NIH for funding. And you're a Howard Hughes Investigator. How has being this interdisciplinary person—

BERTOZZI: Well, it gives me access to a lot of different pots, so there's that. Well, I shouldn't say that on the record. I have enough money. I wouldn't say I have too much money because you can always have more. But funding has never been a limitation. At least I haven't felt it as a limitation. I've never not been able to take students or postdocs because of funding. It's space that's been my limitation, and just being able to handle it psychologically.

But my major funding source is the NIH. I have four RO1s, and it's a lot of work to keep them up. Some of them slip through the cracks sometimes, and I don't know if I can sustain them indefinitely, but right now, at this moment, I have four. And I'm a junior investigator of Hughes, so that means I don't get a load of money from Hughes. It's good money, but it's not like the majority of my lab. My Hughes budget right now pays for two technicians, one postdoc—it used to be two postdocs, but we had to cut our budget so I had to slash a postdoc. And then it pays my salary and it pays some research supplies. And the research supplies are probably on the order of an NIH grant. You know what I mean?

So the big things are my four RO1s, and then I have some money from this prostate cancer organization [UCSF Prostate Cancer Center Developmental Research Grant]. I have some money from Johnson and Johnson [Focused Giving Grant], this pharmaceutical company, and then I have substantial funds from LBL. So this is the great thing about LBL. It's a source of money. It's DOE [Department of Energy] money.

I'd say my total operating budget for a year—direct costs—is probably on the order of two million. It's a lot. I'm not the biggest spender in the department, but I'm probably second to the biggest. And I have probably the second largest lab. I have a lot of people, it costs a lot of money to do what we do. But the reason I can tap into so many funding sources is because I can get money to do tissue engineering from LBL, I have money to do nanoscience projects from LBL, then I have four grants from the NIH, and there're the sulfotransferase grants, and this glycoproteomics grant. I have a metabolic engineering grant and a tuberculosis grant. And then I have the Hughes money, it's unrestricted. And then J and J [Johnson and Johnson] pays for a tumor imaging project, and then I have little awards and things, just little things that I have.

Any one of those projects you can have a whole lab work on. In MCB [Department of Molecular and Cell Biology], that would be more the style. But in chemistry, the culture is more like, more is better. Everyone's always trying to do more, push yourself to the limit, extend yourself as far as possible and see where you snap. That's what we do. I don't know why. That's why I need really good students and postdocs, because otherwise all these balls are up, and it could just crash. And you have to have these really good people you can delegate to. And I do. Really good.

MAESTREJUAN: And why is it that you've been able to attract good students?

BERTOZZI: It's Berkeley, you know. They're all good. Most of them, I think, are really good. It's Berkeley. What can you say? I'm nice to them, I treat them pretty well. Occasional lapses, you know. Yes, we have some really good people. And then they beget each other. You get a few good students and postdocs, and then they'll recruit people in. They now recruit really good people in and keep it going. So I owe them a lot.

MAESTREJUAN: You have tenure here in the chemistry department, and what does tenure mean?

BERTOZZI: Other than the obvious?

MAESTREJUAN: That you can't get fired.

BERTOZZI: That's what I meant by the obvious.

MAESTREJUAN: If all those balls that you kept in the air suddenly—

BERTOZZI: No! If my worst nightmare materializes, the NIH goes bust, none of my grants get renewed, Hughes boots me out, what would I do?

MAESTREJUAN: Yes. What would Berkeley do to your lab space?

BERTOZZI: Oh, you know, the usual. They'd take it away and give it to the next rising star and I'd be a cautionary tale and the butt of jokes and gossip at Gordon [Research] Conferences.

MAESTREJUAN: How much does Berkeley cover your salary?

BERTOZZI: None. Well, Hughes pays my salary because I'm a Hughes Investigator. If I weren't, then I'd get nine months from Berkeley and then three months would be off of my grants, which was my situation before I became a Hughes Investigator and is the standard situation here. Although sometimes, grants. I have LBL money. I used to pay two-ninths from NIH, and I used to have an NSF [National Science Foundation] grant, and one-ninth

from LBL.

MAESTREJUAN: Well, because we've been interviewing on Sunday, and when I left you yesterday you were just getting started with your students and it's nine-thirty on a Monday night, how do you balance a personal life with your professional life if you are here, as it seems, all the time, or else on the road?

BERTOZZI: Well, what qualifies as a personal life? Relationship, family?

MAESTREJUAN: Yes, a long-term relationship, or you mentioned that you don't have children.

BERTOZZI: No, not for lack of effort. It just didn't work. We tried. I had envisioned that as being something that I would have, but we tried for about two years, and it cost a fortune. So for us it was a little complicated because my partner [Cynthia] is female, so this was for us an investment.

Yes, it's hard to balance. I'm not a very good balancer. I get absorbed. I'm a workaholic. "My name is Carolyn and I'm a workaholic." [mutual laughter] I've had times in my life where I did a better job than others, I think. I did a pretty good job at that when I was a postdoc, I thought, actually, at UCSF.

I've been in a relationship for fifteen years with the same person, who I met here as a grad student, as a first-year grad student. And she was a grad student in the [Richard and Rhoda Goldman School of] Public Policy department. When I was a student, I worked really hard, actually. We were here all the time. I worked for a new assistant professor, and it was a total grind, but I liked that. Lab is your social environment in addition to your work environment, and you're working with your friends. So I never felt like coming to work was somehow separate from my personal life. It was all woven around this building, this was like my theme. And we had as much fun here as we had work, and I hung out with people here, and you goof around a lot when you're in the lab. So that didn't seem so bad, and my partner used to come over and hang out, and she became friends with all my friends in the lab, and we were all just friends. We'd all hang out together and it was just a scene, you know.

Then when I was a postdoc we really had a good time because I felt a little more relaxed. I had been in the situation where I was trying to run this lab and get grants. I had a lot thrown on me as a grad student, and as a postdoc I was relieved of that. I finally just got to do research. We lived in San Francisco, which was incredibly cool. We moved to Noe Valley, which is a totally funky neighborhood.

That was the first time I'd ever worked with women in my lab. So, when I was a grad

student, I was the only woman in the lab, which was typical because of the numbers back then. But I had these great guys, and we were really good friends. And when I went to UCSF, there were all these women in the lab, and I was like, "Whoa, there're women here. It's so cool." So I made all these really good friends and then my partner—her name is Cynthia—made friends with them, too. She would come and hang out, all of us would hang out together. And so she was as much part of that social scene as I was, and sometimes she would come to the lab even if I wasn't there, which sounds sick, I know, but just to visit people and then go out to movies with them. So she has remained really close friends with some of those postdocs I worked with in Steve's [Steven D. Rosen's] group.

Biology, the labs in biology have just a more mellow culture than in chemistry. Chemistry has a kind of grind it out ninety-hour work week. When I was a grad student, we had group meetings Saturday night at ten p.m., and that was the standard. And my boss said to us, "Well, you know, you don't really get much research done Saturday night at ten p.m., so you might as well have group meeting."

We were like, "Yes, okay." And so this was normal.

Whereas in biology, people don't live like that. They go home in the evenings and it's just a different culture. So in Steve's lab, Steve would go home at six. He worked really hard from eight to six, but at six he went home and he had dinner with his family and his kids. I had never seen that before. I was like, "Wow, you go home? That's weird. They eat in their house? They have food in their house? God, what do they do with it? Who cooks it for them?" It was so foreign to me.

Whereas Cynthia, my partner, has always had a very normal lifestyle. She would never take a job that demanded more of her time than eight to five. She refuses. She has to go to yoga class and her book club and friends and just stuff. She does stuff, volunteers for this and that, and so she would never be a workaholic. She just refuses to do it. And if her job is like, "Well, you have to stay late all the time," she'd be, "Forget it. I'm not going to do it."

So she always thought we were insane, all of us scientists, but she put up with it because she thought—and I used to tell her—"Oh, well, I'm in grad school now and I have to do this, but eventually I won't be, and everything will be normal."

Then there was a hint of that when I postdoc'd, because I had a little bit more normal life. I would come home some nights for dinner—not every night, but some nights—and I would take off Sunday, I wouldn't go in every single day in the weekend, so she got this, "Oh, Carolyn really is going to—"

Then I took my job here, and it was right back to the old ways and then some. So the first year I was on the faculty I don't think I took a day off, and I don't think I came home for dinner once. And she got pretty fed up. After about a year she was, "I'll see ya later." So I had to clean up my act. So that was my lesson in balance, but actually I've still never really gotten very good at it. And what happened is she changed professions at that time. She quit her job and went to

nursing school, and when she was in nursing school, she had a pretty extreme schedule, so I was like, “Oh, good. I can sneak out and work late because she won’t be home till midnight.”

Now I think she’s just, after eight years, finally resigned to the fact that I’m never going to have a normal life, that I’m going to be on the road a lot, and that I’m going to be home at eleven, and that maybe once or twice a week I’ll come home earlier for dinner or something. But, yes, it’s hard.

MAESTREJUAN: So how much effort do you make time to spend time together?

BERTOZZI: Well, I think I make all these efforts, but I’m sure by a normal person’s standards it’s quite pathetic. Now I might take a day off on the weekends. Like last Saturday I came back from Australia, I got back at noon, and I didn’t go into work, I stayed home. So that was an event. And then Sunday I came in, of course.

I’ve been better about trying to take time off, but, also, since Thios [Pharmaceuticals, Inc.] started, to be perfectly honest, it’s been really hard. Every free moment I get I feel like I need to spend with Thios. So Thios has become my other hobby outside of work. Cynthia would call it my mistress, but it’s very time-consuming.

It’s not easy. I definitely stink at it. It’s a problem. It’s hard on the relationship. Cynthia is heroic to put up with the crap and so on. And the worst part about it, of course, is that not everybody wants to live an extreme life like I do, right? Most, in fact, people don’t. And the worst part about it is that my students, particularly my female students, look at me as a freak, and I’m like their anti-role model. So they’re, “I don’t know what I want to be, necessarily, when I’m in my own career, but I know I don’t want to be like you.”

And, of course, for women in science, all our lives we’re, “I want to be a role model. I want women to look at me and say, ‘Oh, look, she’s doing this. I can do this, too.’” And, in fact, I have quite the opposite effect on my students. They’re like, “Look at her. She’s here at eleven o’clock here every night, she never sleeps, she’s flying all over the place, and I don’t want to live like that. And if that’s what it means to be an academic, I don’t want that job.”

I feel terrible about that, because the truth is that I have a lot of colleagues who don’t necessarily do that. They’re much better, they have families at home, they go home. Like my suitemate next door, he works really hard, but he leaves every day at five-thirty because he has young children at home. He gets in every day at five, he’s here at five in the morning, but the students see him leave at five-thirty. That’s what they see, and they’re like, “Man, family, I can see myself being like him.”

And we have in our department forty-five men, and there’s a man of every type, so you can find a guy, probably, who you can relate to. There aren’t that many women. There’s just a very few of us, and I might be the only one that some of these students ever see. And if I’m the

only woman they see, and I live like this, as far as they can see, that's the way you have to live as a scientist. They don't have enough of a diversity of personalities to relate to among the women faculty. You know what I mean? So some of them might look at me and see how I live and say, "Oh, yes, that's really exciting. She gets to fly around and she's so intense about her work, and she's always making time for us, and she'll stay up late to finish her paper, and how great that is, and I want to do that." But that's going to be a small minority. A lot of them, they envision a different lifestyle for themselves, and there might be women leading that lifestyle in academia, but they don't see it. All they see is me. So this keeps me up at night. I lose sleep over this, and I don't know what to do about it, to be perfectly honest.

MAESTREJUAN: Okay. Let me flip the tape over.

[END OF TAPE 4, SIDE 1]

MAESTREJUAN: Okay. Well, it's not clear to me that this is a choice that you make, or is this something that you're compelled to do? And you seem to think that your students see you as a freak, but do you, yourself?

BERTOZZI: I know it, because they've said it to my face.

MAESTREJUAN: Really?

BERTOZZI: I have a very open relationship with my students. They can say anything to me, and I promise I won't judge them, because we make that pact. And I've had them say to me, "The reason I don't want to go into academia largely is because I look at you and I look how you live, and I just know I don't want to live like that." That's painful for me to hear.

MAESTREJUAN: And what do they see is wrong with what you're doing?

BERTOZZI: No family, no children. Basically here all the time, shoving dinner in my face and going back to work, and just scurrying around and doing a lot of different things and being frenetic, and all the travel. It's exhausting, this job is really exhausting. It's self-inflicted exhaustion. It's within my volition to say no to things, to not be involved in all these different projects, to not be editing books and not be on all these committees. And I'm on NIH [National Institutes of Health] study section full time, and I fly out to Washington all the time.

There's nothing preventing me from saying no. I don't have to have a lab of thirty-five

people. I could have ten. That's within my volition to do that. You know what I mean? It's just not within my nature to do it. That's the problem. I have a fundamental problem with the fact that if someone puts an opportunity down on the table, I really have a very hard time passing on it. I see it as an opportunity and I feel compelled to do it. So I really—like you said—feel compelled, and sometimes I have to stop and what was I thinking? Oh, my god, why have I done this to myself? I haven't slept in weeks, and I really need a break. There're all these things and my calendar is packed for the next two years. My life is literally scheduled until 2005 spring. I can tell you what I'm doing every day.

And so that's not fun, right? But at the same time I feel if I can do it now, I should, because there will be a time when I can't because I'm dead or something or exhausted, I don't know what. But if I can now, if there's any way I can figure out how to make it work now, I should just go for it. That's how I feel, and it's something that's compelling me to do it.

But I try and tell my students that you make those decisions yourself, and you can have a really successful fulfilling career with a smaller group and fewer distractions and a different approach and a family, and there're plenty of examples of that on this campus, just not really in the chemistry department. But I think in MCB [Department of Molecular and Cell Biology] there are.

MAESTREJUAN: Well, if you were to have children, how would your schedule change?

BERTOZZI: Oh, it would have changed completely. It would have to. I would have to have changed it, but what we tried to do, my partner tried to get pregnant. So the reason I said a minute ago that I think I'm going to be lucky is for two reasons. One is that my partner [Cynthia]is female, right, so I sort of have a wife, the way that maybe some of my male colleagues have a wife. So she'll put up with a lot more crap than I think a lot of male partners of female faculty might not put up with unless they are also academics, and then they maybe understand better. So it's a horrible thing to say, but it's true, I think.

She gives me a lot more support than I think some of my straight female colleagues get from their husbands. She maybe doesn't have as high expectations of me with respect to having more of a home life than the male partners of my female colleagues. You know what I mean? So there's that, and that also relieves me from a lot of the social pressures. So I think my straight colleagues—they're supposed to be wives and mothers—have a lot of pressure from their families and from society, and people look at them, and I think they've grown up with that. And I didn't. For me, no one expects anything from me, except to be a freak, and I can do that. And so there really is no expectation of me.

And my male colleagues don't really know what to expect from me. They don't really address me in necessarily the same way that they might address some of my straight colleagues, because they don't see me as the female somehow. You know what I mean? I'm a different thing.

And also, when you grow up in our society, if you're not straight, then you grow up with alienation. You're accustomed to feeling like you're the minority, the odd person out, somehow alienated, not part of the thing, and you assimilate that and you can deal with that. So I have a lot of coping skills for dealing with being just out there on the fringe alone and separate somehow and not included in the majority.

And I think a lot of my straight friends, when they go into academia, that's the first time they've really experienced what it feels like to be just so separated from the major group and so cut out from the center of the universe, and that's not a big deal for me. I'm accustomed to that. So I think this has—I don't know—maybe makes it easier for me because I had less to lose, coming into academia than some of my straight friends, who really felt like they lost. They've entered this world where they don't have a community and they don't have a support network and they miss that. But I don't ever really feel like I ever had that.

MAESTREJUAN: Okay. Well, in terms of women scientists as role models, in fact, you're the standard, right? If you look at Barbara McClintock and Rosalind [E.] Franklin, with the exception that you actually have a long-term relationship, they tended to be single.

BERTOZZI: Kind of loners.

MAESTREJUAN: Loners. Spent tremendous hours in the lab, chose not to have children. If you look at the current kind of science statistics on who the tenured professors are, they are white males with children, and the absolute minority is females of any color without children, but they're more representative than women with children of any color and/or married. And so clearly, from that perspective, this isn't an issue of being a freak, this is the standard face of female scientists. And how much is this just a function of the individual scientist as much as a construction of what science is, that the face of science is?

BERTOZZI: I don't know. See, my contemporaries—there're only five women faculty in chemistry—all of them have kids except me. They all have families. I'm the only one who doesn't. And in biology, at least the tenured and the more senior faculty and most of the junior faculty also all have kids. So at least at [University of California,] Berkeley it's very uncommon for a woman professor not to have a family. Actually, I can only think of one who doesn't, but she's young. She's an assistant professor.

So I don't have a lot of familiarity with that more classic kind of spinster or loner female scientist. I never knew any. Well, I didn't know any female scientists when I was in college, and when I was a grad [graduate] student, there were a few women in the faculty, but they all had kids. So I don't know. But it's certainly easy to imagine how women would find the job so consuming, or maybe they would feel they were at such a disadvantage if they had children, or

maybe their spouses, if they had them, were so unsupportive of taking care of a family. I don't know. Maybe the women who are here now, of my generation, their husband are more partaking in the childbearing. I do know that a lot of my female colleagues, especially in biology, their spouses are also academics, you know, so they are a double academic couple, whereas my male colleagues here, only one of them is actually married to another academic. All of them have wives who—some of them—don't work, and they're just at home taking care of the family full time, and these are people my age. A lot of them have wives that just quit working or work part time. But my female colleagues who are married and have kids, their husbands are all professors here. So I don't know.

I can definitely see how this job is the kind of job where there're this many things to do, and you could never do any more than 10 percent of it. If you didn't sleep one minute ever and you worked every single minute of your life until you died, you'd still get 10 percent or less of what you really needed to do accomplished. So given that reality, you 're going to have to draw a box—you know what I mean?—and you're going to have to at some point just stop and say, "Okay, I'm going to do this much, and then I'm going to stop, and all these things are never going to get done."

And you have to decide where you're going to draw the box. Are you going to draw it at a sixty-hour workweek or an eighty-hour workweek or a hundred-hour workweek? And there's no box you can draw that's going to encompass everything you really need to do. It's just the nature of the job. There's just too much to do.

So we all draw the box in a different place, and I've drawn the box in a place where I can barely maintain my relationship and have a few days off to myself here and there, and also have the time to feel like I give some mentorship to twenty students and twelve postdocs. That's all I can say. And if I had a family to fit in there, it would be a smaller box.

And again, it wasn't from lack of effort. We've been trying for two years, and when you're doing artificial insemination, it's very difficult, because it's not, oh, you just randomly mess around for two years. Every month you have to schedule things very carefully and spend a lot of money and you have a lot of doctor's appointments, and, again, every month, month after month after month. This is really exhausting.

And after two years, we just couldn't do it anymore. It was too painful. It was too costly. We just decided to call it quits for now. But my partner is forty, and so, she can't really wait forever, but I think she's basically decided that's it. So if we're going to do it again, it's going to be me.

MAESTREJUAN: Okay. Well, I wanted to ask, because you're in a unique situation, how did you choose who was going to conceive?

BERTOZZI: That was easy. She was older than I am, so she's kind of running out of time

faster than I was, so she was thirty-seven actually when we first started, whereas I'm four years younger than she is. So there was that.

Also, she had the biological urge to conceive, and there's no other way to put it. I wouldn't have believed it if I hadn't seen it with my own eyes. She just wanted to be pregnant in a way that you just couldn't explain, whereas I felt like take it or leave it. For me, I could have a hamburger or a pizza, you know. I didn't really feel strongly. I thought it would be kind of interesting, but if it didn't happen, whatever, I was perfectly happy to have her do it.

And then when it didn't work for her, I said, "Well, you know, maybe we should switch universes, and I'll give it a go." And she didn't want me to, because she thought it would be too hard because she was so disappointed. She felt like such a loss at not being able to conceive that she thought it would be really hard to have me hanging around pregnant, that would be really hard for her to witness. Although I'm not really sure, actually, I think she would have been fine with it in the end. But now, if I'm going to do it, I'd really better start thinking, because I'm thirty-six, and when you do artificial insemination, it's that much harder. It's hard enough to get pregnant when you're forty the old-fashioned way, but it's really hard when you're doing it this way.

But, I think at this point it's very likely that we'll just not have children. We'll just have more cats and a dog, you know. But again, for me, I don't feel such a loss like she felt, because I have my grad students. And they certainly act childish enough at times, so I feel like I'm fulfilled in that regard.

MAESTREJUAN: Okay. Well, do you consider there's a life cycle to the life of a scientist, and then there are windows of opportunities when scientists can decide to have children? And, it certainly is different for men and women, but when you're counseling your graduate students and they're presented with these issues, how do you advise them?

BERTOZZI: You know, I don't know. I've never had a student come to me and say, "I'm trying to figure out when's the best time to get pregnant." That's never happened. I've had postdocs [postdoctoral fellows] come to me and talk to me about that, and I've had postdocs get pregnant in my lab and have babies. Like Jie [Song], my über-lieutenant at LBL [Lawrence Berkeley National Laboratory], she had a baby last December, and so did another postdoc just around the same time. And I've had a lot of friends have babies when they're postdocs, and I think it works pretty well as long as you don't work for some asshole, you know, you work for someone who understands what it's like to have a baby and have a family and how that changes things. So I would say just watching my own friends having their kids as postdocs and watching Jie and GooSoo [Lee] do it, I think that that's not a bad time, if you can get pregnant. You can't often snap your fingers and get pregnant when you want to.

I think it would be hard as an assistant professor. In chemistry, most faculties start when they're a little bit younger than in biology, because they haven't done the six-year postdoc thing,

and they've finished their Ph.D. in four or five years. So when I started my job at [University of California,] Berkeley, I was twenty-nine and that was standard. Some were even younger, twenty-eight, twenty-seven, and that's really nice. In chemistry, they tend to rush you through. Everything is accelerated and overblown and we have big labs and we do things really quickly, and so we often tenure people in three years in this department. In three years, either you're hired or you're not, and that's the decision, that's it, you know.

And so I was tenured. I was tenured when I was thirty-two, and so that would have been easy for me to start a family at the age of thirty-two, if I were a straight person, and be tenured. So in chemistry, I think you can do it. Biology, you know, by the time they get tenure, often they're thirty-nine or forty, and then you're pushing the envelope, and they really feel like the pressure's on, "Got to have kids now." Maybe they're thirty-eight, just about to reach that age.

But most of them are certainly over thirty-five, and everyone teaches you that thirty-five is the point at which your fertility plummets into the basement, and you can just hear it crashing. [Laughs] So my friends in biology definitely feel a lot more pressure than in chemistry. In chemistry, we're just a bunch of young, like little babies when we get our jobs. But that's actually really good, I think.

MAESTREJUAN: Well, you mentioned that you came to the Bay Area because of your sexual orientation, that you thought it might be a more tolerant environment, but you've thrown out, "Well, nothing is perfect."

BERTOZZI: Good memory.

MAESTREJUAN: Yes. I want to talk about both homosexuality and science, but how has the Bay Area been? Has it met your expectations?

BERTOZZI: It's a totally funky place. It's completely funky, orders of magnitude better than Boston. I can't really say anything negative about the Bay Area. Just relative to any other place, it's the best place I've ever lived. In the sense just basic life: People don't get in your face. You can live like a human being here, which I appreciate. Like we can buy a house, and the real estate agent isn't like [gasps]. It's no big deal. We can buy a car.

And Cynthia comes to all faculty events with me. She's my official guest. You know, so when I get invitations, it's Carolyn and Cynthia. She's always invited everywhere, and she knows the faculty. She's gone to faculty baby showers even without me. And I know that there are certainly faculties throughout the country that would not welcome her so openly as a spouse of a faculty member. Not every member of the faculty here, I'm sure, feels comfortable with that idea, but it's such a big faculty that I don't even know all of them, anyway, and there're enough of them that my most immediate colleagues treat her like any other spouse. So that

has immeasurable value, you know what I mean? In that sense, they treat me like a human being with respect.

But the students here are not like people from the Bay Area. They're just people from all over the place that come here for grad school, right, and a lot of them come from the Midwest. We have a lot of students from Michigan, Illinois, Wisconsin, really good flagship state schools, and these are kids who like the concept of big state schools and they want to come to the coast where it's warm. And so the hardest thing is dealing with the young students who come here clueless and from very conservative backgrounds, a lot of them who don't really understand the concepts, and they have to deal with me in some way. Maybe they join my group. Fortunately, students and, in fact, human beings are such gossip hounds that I don't think there's any student that would join my group who hadn't heard through some gossip mill that their professor is this big dyke, okay.

So that's kind of a filter, and I can't imagine a student ever joining my lab who couldn't handle it or for whom it was issue that would interfere with our professional relationship. So I've never had to deal with a student in my own lab who was like, "Ack!" You know what I mean? That's never happened. I think the clue is out there.

But there are students in other groups, who I might have to interact with here and there, and sometimes I can tell they're very uncomfortable, and they can't look at me in the elevator. I'm on the qualifying exam committee, and they're weird, uncomfortable. I'm sure there are a lot of jokes. I'm sure I'm the butt of many jokes of young twenty-one-year-old males. These are young men that come here, most of them, and so I have to somehow exist among them and somehow command authority. So that can be tricky.

It was hard when I was a student here, because there were ten guys for every woman and for every hundred women there was one lesbian. It was just like I was it, and I got a lot of harassment from students, other students. Never from the faculty, of course not, they were too cool for that.

Fortunately, I had a couple of gay friends—men—and we insulated ourselves with our little group. But I was afraid to go to the bathroom. I was working on the seventh floor of this building, and there was no women's bathroom on that floor, so I needed to go up or down. And when I went down, I would just get names. There was this one hallway full of these guys, and they would just sling names at me. So I became afraid to go to the bathroom down there and stuff like that. This wasn't the Dark Ages. This was the late eighties.

But this was a different culture even than now. You have to put yourself back in that time. This was before [*The] Ellen* [*Show]* [Ellen Degeneres] and before *Will and Grace.* You could never have even thought of such TV shows back then. It was so taboo, and this was the [President George H. W.] Bush years, right after the [President Ronald] Reagan years, and so that was the climate amongst students here.

So it was hard, to work amongst those students, although I had a couple of incidents. I

had one particularly bad day where someone was calling me weird names, and I let it get to me somehow. And I went back up to my lab and I was crying, I was really upset.

And my boss came in, my graduate advisor [Mark D. Bednarski], this group meeting at ten p.m. guy, and he was a real tough guy and everything. He knew and he didn't care, because I worked hard for him. That's all he really cared about. The guy was really practical. And he came in and he was like, "What? What are you upset about? Your reaction didn't work or something?"

I was, "No. These guys down there, they were just calling me all these names. I'm afraid to go down there, and it's so hostile. And how can I work when I feel like I'm just in a combat zone or something?"

And he was, "What did they say to you?" He was infuriated. He went down there and he kicked their ass. He went down there, and he was, "You've got to learn how to treat people with respect. What is this, a junior high school here? You don't belong in a graduate program." I couldn't believe it, because this was, to me, so out of character for this guy. He went down there, and I was, "Oh, my god." And I was so relieved, that this boss would go and do that for me, he cared enough, so it wasn't all bad.

But, yes, it was tough then. And now, I think it's better. There're gay students around here. You know who they are, and actually there're a few of them in my lab and there're a few of them in other labs, too. There're a lot more women here now than there used to be, so our student body is 35, 40 percent women. My group has always been about 50-50, and so that changes the whole climate. When you just have some women around, that really helps a lot, makes it a more professional, somehow sane environment. Men act differently when there're women around somehow, thankfully.

And so I think now you wouldn't hear that kind of stuff. Maybe the students' sensibility—the culture—has changed a little bit, more tolerant. But I also know that if they said things, if they treated a student like that and it got back to me, who's a professor here, I would come down on them like a ton of bricks, and I would be, "Your career is over today, and I will see to that." You know what I mean? They know that, so certainly out loud you couldn't imagine hearing that kind of thing now, so it's gratifying.

MAESTREJUAN: Right.

BERTOZZI: There's a colleague of mine in the department who's gay, a young assistant professor, a guy. He had an offer at Princeton [University], an offer at the Rockefeller [University], and he said he came to Berkeley because I was on the faculty here, and he knew that if I could get a fair shake here and be successful, so could he. That was gratifying.

MAESTREJUAN: Yes. Well, I think you're right in that sensibilities, I'd like to think, have changed, in that overt harassment is much more—

BERTOZZI: It's not PC [politically correct].

MAESTREJUAN: Right, it's not PC.

BERTOZZI: But it happens.

MAESTREJUAN: But the bigger problem is covert discrimination.

BERTOZZI: I know.

MAESTREJUAN: How prevalent is that?

BERTOZZI: Well, since it's covert, I probably wouldn't know about it, by definition. But I don't know, because, again, I can't do the control[led?] experiment. I don't know what my life would be like here as a straight person. I don't know how successful I would have been. Would I have been more successful? I think I've been pretty successful, so I can't honestly say that I've been mistreated. I've had problems with certain faculty, rarely. I tend to get along with most people here, and they get along with me.

But I had one bad encounter with a very senior person when I first got here, and it was very unpleasant to work with him in the same department, but then he left, thankfully. So that problem solved itself, or at least it became a long-distance problem, because he's still in the field. He was one of these people who didn't like having young people come up and challenge him, and so on. And he felt very uncomfortable. He was one of those guys who—you could tell—felt very uncomfortable around me, couldn't look me in the eye, especially when Cynthia was around. Thought it was disgusting and so on.

But again, it certainly hasn't undermined my career. I don't think you could really say that. I think if I were a guy, it would be harder. It would be harder on my younger male colleagues.

MAESTREJUAN: Why is that?

BERTOZZI: Well, because this is a very macho culture, and it's, I think, easier to be a lesbian in a macho culture than a gay man. You know what I mean? I'm already female, I'm already kind of a freak and out there on that fringe, and so I'm also a lesbian, whatever. I'm already out there.

But this guy is expected to be one of the boys, and he's not, and I think that will be ultimately harder for him. And I can see it. Again, most of our students who do synthesis are these guys, they're these tough guys, and I think it's going to be harder for them to work for someone like him than me.

MAESTREJUAN: Does that mean that you have less credibility as a scientist than this other guy?

BERTOZZI: No, well, we're sort of apples and oranges, because we're in two different types of chemistry. He's a synthetic chemist, which is the most macho of all forms of chemistry, and I'm a bioorganic chemist, which is a little softer. And so I have more women in my group. He has mostly men in his group, which reflects that type of chemistry and the demographics of it.

No, I don't think I have less credibility, actually. I really don't.

MAESTREJUAN: What about on the level of professional societies?

BERTOZZI: Like the American Chemical Society?

MAESTREJUAN: The American Chemical Society, for instance, and this issue of covert-overt discrimination and harassment.

BERTOZZI: I don't know. I'm a member of the ACS [American Chemical Society]. I go to ACS meetings, but there're one hundred thousand members of the ACS. Of course there are places in the country where they wouldn't even look at me, even just because I'm female. Forget anything else. It's just that I don't hang out there, you know. I go to ACS meetings, I give my talk and I leave. These are huge meetings, and I don't really know anybody.

I keep to myself. Maybe I'm not that involved in these things. I don't expose myself a lot to potential for that. But, I get invited certainly, being on a lot of committees, mostly because "We need a woman. You want to be on our committee?" Despite my shortcomings, I guess, as a human being—as they might see it—they still need a woman, and I'll be there. And I'm on NIH study sections. I'm on a lot of these things.

So put it this way. If my being a lesbian excludes me from being invited to be on certain committees or participate in things, good, because I already have too much of that to do, and I really don't need any more.

MAESTREJUAN: Yes. Well, you had mentioned yesterday that women have been persistently absent in the field of organic synthesis, but other fields of chemistry have been more appealing or have more of a presence to women. Some have made that argument with medical specialties as well.

BERTOZZI: Like surgery versus pediatrics.

MAESTREJUAN: Cardiology, there were more women. Neurosurgery became more male-dominated.

BERTOZZI: So cardiac has more women?

MAESTREJUAN: Well, cardiology as cardiac surgery, and, that there were these shifts. What do you think accounts for why one particular field in chemistry would have a greater representation of women than other fields?

BERTOZZI: Well, you probably have to trace it back to the attitudes of the professors who were the forefathers of the field, I think. And if early on in the development of a field you had a couple of influential academic types who were either women or very supportive of women, that would make a big difference because of the propagation effect. It's geometrical.

Like in my career, I'll train hundreds—hundreds of students and postdocs— and each one of them will train hundreds, and so the people who I will, propagate exponentially with each generation of people that I've trained. And so if I've trained them in such a way that they have this intrinsic belief that women are competent scientists and can have leadership roles in science and can be superior graduate students and so on, that will make it that much more likely for them to have women in their own groups and train them with the same vision.

And, conversely, if I don't accept women into my group categorically, ever, and I send the message to my own students that women will never be as good chemists—"That's why I don't take them, neither should you"—then that's going to propagate exponentially, too, and that's what happened in organic synthesis. So there were a couple of very influential founders of the field that had that mentality, and it wasn't hidden, they wore it like a badge. Two of them were on the faculty of Harvard [University] when I was an undergraduate, and they refused categorically to take women into their group as students, never had one and never would. And

you knew that, so if you were a grad student and you went to Harvard, you knew that these were the two groups that wouldn't take women, so don't bother. And these were the two groups that would take women, and you'd have to go to them.

And people accepted this. They weren't, "Oh, my god, that's a lawsuit. Let's hire a lawyer and sue." It was none of that. It was, "Okay, that's life." Now it would be really hard to get away with that so publicly, but back then it was just part of life and you just dealt with it.

One of those guys won a Nobel Prize, was a very influential person. And then later, I think the last few years of his career, before he retired, he had one woman grad student finally. Because what could it hurt him at that point? He already had the Nobel Prize, right? So it's that kind of mentality, and that combined with the amplification effect of the fact that this is a person who ran a group of fifty people at any given time and was turning out five Ph.D.'s a year over a forty-year career, and that is a lot of influence. And so a lot of his spawn then later started to adopt the same reputation as being not a friendly lab for women, you know. They had this attitude, and that takes a long time to heal that, because all these people, basically, have to die. That's how I see it. [laughs]

And these are great people who have made, scientifically, enormous contributions, and you have to respect their science, but at what cost? Is it worth it? Did that guy deserve a Nobel Prize? It's a loaded question, because, yes, it's true, this person had a huge impact on the field in terms of the creativity, the chemical discoveries, and certainly trained a lot of people who then went on to brilliant careers, and so he had a longstanding influence and did maybe irreparable damage to the women who might have had aspirations to be an organic chemists.

So what discoveries did we lose because those women will never realize their creativity and their potential as organic chemists? We'll never know. But the fact that that was rewarded with a Nobel Prize kind of tells you where the priorities sit in the field, and I think you have to look very carefully at those kind of stories.

So now those are the old days and not the new days, so here I am privileged, because I have this lab where half my students and postdocs are female, which is rare in chemistry. That's sort of a lopsided demographic. So I have the opportunity now to propagate things, right, exponentially, and, again, hopefully a lot of these women will end up taking academic careers despite the freak influence. And it doesn't matter, because even if they don't, and only the men do, the men will have worked for a woman boss, and will have worked alongside peers who are women who are equally competent, if not more so. And in ways that I will never be able to quantify, that will have influenced their opinion of female scientists.

So I think it's still, even if only my men ever became professors, which hopefully that won't be the case, it's still something that will help. Not just me. There're other women, too, of course, who have their careers now. It would be great to have more in organic synthesis, but, again, the damage is significant.

MAESTREJUAN: Well, to talk about these numbers and representations, and I'm not as familiar with it in the chemistry departments as I am in molecular biology departments, cellular biology, developmental biology departments, is that, yes, now we're seeing 50-50 graduate students. At the postdoc, it's maybe 60-40 percent women. But when you look at the tenured full-professor ranks, those numbers then get distilled down. That would be one argument against this exponential view.

BERTOZZI: But to have the exponential effect, you have to have faculty, you know what I mean? You can't even start the geometry.

MAESTREJUAN: Right. So how optimistic are you that these discrepancies will ultimately be overcome?

BERTOZZI: I don't know. I'm contributing to it, because if I'm a deterrent to women going from postdoc to academic, then you're right. You have to divide the amplification effect by the anti-role-model factor.

I don't know. Again, I only have my own experience to go on, and I'm just looking at my life. I've produced fifteen Ph.D.'s, and about half of them are women, and I'd say half of those women are planning to go into academic careers. Some of them are still postdocs right now, so they haven't yet made the real commitment. But the first one to finish her postdoc this year did take an academic job, so that's a good sign. My postdocs, most of them want academic positions. That's a good sign.

MAESTREJUAN: Well, you keep coming back to this idea that you're somehow different.

BERTOZZI: No, I'm not.

MAESTREJUAN: Yes, right. Okay. So your students have told you to your face. But how prevalent is a traditional role for women within the family structure among scientists, or women who want to pursue a professional career in science? The traditional role of women has always been to be the caregiver and child-rearer— bearer, obviously—and take care of the home. How—in all these advances that we've made, and we have a lot of examples of dual careers—prevalent is this traditional notion of women's roles?

BERTOZZI: Yes, I don't know. I don't travel in those circles. You know what I mean? I hang out with a bunch of lesbians. I really don't know what it's like for them. Again, I can only tell you by inspection, by looking at my students.

MAESTREJUAN: Well, exactly, exactly.

BERTOZZI: And most of them don't have kids yet, so even they don't maybe really know what pressures will really fall upon them when they start a family. I'm sure a lot of them, most of them, probably plan on having a family at some point, but haven't really thought out the logistics yet as grad students. When they become postdocs in someone else's lab, maybe they might start doing the math and say, "Oh, my god, how can I do this?"

But again, most of my postdocs, right now they seem intent on an academic career, despite the fact that I think they also have ideas for having a family at some point. And either they haven't done the math or it doesn't scare them, and I don't know which it is.

The two postdocs had two babies in my lab, and I was really happy when they did, I was thrilled that they were both pregnant and both going to have babies, because I thought that would be really great for my students to see that, that, "Look, people having babies and can have a life, and take time off and come back and do what you need to do." And I had a baby shower for them. I made a big deal out of it, because I was, "Great, okay. This is good. This is good." Because that provided them a different view of a thirty-something female than me, because I couldn't provide that. I couldn't provide that for them.

MAESTREJUAN: I guess what maybe I'm trying to get at is how optimistic are you that we can—as both larger society, but also as a scientific community—move away from these notions of life choices have to be labeled either freakish or normal or abnormal or that why would you just automatically assume that the choices you made are normal, and these students are not correct, that they're wrong to think that that you're aren't just a role model?

BERTOZZI: Yes, well, I think the important thing is that they have choices. That's how I see it. They should know that this is a choice I make, and that on a dime I could change my mind and make another choice, and that one of the great things about an academic job is that I have the flexibility to do that. And I haven't given them any evidence of that, but hopefully they would understand that it's true.

I think what's going to be important for a lot of these women is that there needs to be more participation from their partner. Or maybe they need to find a partner who understands that they have ambitions and that they might want a job that is going to take more of their time than June Cleaver—you know what I mean?—and so they need to fill in those gaps. And I think a lot of them actually are not deterred by the notion that it's a job that has hours that are sometimes extreme and that it comes in fits and spurts and sometimes you have these moments where you have to work hard and that you might have to travel a lot and stuff. A lot of them, actually, I don't think that intimidates them. I just think they're going to have to find a spouse

who can really wise up to it, you know. They need to have pretty high standards for their spouse, and hopefully they can find one like I did.

But it's not easy. I know there's a lot of pressure on these women from all different sides. They feel pressure from me. "Carolyn expects me to be a professor, and she's going to be really disappointed if I don't." They know this. And I would never say it, I don't say it, but I know they feel it. And then their family, their spouse. I don't know how they deal with it.

My life is easier. I came from an academic family. I had a lot of support for being a professor and working like a dog. We're supposed to do that. My parents would never say to me, "Oh, you shouldn't be working so hard. You should slow down and have a family." They would never say that. They wouldn't say that to my sister, and she's straight and has a husband and could have children at any time now. But they would never tell her, "Oh, you're thirty-eight already, and you should really start a family." Are you kidding? She's married to her career, and that's laudable. You know what I mean? So I never had these pressures. I'm really lucky in this regard.

And then I have a spouse who's female, who's basically a wife. I'm like one of the guys in my department. I have this wife at home who's cleaning my house, doing my laundry. So how could I possibly understand what these women are going through? I have a very lucky situation. No, it's really hard. I don't know.

I would really like to get my students to talk to me about it more, really what do they think. But they're afraid to, because they're reticent, because they don't want me to think—I'm their boss—that they're not ambitious or something. I think they'd be afraid to say to me, "I'm having serious doubts about whether I want to be a scientist or even have a career at all. I'm starting to think maybe I would like to just focus on a family." They would never say that to me, because they would think I would judge them. You know what I mean? Would you say that to your graduate advisor?

MAESTREJUAN: My graduate advisor, no.

BERTOZZI: Yes, because what are they going to think of you: That you're not serious? And so I'm worried my students probably would think that of me—that I wouldn't take them seriously—and so if that's really what they thought, they would never tell me that. So, it'd be hard to have an open discussion.

And I've had the best luck with the ones that just graduated, because they're leaving, they don't have to deal with me anymore, and I've had some that were right on the way out be very honest with me about things like that. I had one who she was so gifted, and from the very minute she joined my lab, I was, "This one is destined for greatness." You could see it. She was brilliant, and she's the one who developed the Staudinger ligation. She had a *Science* paper in her second year of grad school. She was just absolutely brilliant. Everything she touched turned to gold,

brilliant writer from Bryn Mawr [College].

And somewhere around her third year of grad school, she started to pull away. I was always, "Oh, I want you to go give a talk at this conference. I want to send you to this meeting and introduce you to all these people, and I want to network you, I think you should meet all these people." I was trying to network her, and she could tell I was grooming her.

And she didn't want to be groomed, and she started to pull back. She's like, "Well, I'm not sure I want to."

And finally I went to her. I said, "What's up with you? You get this great result, you have all these papers, all this success. I want to groom you. I want to send you out to all these places and show you off, and you sound like you're—"

And then she said, "You know, the bottom line is I feel like you're grooming me for some kind of high-powered academic job like yours, and I don't want to end up like you."

And I was, "Oh no." And that was why, because she said she wanted a family. She was engaged to one of the other students in my lab. They were planning to get married. She wanted to raise a family. She didn't want to have to deal with the stress of having to be responsible for paying thirty salaries every month. She didn't want the stress. She didn't want the time commitment. She wanted a nine-to-five job, like in a biotech [biotechnology] company, have a nice salary, go home, and have a family and stuff.

MAESTREJUAN: And do you have the same level of discussions with your male students?

BERTOZZI: Not really. Never seems to be an issue. Or they don't say it. Maybe they're embarrassed. I don't know. No, none of them.

Some of them have said things like, "Oh, I want to have a life." That's how they would phrase it to me. "I don't want to go to academia. I want to go to industry, because I want a life." But they would never say because of the family thing, just, "I want a life," which could mean they want to go out drinking. I don't know what their life is.

Also, they're very confident. The male students I have are very confident in their abilities. Or they don't express it if they're not. I've never had a man say to me, "Oh, I don't think I could handle an academic job. I'm not smart enough." They would never say that to me, whereas almost every woman has said that to me. "Oh, are you kidding? I could never do what you do. I could never have a job like that." They have a confidence crisis. What can you do?

MAESTREJUAN: Let me pop in another tape.

[END OF TAPE 4, SIDE 2]

MAESTREJUAN: Do women and men learn science differently?

BERTOZZI: Not that I know of. Not that I can tell. They seem comparable to me.

MAESTREJUAN: What about the cultural diversity in the lab?

BERTOZZI: There's not much.

MAESTREJUAN: How true is that across chemistry departments?

BERTOZZI: Right now I have three students in my lab of thirty-whatever that would qualify as underrepresented minorities, and that's actually a lot. Right now I happen to have that, but in the past I might have one, and most labs might have none.

I'm the affirmative action advisor—I guess I'm called—for the department, which no one really knows what that means, but what that means is I do a lot of admissions. I'm also a vice-chair. There're three vice-chairs and I'm the one who handles the chemical biology.

[tape recorder off]

BERTOZZI: Underrepresented minorities. Yes, all it means is that I go through the applications and really look hard to find underrepresented minorities that we might be able to get into the department and then try and recruit them.

MAESTREJUAN: At least in biology there seems to be a greater increase in the number of Asian or Asian Americans interested in molecular biology, but that's about the only ethnic minority making progress. What is it about chemistry that does not seem to reflect the student population?

BERTOZZI: Well, chemistry doesn't have a very good public perception. Most kids don't know what chemists do. We don't do a very good job, I think, at public relations. Biology's great, it's all about medicine and curing human disease and there're TV shows on PBS

[Public Broadcasting System] about some human genome stuff and everything. And the same with astronomy. Everyone knows black holes, and it's really cool, outer space.

But chemistry, no one really knows what chemists do. We spill oil in Alaska from oil tankers. We pollute the environment and make carcinogens. In movies we're these weird old guys with crazy hair and lab coats, buried in the basement. You know what I mean? So I think that a kid, just in general, growing up in the world, would not necessarily think, "I want to be a chemist." You have no idea what that is. There's no TV show about it like *ER* [television show] or *L. A. Law* [television show], or something like that.

And so the question is, where do you get your information about what chemists do? If you don't get it from your parents or your family or something, you don't get it at all. We get a lot of kids from the Midwest. The Midwest, these are the states with the big chemical industry and a lot of their parents are chemists or they know chemists, so they have some familiarity with what that means. Most of our science majors at [University of California,] Berkeley, undergraduate science majors, who are African American, they want to go into medicine. They're not interested in a Ph.D. in chemistry. Doctors are held in very high esteem in virtually all cultures, and it's considered a pretty sure way of getting a high-paying job. And, again, what do chemists do? We don't know. What do they get paid? Who knows. [laughs] No one really knows. And ACS [American Chemical Society] is very well aware of this problem, too. So there's a lot of talk about increasing public awareness of chemistry, trying to make it sexier to young kids so that they get interested at a younger age so they're more likely to recruit them in based on interests.

MAESTREJUAN: It's too bad how they banned all those chemicals in the Sears [Sears, Roebuck, and Co.].

BERTOZZI: Yes, chemicals are bad. I mean, you want food with no chemicals in it, right? And makeup with no chemicals.

MAESTREJUAN: Did you have one of those little chemical kits when you were growing up?

BERTOZZI: No, actually. I had no idea what chemists did. I had no idea. At the burrito place down the street, it's like, "We don't use chemicals in our burritos."

And I'm like, "Let me tell you, you do." All that stuff is chemicals. But that's public perception, is what it is. So there's a mission of the ACS, which is to improve the public relations with the community, which means get cool chemistry demonstrations into the K [kindergarten]-through-12 science classes and have little science fairs where chemists go on the road with cool demonstrations about how an airbag works in a car and stuff like that, which is

chemistry. So hopefully that will help. But, yes, it's a problem. It's such an ancient problem, again, how do you even trace the origin of that one? It's pretty far back.

MAESTREJUAN: Affirmative action is certainly a contentious issue at the University of California, with the regents standing on one side of it and several— including the Berkeley chancellor—standing on another. What is the Department of Chemistry or the College of Chemistry's stance on the notion of affirmative action?

BERTOZZI: Officially?

MAESTREJUAN: Yes.

BERTOZZI: Well, officially, we don't have quotas, but we do the admissions as faculty, so there're myself and two other guys who sort through all those folders and do the admissions, and, yes, we pay attention to if we have a qualified candidate who's an underrepresented minority. Yes, we work pretty hard to try and recruit that person. No question. There aren't that many applicants. We have such a small applicant pool that it's not like there're all these candidates to choose from. You're lucky to have five applicants who would qualify themselves as an underrepresented minority in a year. And everybody wants them in their department, so you're fighting over them. They all get fellowships. It's great. They're free if you can get them, everybody wants them in their group. I'm thrilled to have three of them. One of is a Ford [Foundation] Fellowship. But they just don't apply to grad [graduate] school, Berkeley, anyways.

Where we've had the best luck has been recruiting out of the local state schools, like San Francisco State [University], Hayward State [California State University, Hayward], Chico State [California State University, Chico]. Well, actually, some of those schools, like San Francisco State, actually qualifies as a minority institution because their student body is over 50 percent underrepresented minority students. So they actually now have minority college status. And their students are great and they have, actually, a pretty strong biochemistry program over there. They train them really well, they try to get them interested in graduate programs and so on.

And so one of us will go over there every year and give a talk on our research and sell Berkeley as great, come to the graduate program and so on. The great thing about that is, if we can manage to recruit a student from one of those schools, because they're local and most of these are commuter schools, the state schools—kids at SF State [California State University, San Francisco], most of them are from San Francisco—they live at home with their parents or their family lives close by. So that means that they have family in the area, which I think helps tremendously, because one of the problems that a lot of these departments and also we have had is that we recruit— Let's say we recruit a minority student away from some other state. They've come all the way out and come to California, and they're just planted in the middle of this

chemistry program with all these white kids from Minnesota, and they're totally out of their element and they have no network, no community, no friends network, no family network. So they're already alienated anyway, then we put them in this environment and further alienate them. And a lot of times they'll leave after a year or two, like, "Screw it." They just don't feel comfortable here or whatever, they're lonely for their family.

Whereas if we can get a student from SF State or Hayward State, their family's here, so even though they're a singularity in our department, sticking out like a sore thumb, outside of work, they have a friends and a family network, so they have a community outside of work, and that's really important, I think. So we have a great success rate with retention of those students and they tend to do very well. That's kind of how I felt. I came here and I felt, okay, I'm going to come into this chemistry department with all these people who are going to be, at worst, hostile to me, or, at best, just ignore me, but outside of that I'm going to have a community, which is my community, separate from work, and that's going to sustain me. And I think that's what we can offer these kids if we can get them locally and their family's here and their friends are here. So we've had some great students. SF State is a real feeder school for minorities, but, again, one a year we're lucky. It's not that many.

MAESTREJUAN: One final question I'd like to ask is what does it mean to be a Pew [Scholars Program in the Biomedical Sciences] scholar?

BERTOZZI: For me, obviously. I was going to say, they send you this check. It's fun because you're in a little club and it means you get to interact with people from all these different disciplines that you know nothing about. That's really fun. It's this whole little world and universe that will open to you, this little window opens to you and you get to look inside and it's like, "Oh, that's really cool."

For me, being a Pew [Scholars Program in the Biomedical Sciences] scholar was all about getting to hang out with developmental biologists once a year. They really have a sense of humor, those developmental biologists, and I learned a lot of terms and we had some kind of inside jokes. I learned all these terms for the different parts of your body that develop during embryogenesis, like the notochord, and I never knew what any of these words meant, and these friends of mine are developmental biologists, would get up and give these talks about the mesoderm and the notochord, and I'd say, "I don't know what the notochord is, but I think mine is killing me right now." [laughs] That was such a Pew [Scholars Program in the Biomedical Sciences] scholar thing.

To me that's what it was all about, making friends in other areas of science that I never would have encountered in some other way. It also was really good because for me, I was kind of an amateur biologist and more of a chemist, and I had biology aspirations and I wanted to hire postdocs [postdoctoral fellows] and grad [graduate] students, I wanted to get grad students from biology departments and so on, and being a Pew [Scholars Program in the Biomedical Sciences] scholar gave me credibility in biology, because biologists had heard—

chemists never even heard—of Pew [Scholars Program in the Biomedical Sciences], but every biologist knew what that meant, so people who might have been considering joining my lab were like, "Well, she's in this chemistry department, I'm not really sure what kind of biology, but she's a Pew [Scholars Program in the Biomedical Sciences] scholar. That's got to mean something." Right? So that was helpful early on for my career.

And, again, so now I'm a Hughes Investigator [Howard Hughes Medical Institute], it's the same concept. Right? It gives you some credibility, and when you're on the fringe of a discipline, that is really helpful. People might not give you the benefit of the doubt otherwise. And, to be honest, I don't know that I would have been elected as Hughes Investigator if I hadn't been a Pew [Scholars Program in the Biomedical Sciences] scholar, because I got a lot of exposure in biology from Pew [Scholars Program in the Biomedical Sciences], and Hughes is a biomedical research foundation, there're not a whole lot of chemists hanging around there. And awards beget awards, so the more awards you get, the more you get. So Pew [Scholars Program in the Biomedical Sciences] was really great for me.

MAESTREJUAN: How are the Howard Hughes annual meetings?

BERTOZZI: That's fun. It's totally different, obviously. It's not like a party at the beach. I mean, Hughes annual meetings you go to Chevy Chase, Maryland, and just live it up, let me tell you. But Hughes, it's great because you get to hear great science and you get to meet all these people. I go to a different meeting every year because there really is no meeting that's really my meeting, I don't really fit into their categories neatly. So this year I'm going to cell signaling, and last year I went to structural biology, and the year before that I went to immunology. That's cool, so I get to see everybody. I like Hughes. It's pretty incredible, actually, when you think about the magnitude of what they fund. Even with the cuts, it's pretty impressive. And they treat you pretty well.

But Pew [Scholars Program in the Biomedical Sciences] was a party. Of all those young investigative things, the three that compete with each other are Pew, Searle [Scholars Program]—What else?—and Burroughs-Wellcome [Fund]. And you're only supposed to have one of those, so some people collect more than one somehow, but the rule is that if you're a Pew [Scholars Program in the Biomedical Sciences] scholar, then you're not supposed to take a Searle scholarship and so on. So sometimes you have to choose which one are you going to be. The money's about the same, all three of them, and the prestige, I'd say, it's pretty comparable, all three are very well known.

But Pew [Scholars Program in the Biomedical Sciences] throws the best party by a long shot. Searle, are you kidding? They have their annual meeting in the Chicago-O'Hare Hilton [Hilton O'Hare Airport], and they wear suits and ties. It's really stuffy. Whereas Pew [Scholars Program in the Biomedical Sciences], Silvia [Montano de Jimenez] and Ed [Edward O'Neil] put on Hawaiian shirts and muu-muus and then you go and hang out in Cozumel [Mexico]. That was great. That was the best part about it, was those parties. And apparently now they're

doing five-year reunions, so I'm counting the microseconds till I get to have my five-year reunion with all my notochord friends and we get to go swimming with dolphins and come up with interspecies mating jokes. That's the whole thing.

MAESTREJUAN: Well, at least you can take comfort in knowing that rather than cutting back on the expense of the annual meetings and the exoticness of it, they have decided to fund fewer scholars.

BERTOZZI: [laughs] Spare the party? No, the party was the best. I told you yesterday, I lived for those meetings. That was my one vacation kind of thing, you know. And everyone there was so nice and so friendly, and those were the first biologists I really met, because I wasn't in the MCB [Molecular and Cell Biology] department when I first joined the faculty, I was just in chemistry and they added me to MCB a couple years later. So for the first few years I really didn't know anyone in MCB, I was just surrounded by my chemistry guys, and they're nice guys, but a little uptight, not as friendly. And, also, there were no young people here at the time. It was older faculty, and so I got to meet all these assistant professors who you could bond with and stuff. It was great.

MAESTREJUAN: Did you take your partner?

BERTOZZI: Yes. I took her [Cynthia*****] to two of them. She couldn't come to the other two. Yes, it was great. These guys, Pew [Scholars Program in the Biomedical Sciences], they're infinitely cool. This is a San Francisco-based operation, so they're totally cool. And also, young biologists tend to be this really funky, cool set. You've met these people, right, so you know what I'm talking about. And young chemists now are getting kind of funkier with time, but there's still room for improvement. Chemists are a bunch of dorks. We're a bunch of nerds, and biologists, somehow, they seem to have—I don't know—a more diversified history somehow. I don't know why. They've read books. They just have more fun somehow. The culture's different. They have a more relaxed culture. I don't know why, because in many ways they make life miserable for themselves with all this, if you don't get a paper in *Cell*, then you're dead. You know what I mean? Which is unbelievably stressful, but somehow around that they manage to be this sort of funky set.

MAESTREJUAN: Okay, well, I've come to the end of my questions, and I'll turn it over to you and ask you what you would like to add that we haven't talked about.

BERTOZZI: Do you get to go to any of these Pew [Scholars Program in the Biomedical Sciences] meetings? Is that like a perk [perquisite] of your job?

MAESTREJUAN: Yes.

BERTOZZI: Do you get to go to the five-year annual reunion thing?

MAESTREJUAN: It just depends on—

BERTOZZI: When you finish this oral history thing, then are you cut off from Pew [Scholars Program in the Biomedical Sciences]?

MAESTREJUAN: Yes.

BERTOZZI: They won't invite you as an honorary—

MAESTREJUAN: I doubt it.

BERTOZZI: As a former participant in oral history, you don't get to go to the five-year? I'll talk to Ed and Silvia about that. It seems like an oversight, because you've met all the people, so you're part of the class now. Right? You've heard all of our stories, you know more about us than anybody, more than my mother knows, actually, now, because I have nothing else to say, and you should be invited to these things.

MAESTREJUAN: I second that motion.

BERTOZZI: Okay. Do you know where the next one is?

MAESTREJUAN: Puerto Rico.

BERTOZZI: I've never been to Puerto Rico. When is it? 2005?

MAESTREJUAN: 2004.

BERTOZZI: Oh, that's, like, next year. Because I wasn't invited to the last one because it was the last year of my Pew [Scholars Program in the Biomedical Sciences] thing, so we just missed the boat on that party.

You know, at a Pew [Scholars Program in the Biomedical Sciences] scholars meeting in Puerto Vallarta, they had me on the forty-first floor of the Westin [Regina Resort Puerto Vallarta] hotel, and I was overlooking that bay, and wafting across my window was a parasailer. I was, "This is the life." I was, "Wow." I'd never had a vacation. When I go on vacation, I stay in some cheap motel somewhere. That was cool.

Yes, Cynthia came and went scuba diving at one of those meetings and went snorkeling. I miss those days. It sure beats that O'Hare Hilton [Hilton O'Hare Airport].

MAESTREJUAN: Yes, I guess.

BERTOZZI: I really don't have anything to add that I can think of.

MAESTREJUAN: Okay, that's good. We appreciate you taking the time out.

BERTOZZI: No, it's your time, I appreciate it.

MAESTREJUAN: Thanks a lot.

BERTOZZI: You have to listen to this thing again, huh?

MAESTREJUAN: Yes.

[END OF TAPE 5, SIDE 1]

[END OF INTERVIEW]

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