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Interview with Prof. Ivet Bahar

It has been a typical mode of communication between two scientists in the post-Covid era. Surprisingly, we were in the same time zone, and the time was 13:30 in South Africa and Israel. Ivet joined the Zoom interview from her hotel room in Cape Town, with a magnificent background view. She took a break from an intensive conference - the Human Frontier Science Program (HFSP) meeting. She delivered her lecture the previous day as an HFSP awardee.

By Ehud Keinan

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Professor Keinan of the Technion is President of the Israel Chemical Society, Editor-in-Chief of AsiaChem and the Israel Journal of Chemistry, Council Member of the Wolf Foundation, and past Board Member of EuChemS. He was Dean of Chemistry at the Technion, Head of the Institute of Catalysis, and Adjunct Professor at The Scripps Research Institute in California. His research program includes biocatalysis, organic synthesis, molecular computing, supramolecular chemistry, and drug discovery. He received the New England Award, the Herschel-Rich Award, the Henri Taub Prize, the Schulich Prize, the Asia-Pacific Triple E Award, AAAS Fellowship, the ACS Fellowship, and the EuChemS Award of Service. Since January 2024 he is IUPAC President.

Ivet, you are a role model for many young Turkish scientists, with over 400 research papers, an h index of 93, over 36,000 citations, the first Turkish female scientist elected to the National Academy of Sciences of the United States, an elected member of the Science Academy of Türkiye, elected member of EMBO, Invited Speaker at the White House, to name a few of your accomplishments. I want to go back to your very early experience with science. How early in your childhood has science triggered your curiosity? And when and why did you consider choosing a career in chemistry?

I was born in Istanbul. My family always valued education. Neither of my parents had the opportunity to go to college, although they wanted to. They were active socially and culturally and spoke multiple languages but were mainly self-educated. They wanted their children, my brother and I, to receive the best education. One of the best things they may have done, in addition to constant support and appreciation of hard work, was to hire a piano teacher for private tutoring, Mrs. Viktoria Akinoğlu, whose guidance, warm sensitivity, and attention to perfectionism, especially during our recitals have been motivating and inspiring me, starting from the age of five, till college years.

Mathematics was my favorite topic in primary and middle school years. I did dream then of a career centered around mathematics, perhaps as a schoolteacher; this was my vision then, like probably many children of that age. Then, during high school years, I discovered that I had an aptitude for physics and chemistry. At my graduation from the French High School, Notre Dame de Sion, in Istanbul, I was honored to receive the Prix d'Excellence from the French government as the best

A childhood photo with my parents Sela-Albert Razon, and brother Viktor, in Istanbul, Suadiye;

Toddler in 1959.

Piano recital at the primary school.

student among graduates, in addition to three awards for excelling in specific topics: Mathematics, Physics, and Philosophy. But it never occurred to me that I might pursue an academic career in science until my then-boyfriend, now-husband, came up with this idea while I was contemplating many (other) topics for college studies. Frankly speaking, I didn't have any science aspirations – perhaps due to a lack of a role model in 'my world' of close family and friends.

In Türkiye, all high-school graduates used to take, and still take, a centrally administered entrance exam for placement to universities. Student matches with departments are made based on their points in that exam and their rank-ordered preference list of departments in all universities. At my graduation from high school, I had to write a first choice, and I knew that this choice could impact my future career. The decision was basic sciences, and among them I had to choose between mathematics, physics, and chemistry. I wasn't even thinking of biology, then. I wasn't sure whether I wanted to pursue an academic career either, and I wanted to have the option of working in industry or private sector if academic life would not be fulfilling enough. Mathematics or physics did not seem to offer such alternatives then. So, I wrote chemistry because I could have a job in a lab if I didn't want to stay at the university. Not surprisingly, I was admitted to my first choice, Chemistry Department at Boğaziçi University. This was the beginning of my journey to discover the world of science and academic life, which led to BS and MS in Chemical Engineering at the same university, and a PhD in Chemistry at Istanbul Technical University.

Did you receive appropriate formal education to become a scientist?

I wouldn't say I received a formal education to become a scientist, but several incentives and experiences added up to drive me in that direction. I attended a regular public school during my primary education and then the French High School Notre Dame de Sion, in Istanbul. I was lucky to have an exceptionally talented and passionate mathematics teacher, Dr. Yomtov Garti (1915-2011), during high school years,

With classmates as a high school senior at Notre Dame de Sion, 1974.

whose depth and kindness could not be matched by any other mentor. He was one of the most influential teachers in my career. I remember him saying, “This girl has intuition; I’d like to see what she will do in the future” which was truly motivating. I was honored to receive a mathematics prize from him at my graduation from high school - the only prize I received for mathematics. I am sure the rigorous education in mathematics (and physics) and the highly motivating prizes I received at Notre Dame de Sion paved the way to my future career, along with the self-discipline and working habits I developed during the eight years I spent there. I think regular piano lessons also contributed to appreciating the significance of technical work behind the harmony/coherence/aesthetics of a beautiful product.

I had excellent professors during my undergraduate studies at Boğaziçi University, as well. Boğaziçi U, formerly known as Robert College (a private American University) had changed status to a state university a few years before I started my studies, but the tradition of teaching all science and engineering courses in English was kept. This gave us the opportunity of learning from the best ‘classical’ textbooks as well as being exposed to scientific literature. The first year all Engineering and Basic Sciences students used to take the same courses, providing us with a firm multidisciplinary foundation. Notably, I was one of two freshman students, among all admitted in 1975, who succeeded in obtaining a GPA of 4/4. The other student left for the United States; I stayed in Türkiye, close to my family and friends, probably prioritizing my family life then. It turned out to be a good decision on professional grounds too. We had excellent instructors in chemistry (e.g., Hadi Özbal, Bedi Ziver, and Selim Küsefoğlu), physics (e.g., Haluk Beker, Ömür Akyüz, and Mahmut Hortaçsu) and mathematics (e.g. Ayse Soysal and Yomtov Garti who also taught at Boğaziçi U), to name a few. I switched from chemistry to chemical engineering during my undergraduate studies because the chemical engineering program offered a course in computer science; chemistry did not. I was fascinated by the speed, power, and precision of computers, and enjoyed writing algorithms. We didn’t have personal computers/laptops then; instead, we used to submit jobs on punch cards to a huge machine in our computer building. I would submit multiple jobs simultaneously, using whichever monitor I could have access to (which were on high demand), eager to maximally take advantage of the available computing facilities at the university.

First year of primary school, with standard uniform of all public schools (in 1964)

Ivet with her high school mathematics teacher, Dr. Yomtov Garti, at the graduation from Notre Dame de Sion, in 1975.

None of this could be viewed as a formal education to become a scientist, but probably equipping me with the basic sciences and quantitative/computational skills that would be essential to do research, starting from my Masters years. My MS thesis advisor, Prof. Burak Erman, was a pioneering scientist in the field of polymer science and a former postdoc of the 1974 Nobel Chemistry Laureate, Paul Flory, from Stanford University. Dr. Erman, now retired from Koc U but still active, introduced me, not only to scientific literature and methods in polymer physics and chemistry, but also to scientific conduct and professionalism. He encouraged me, for example, to read the book "Surely You're Joking, Mr. Feynman!" by the physicist Richard Feynman (1965 Nobel Physics Prize). I also remember vividly the moment he introduced the 1969 book 'Statistical Mechanics of Chain Molecules' of Flory to me, as the 'Bible' in the field. I knew that I had to learn/understand all concepts and derivations in that book, but I didn't know then these were the first steps to my future scientific life. I read the book, derived all equations in it, during the summer of 1982, at home, while also spending precious time with my sons. Yes, I got married and had two sons by the time I completed my undergraduate studies at Bogazici University.

Ivet with her husband Izzet and two sons, Yusuf Joseph and Alper Albert (newborn) in 1980.

Ivet with her family in 1981.

What happened after graduation?

It was not easy to be a mother and a student at the same time during undergraduate studies (despite the tremendous help of my husband and my mother), and I simply decided to take a break and dedicate my full time to my kids after graduation. I believe it is important to take a step back, when needed, to be able to make a bigger leap forward afterwards. I truly enjoyed this 'family' break of 20 months, after which I was attracted to go back to school, for my MS in Chemical Engineering at Boğaziçi, followed by my PhD in Chemistry at the Istanbul Technical University. My research studies, on statistical mechanics of macromolecules and thermodynamics of polymer solutions, gradually became more and more interesting. I was pleasantly surprised to see that my findings were accepted for publication in leading journals in the field.

Ivet with her two sons, Yusuf Joseph and Alper Albert at the graduation from Boğaziçi University.

Ivet with her family in 1982

Ivet *(left)* with Dr Erman *(middle)* and her first PhD student, Dr. Turkan Haliloglu *(right)* in the first row and student researchers *(back row)* at the PRC in 1997; Dr Haliloglu is currently the Director of the PRC; at the right end of 2nd row is Banu Ozkan, Ivet's 5th PhD student, now a Professor and Director of the Center for Biological Physics at Arizona State U.

At the MS graduation of Başak Işın in 2000, co-mentored by Ivet Bahar and Pemra Doruker, on both sides of Başak. All PRC student researchers in this photo pursued doctoral studies at the PRC of Boğaziçi U or in the USA. Several are now academicians: Neşe Kurt Yılmaz *(front row, left)* at U Mass Amherst, USA; Zerrin Bağci *(front row, middle)* at Tekirdağ Namık Kemal U, Türkiye); and Nuri Alpay Temiz *(next to Ivet in the back)* at the University of Minnesota. Ivet's two first PhD students, Türkan Haliloğlu *(middle row, rightmost)* and Pemra Doruker *(middle row, 2nd)* were already faculty at Boğaziçi U Chemical Engineering Dept when this photo was taken, shortly before Ivet's relocation to the U of Pittsburgh.

I was offered an Assistant Professor position at the Chemical Engineering Department of my alma mater, Boğaziçi University, immediately after completing my PhD (Feb 1986). Boğaziçi U was, to my view, the best university in Istanbul then (not to mention that it was hard to secure a faculty position). A year later, I was promoted to associate professor position, and in my mid-30s to full professor. By the age of 40, I was an elected member of the Turkish Academy of Sciences, and recipient of several national prizes. Between 1993 and 2001, I served as the Director of the Polymer Research Center (PRC) that we founded together with Dr. Erman in 1989. The PRC was a true Center of Excellence, a research hub. Several talented students (mostly girls) found the opportunity to do research there and become future scientists.

Interestingly, with my shift in interest from synthetic to biological polymers (mainly proteins and their complexes/assemblies) starting from the early 1990s, the PRC literally became a protein research center (and the acronym PRC still fitted). This is where we laid the foundations of elastic network models (ENMs) for predicting the equilibrium dynamics of proteins, starting from the Gaussian Network Model (GNM), which we formulated together with Drs. Erman and Ali Rana Atilgan. Ali Rana was a young Faculty at the Civil Engineering Department then, with excellent insights in material science (he is now a Professor at Sabanci U). Together, we published our first paper on GNM (Bahar, Atilgan and Erman, Folding & Design, 1997). Notably, the journal was discontinued in subsequent years, but our paper has been consistently cited, as it provided a simple framework for bridging biomolecular structure and function through dynamics.

"We, all women scientists, benefited from Atatürk's reforms that removed gender barriers and promoted education and science."

Your list of prizes and awards is very long, but I want to focus on your early career as a young female scientist in Türkiye, already a mother to two children. Were any of those recognitions dedicated to encouraging women in science?

Not at all. At that time, there were **no** specific prizes for women in science. Let me take this opportunity to acknowledge my deep gratitude for all recognitions from academia as well as government, during my early career in Türkiye. This started as a student at Boğaziçi University, when I got a fellowship from the Scientific and Technological Research Council of Türkiye, TÜBİTAK. Being a TÜBİTAK fellow motivated me to work harder to deserve the honor. Immediately after I became an Assistant Professor, I received a UNESCO fellowship to do research in the USA during the summer, thanks to an initiative led by Prof Zeynep Ilsen Önsan at Chemical Engineering Department, who was then the Dean of the School of Engineering at Boğaziçi U. I had the opportunity of selecting any lab in the USA (if they would accept me as a researcher), and of all the places, I chose the University of Akron; or more exactly, I chose Professor Wayne L. Mattice at the Institute of Polymer Science of the U of Akron. Dr. Mattice was doing pioneering computations in polymer science, and I admired his work as well as the computing resources in his lab (which we emulated a few years later at the PRC). This was my first exposure to the scientific world in the USA. I learned from him how to run a lab, how to work very hard to be able to engage and inspire all lab members, and how to be very patient and positive during research. This first visit was followed by four more summers, funded by Dr. Mattice's grants, who also continued to host many students of mine, after my interests shifted to biological systems and I preferred to spend the summers (of 1992-2000) at the National Institutes of Health (NIH) in Bethesda, while being a Faculty

Ivet receiving the TÜBİTAK -TWAS award from the President of the Turkish Republic, Mr. Süleyman Demirel in 1995.

at Boğaziçi U. These visits to the lab of Dr. Robert Jernigan (another former PhD student of Paul Flory) at NIH were a decisive factor in my scientific career change from polymer science to computational biology.

Back to my early career years in Türkiye. As an Associate Professor at Boğaziçi University, I received TÜBİTAK Teşvik (Encouragement/Incentive) award for young scientists (in 1990); and in 1991, a popular newspaper awarded us, my mentor/collaborator Erman and me, the Sedat Simavi prize for our work on developing polymeric materials with upgraded mechanical properties. A few years later, as a professor, I received the TÜBİTAK -TWAS (Third World Academy of Sciences) Award, a highly prestigious science prize awarded by the President of the Republic. I was honored to receive the prize from President Süleyman Demirel.

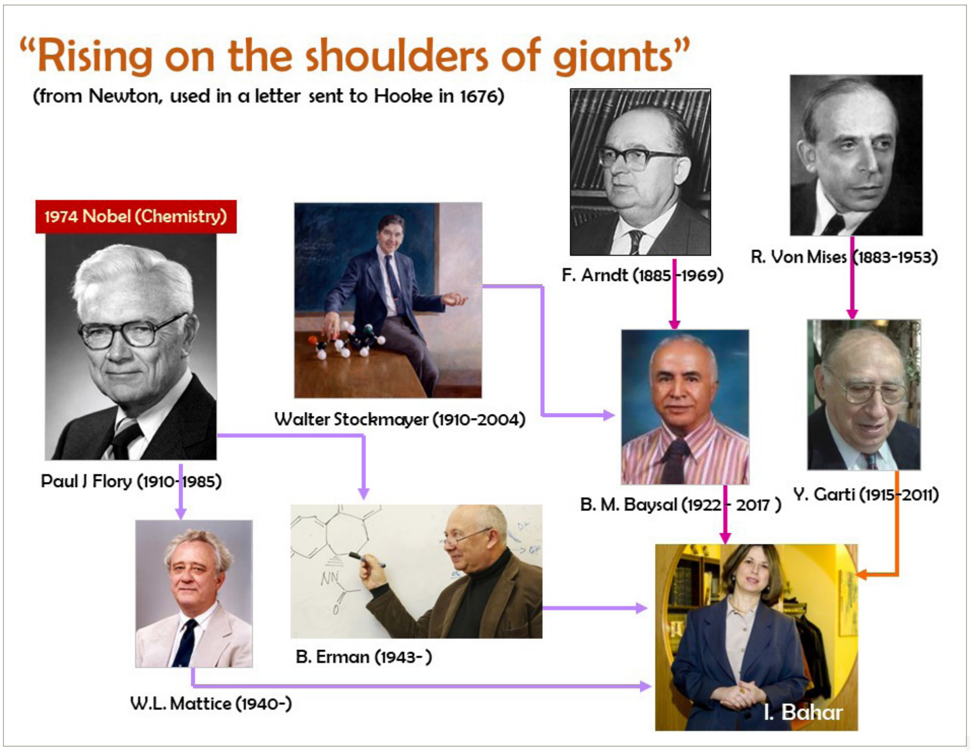
In the fall of 2000, in my early 40s, a few months before my departure to the USA, I was elected a lifetime member of the European Molecular Biology Organization (EMBO). They elected me, not as a woman scientist, but as developer of innovative models and methods for studying protein dynamics in silico. At least this is what I would like to believe. On the other hand, it is true that female scientists were, and are still, underrepresented among EMBO members (currently the ratio of female to male members if 1:4), and understandably female scientists could and should be given serious consideration. It all starts by nominating them, bringing them to the table, but then the selection should be merit-based. As a parenthesis, I am very proud to say that two former (female) PhD students of mine from the PRC years, Özlem Keskin (now Professor and Vice Dean at Koç University) and Canan Atilgan (now Professor at Sabanci University, and President of the Academy of Sciences in Türkiye), were elected EMBO members this year, increasing the total number of Turkish members from four to six. I hope and trust that many more scientists will follow in the coming years, both female and male.

This special issue of AsiaChem is dedicated to the anniversary of the 100 years of the establishment of the Republic of Türkiye by Mustafa Kemal Atatürk. Do you feel indebted to his legacy, assuming that if he were not successful in establishing Türkiye as a modern, secular country, women like you and your students would not be able to develop a science career?

Absolutely. There is no question that women scientists would not have found the opportunity of doing academic careers, let alone science, if it were not for the reforms of Atatürk. I am the second generation of women scientists in Türkiye. Most of the first generation, who pioneered in various scientific areas, now retired, or passed away. I would like to mention, en passant, an excellent book put together by the Science Academy in Türkiye (with the leadership its President, Dr. Canan Atilgan) on this first generation of women scientists (entitled "Sahada: Cumhuriyetin Harcında Bilim ve Kadınlar", that translates as "In the Field: Science and Women in the Mortar of the Republic"). We, all women scientists, benefited from Atatürk's reforms that removed gender barriers and promoted education and science. You know, one of his famous sayings was "Hayatta en hakiki mürşid ilimdir", which means 'The most genuine/authentic guide in life is science". My generation grew up with this concept, this wisdom. You may know that Turkish women are very active in academia and science, not only in Türkiye, but in the entire world. I am also very proud of five female PhD students whom I mentored during our PRC years, all of whom became scientists.

I might add that the first two generations of scientists in Türkiye, and perhaps indirectly new generations too, also benefited from the modernization of higher education initiated at the 10th anniversary of the Turkish Republic, in 1933, under the visionary leadership of Atatürk (and the dedicated efforts of the National Education Minister Dr. Reşit Galip). Several German scientists (of Jewish origin) who were also trying to flee Nazi Germany, were invited to Türkiye to launch new training and research programs. The goal was to replace the old system of Darülfünun by research-oriented departments in the newly founded Istanbul University. This initiative led to a complete transformation of high education in Türkiye. More than 40 such scientists joined Istanbul University only in 1933 (and

Ivet giving a talk at the same award ceremony.



Ivet Bahar’s academic genealogy. Immediate mentors were Garti (mathematics teacher), Erman (MS advisor), Baysal (PhD advisor) and Mattice (advisor/mentor during summer visits as a new faculty). These individuals were mentored by Flory (1974 Nobel prize in Chem, at Stanford U), Stockmayer (pioneering polymer scientist, at Dartmouth College), and Arnd and von Mises (German scientists at Istanbul U).

100+ were recruited by many universities in subsequent years). My Ph.D. advisor, Prof Bahattin M. Baysal (1923-2017), for example, was a student of a renowned chemist/scientist, Fritz Arndt, who chaired the newly founded Chemistry Department of Istanbul University. Arndt served more than two decades in that role. He learned Turkish, taught in Turkish, and even established the early scientific chemistry terminology in Turkish, which helped ‘democratize’ high education. My high school mathematics teacher, Dr. Yomtov Garti, was a PhD student of Professor Richard Von Mises, again a worldwide renowned mathematician who served as the Chair of Pure and Applied Mathematics in Istanbul University. In a sense, we rise on the shoulders of giants, and I had my share too.

Is it also the situation over the last 20 years that the same opportunities exist for women in Türkiye?

I believe so. In general, there are no **obsta**cles for women in Türkiye to pursue careers in academia or science, at least not more than in other countries. It is, however, a reality that there is still a gender gap, and women are generally underrepresented in academia especially in STEM topics. I believe the situation in Türkiye is not worse, and is probably better, than many European countries. But we still have a long way to go.

What may have become more challenging for scientists in Türkiye, for both female and male scientists, is to secure adequate support to conduct research. This is not only about research funds to run their labs, but also about research infrastructure and/or equipment, which is a major determinant of success. I hear from my former students that national support is more challenging compared to 20 years ago. This presumably originates from an increase in demand, with a mismatch in supply, and signals a requirement to increase the percentage of GDP allocated to R&D. Furthermore, not only government but private industry and foundations should contribute. The good news is that Turkish scientists are truly innovative and competitive when given the opportunity. So domestic support to promote their research would more than pay off in international arena. Several brilliant scientists, including female scientists, already benefit from research and training funding programs offered by international (especially European agencies, including Horizon and Erasmus programs of EU, ERC grants, EMBO fellowships). Association of Türkiye to such research organizations and programs is vital to promoting research in Türkiye.

What are your most significant scientific contributions to science?

The most important discovery we made during my years as the PRC Director and Chemical Engineering Professor at Boğaziçi University is the demonstration that a simple model, known as elastic network model (ENM), can successfully explain the structural dynamics of biomolecular systems. Structural dynamics here refer to conformational changes the biomolecular systems undergo under physiological conditions, due to thermal fluctuations or environmental effects including their interactions with other molecules. Biomolecular systems encompass proteins and their complexes/assemblies with other proteins, DNA/RNA molecules, lipids, and small molecules (e.g. drugs). Despite the complexity of biomolecular structures, their equilibrium dynamics are uniquely ‘predictable’ by ENMs. More importantly, dynamics define mechanisms of function. The intrinsically accessible motions are needed for signaling, catalytic, transport, transcription, and regulation activities in the cell. Thus, ENMs permit us to gain an understanding of the mechanisms of function, and consequently opened the way to designing methods for modulating/altering them, i.e. designing drug candidates– a major research topic in my lab.

ENMs typically apply to solid-like materials whose overall structures are maintained/restored despite changes/fluctuations that induce temporary deformations. Flory, Erman, and coworkers introduced such models for polymer networks. We were inspired by these studies as well as a paper of Monique Tirion that appeared in Phys Rev Lett in 1996, which showed how uniform harmonic potentials could be adopted for describing the motions of a protein. This paper stimulated our curiosity and led us to build the theory and mathematical framework of a simple ENM, the Gaussian Network Model (GNM) in 1997. GNM was followed a few years later by a more advanced model, the anisotropic network model (ANM), (Atilgan, Durell, Jernigan, Demirel, Keskin & Bahar, Biophys J, 2001). The latter turned out to be my most widely cited paper.

ENMs represent the proteins as an elastic network, as the name indicates. Information on inter-residue contact topology is sufficient to build the network, where the beads represent the amino acids, and elastic springs connect the pairs within an interaction range. Any such structure of beads and springs is subject to a spectrum of motions uniquely dependent on its

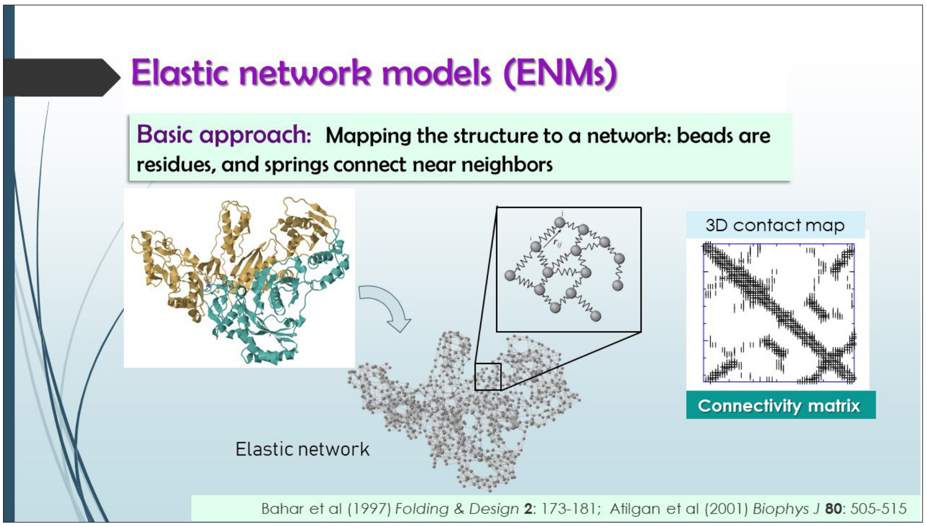


Illustration of the mapping of a protein structure, usually shown by a ribbon diagram, to its elastic network representation.

network connectivity. Our work demonstrated that the most easily accessible modes of motion, also called 'soft modes,' are utilized to achieve function. The model also brought into consideration profound arguments on evolutionary selection. Our view is that structures that lend themselves to functional movements are selected by evolution, and this explains why structurally favored motions are functional.

In recent years, we extended ENM predictions to examine the effect of mutations, by using them in artificial intelligence (AI)- or machine learning (ML)-driven sequence-based studies at the proteome scale. Such studies become increasingly important with advances in personalized medicine.

Can I say that your keys to success have been your unusual angle at biological systems?

Yes, I come from chemical engineering, chemistry, material science, and polymer chemistry, which allowed me to adapt the theories and methods chemists have been developing, especially in polymer science, to biological sciences. That's what I've done, so it made a difference.

In Türkiye at that time, if we aspired to do something internationally competitive, the best thing we could do was computational research because computers were inexpensive, and we could acquire the latest technology. We found it most productive to do computational chemistry at that time. As I mentioned earlier, I benefited from Flory's school on the one hand, and German scientific tradition on the other. We adapted the theories and methods that scientists developed for polymers and adapted them to proteins. For example, in polymer science there is a classical model, the Rouse model, that represents the polymer as a sequence of beads and springs and yields an analytical solution for the polymer equilibrium dynamics. In the case of proteins, the counterpart of the Rouse model became our GNM. The critical difference was that GNM springs connected not only sequential, but also spatial neighbors, but the underlying mathematical framework and physical concepts were the same.

ENMs became the foundation of 20+ years of work since then, which led to my election to the US National Academy of Sciences and broadly recognized and cited studies. We would not have pursued this line of research at the PRC, if it were not for the summer visits that I used to make to NIH (in 1992-2000). Each summer, I used to learn the state-of-the-art in protein science, and bring new knowledge and ideas to my students and colleagues at the PRC. It was exciting to model and visualize in silico how specific proteins interact, how those interactions underlie their actions as workhorses of the cell. This was a whole new world that we could explore by adapting models and methods of molecular physics and chemistry to biomolecular systems. Everything the proteins did under native state conditions could be related to their chemical and physical dynamics while maintaining their fold.

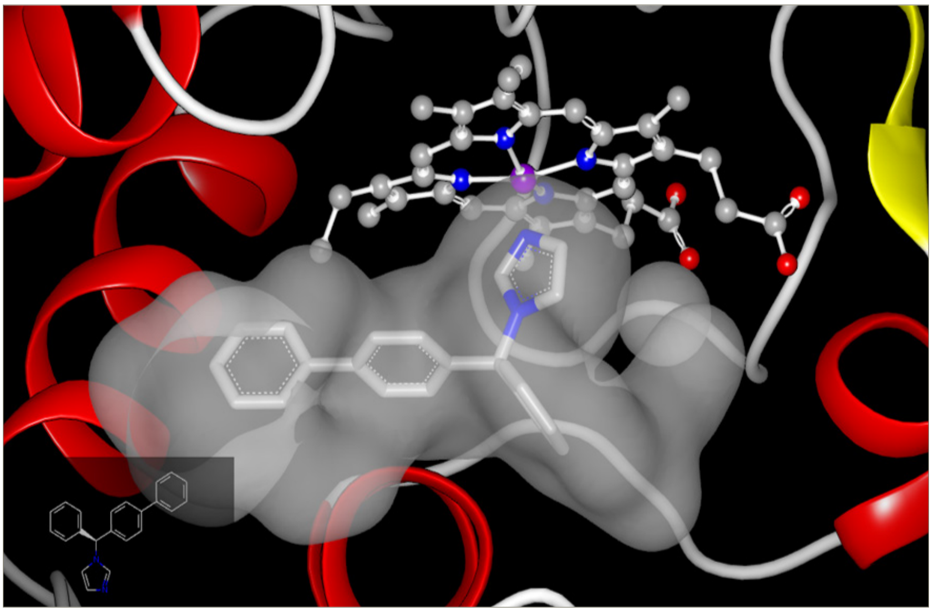
In the past 20 years, I got increasingly interested in understanding the machinery of biomolecular assemblies and designing molecular intervention strategies. My lab works extensively on drug design in collaboration with experimentalists and clinicians]. For example, we have a recent patent for the treatment of COVID-19 infection. The difference we made in this area was to consider the protein as a moving target, not a static entity. The goal would then be to design a small molecule modulator that would bind the moving target, considering the two-body problem's dynamics. We also introduced the concept of signature dynamics of protein families (Zhang, Li, Krieger & Bahar, Mol Biol Evol 2019) and determined how specific members distinguish themselves. This is important because we want to design selective drugs that target those members and overcome drug-resistance mutations. Therefore, understanding how structure evolved to enable functional dynamics opened many new avenues for drug design and repurposing, which we and others are now pursuing.

"Turkish scientists are truly innovative and competitive when given the opportunity. So domestic support to promote their research would more than pay off in international arena."

The late Prof. Ephraim Katzir of the Weizmann Institute, who later became the fourth President of the state of Israel, once advised me to take chemistry for my undergraduate program, arguing that I could always switch to biology. Still, if I started with biology, I'd never become a chemist. And I have seen highly successful biologists, educated initially as chemists. Do you agree that the more rigorous sciences and thorough understanding at the molecular level are essential for a career in the life sciences?

That's a good point. Doing my Ph.D. studies in chemistry was a good starting point for me too. It provided the foundations that I used in biology.

But I also recognize that things are changing. I have seen biologists with solid quantitative skills who ask the right questions, and this is the first logical step toward addressing a problem. In that respect, some biologists have deep insights. While rigorous education in a single discipline such as chemistry works well, there are



Computer-aided discovery of a drug candidate: an imidazole-containing compounds that binds the heme-group of cytochrome c to inhibit its peroxidase activity (from Bakan et al Mol Pharmacology 2015)

now rigorous quantitative theories and methods in biology. I believe the key to success nowadays is to master two fields, e.g. a basic science (chemistry, physics, or biology) and quantitative science (mathematics, computer science, or engineering), in the face of increasingly complex research problems. For example, in my area, it is important to have strong computational skills alongside basic sciences.

We are now in the artificial intelligence (AI) era; we see AI or machine learning (ML) solutions everywhere. AI/ML took the center stage at the turn of the millennium in life sciences, with the elucidation of human genome and explosion of data. My group was already doing computer-aided research since the late 1980s, and we were well-prepared when AI/ML gained even more importance in recent years with advances in both biotechnology and computing technology. For example, my lab built a web interface, named Rhapsody, to predict whether the mutations in proteins would be pathogenic or neutral. The underlying computer program combines ML/AI and physical-chemical sciences, making our tools superior to many others.

A new era of scientific research and training emerged in recent years at the interface of biology and computations, fueled by fundamental theory and methods of physics, chemistry, mathematics, and engineering. Many PhD programs have been launched in this area. One of first was the Computational Biology PhD Program that I have co-founded between the University of Pittsburgh and Carnegie Mellon University (CMU) in 2005, a program that has been continually supported, first by HHMI then by NIH. Notably, none of us, the instructors, received a formal education in computational biology. We all came from different fields. However, based on our experience, we knew the background and skills necessary to do research in this area. So, we designed the curriculum, the content of courses, and we wrote textbooks to provide a rigorous education. One of them is the graduate level textbook I wrote together with Robert L Jernigan and Ken A Dill, Protein Actions: Principles and Modeling.

The concept of a transition state analog serving as the perfect inhibitor has been central to understanding enzyme and antibody catalysis. Can your methods help design such analogs as potential drugs?

Of course. Between two endpoints, there are intermediates and transition states you would like to understand because you want to understand the mechanism. It's all about understanding mechanisms and then pushing the molecules along that mechanism. Chemical reactions are hard however, we mostly simulate physical events.

What are your most significant scientific contributions to society?

I am a 'methods' person rather than specializing on specific systems or diseases. So, I have been developing new models and methods, and applying them to many cases, especially to complex problems in biological and biomedical sciences. Between 2012 and 2020, I ran a center on multi-scale modeling applied to neurological disorders; we came up with new compounds for Parkinson's disease, for example, we have funded projects on triple-negative breast cancer immunotherapy; we worked on developing therapies against COVID, etc. You know, there are two phases in drug design: discovery and development. Discovery is a lot of fun because we discover new compounds, and this is what I enjoy doing. Then comes the tedious stage of development with systematic modification of chemical groups and examination of absorption and excretion properties, delivery methods, etc. That part, essential for successful completion of clinical trials, is not an area I specialize in. I am more productive at discovery.

Coming back to contributions to society, a significant aspect of my lab's work is to make all theories and methods we have developed accessible through user-friendly interfaces. One such API (application program interface) is ProDy, for protein dynamics using ENMs, which we extended to comprise multiple modules from druggability simulations to cryo-electron microscopy data analysis. We launched ProDy in 2011 during the doctoral studies of my Ph.D. student Ahmet Bakan, now a senior software engineer at Google. He was the first Turkish student to join the Comp Biol Ph.D. program I established with Carnegie Mellon University. ProDy has been used by more than 150,000 researchers and downloaded more than 2 million times since then. Having something so broadly used is unusual in scientific community. ProDy is user-friendly, straightforward, logical, and adaptable to many problems. We started with very simple elastic network models using chemical structures; now we push the boundaries of molecular design, engineering, and drug discovery.

Another obvious service to society is the training of future scientists, or doctoral students. I mentored a total of 20 to date, including five girls at the PRC in Boğaziçi University. They all became resourceful scientists and trained new generations of scientists. A scientific generation is about ten years in academia, and one can easily see academic grandchildren or off-springs. This is one of the most satisfying aspects of our profession. The PRC has been successfully led by my first PhD student, Dr. Turkan Haliloglu since my departure from Türkiye in 2001. Another former PhD student, Dr. Canan Atilgan, is the President of the Academy of Sciences, recognized by the All-European Academies (ALLEA).

Do you collaborate only with scientists or also with companies?

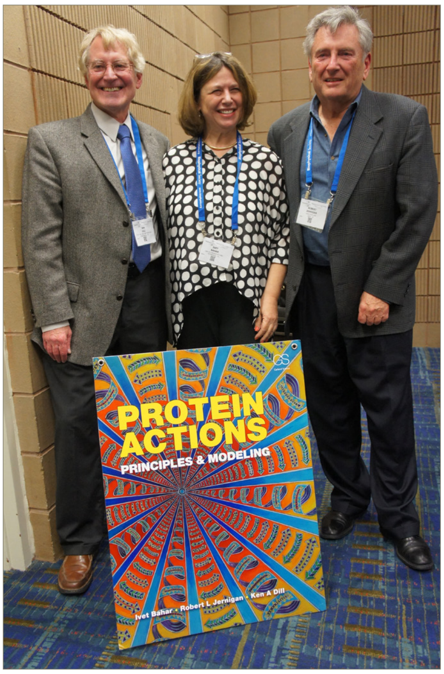
We collaborate with both. For example, I am currently collaborating on metastatic lung cancer therapy with a company that is a spinoff of the Memorial Sloan Kettering Cancer Center. We are working together to design a drug that would act through a new mechanism – via triggering a ferroptotic response. Ferroptosis is an iron-dependent cell death. The goal is to promote the death of cancer cells, while healthy cells will survive, by inhibiting a protein that would otherwise prevent ferroptosis. I am also working with another company to design drugs for a series of rare diseases. I've been lucky to have support from both federal agencies and private companies.

"A new era of scientific research and training emerged in recent years at the interface of biology and computations, fueled by fundamental theory and methods of physics, chemistry, mathematics, and engineering."

Do you remember Eureka moments in your career?

Yes, at least once. During a regular lab meeting at the PRC, one of the students brought to our attention a paper by Monique Tirion, which she published in Phys Rev Lett during her postdoctoral studies at the Weizmann Institute. Tirion used uniform harmonic potentials and reproduced the soft modes of motion of a protein which are otherwise computed using sophisticated force fields. That paper and that group meeting became the basis of further studies that opened new avenues for us. That student who was intrigued by that paper, Melik Demirel, is now Huck Chair in Biomimetic Materials and Pearce Professor of Engineering at Penn State. Immediately after the group meeting, three of us, my former MS advisor Burak Erman and Melik's advisor Ali Rana Atilgan (faculty at the Civil Engineering Department) and myself, got together and tried to understand why this simple model worked so well and to explain it with a theoretical model (which then because the Gaussian Network Model, GNM). We said that if this theory worked, it would be a significant breakthrough in protein science. I remember very clearly how I wrote the computer code to test the predictions of GNM. I was in front of the computer together with Ali Rana Atilgan, waiting to see what the output would be. As a validation, we wanted to see how well the mean-square fluctuations of the protein's amino acids predicted by the GNM would compare with the experimental B factors or Debye-Waller factors measured for that protein. The Protein Databank provides the XYZ coordinates plus the B factors representing the fluctuations from the mean positions. I applied the method to a first protein, got to our surprise, an excellent agreement with experiments, and then I applied to a second and so on, all with the same program, just changing the input. One after another, we could not believe with Ali Rana that the simple theory worked so well; we were absolutely ecstatic. Usually, to obtain such results by molecular dynamics simulations would take weeks for each protein (in 1997), and there we were obtaining them within seconds for every protein.

So that was the Eureka moment, and that was the first paper in this area (Bahar, Atilgan and Erman, Folding & Design, 1997). And this happened just in front of the computer rather than observing something in a wet lab. The outputs from the computer program, in agreement with experimental data became the foundation of the more elaborate theory and methods we built after that.

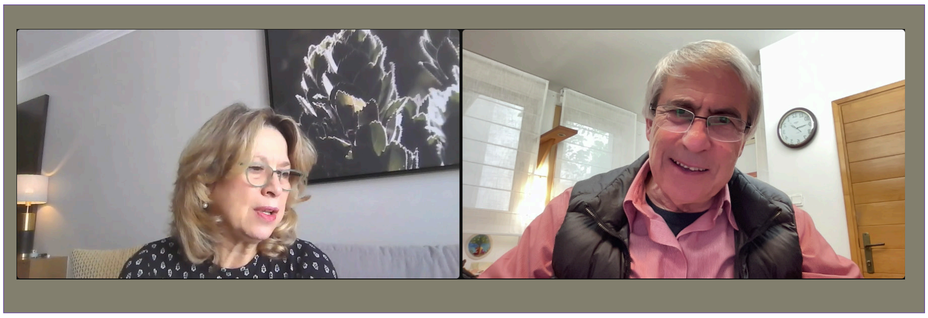


Bahar with co-authors, Ken Dill *(left)* and Robert Jernigan *(right)*, introducing their textbook, Protein Actions, at the Biophysical Society meeting in 2017.

You mentioned several interdisciplinary interactions, including civil engineering, chemical engineering, physics, and mathematics. Which university deserves the credit for offering such productive multidisciplinary interactions?

Everything I described, my BS and MS education and early academic years took place at Boğaziçi University, except for three years of PhD studies (1983-86) at the Chemistry Department of Istanbul Technical University (ITU). My experience at ITU was also useful, but I view that as a way of gaining experience in another institution to be eligible to become a faculty at Boğaziçi U. Immediately after completing my studies at ITU, literally the next

From a workshop organized by Ivet Bahar, Klaus Schulten (pioneering (late) computational biologist from the U of Illinois Urbana-Champaign) and Markus Dittrich (all three sitting from left to right) at the Pittsburgh Supercomputer Center in 2017.



A snapshot from the interview

day, I became an assistant professor at Boğaziçi University. I never did postdoctoral studies or other studies abroad. I learned everything in Turkish universities. I credit Boğaziçi U for offering an open and multidisciplinary research environment in my early years.

It is not straightforward to see such interdisciplinary interaction, even in European and American universities. Many universities are physically so large that when you stay at one part of the campus, you have no idea what's going on in the other parts. Boğaziçi University was relatively small; the engineers were close to each other, as well as the basic scientists. I was always commuting between the basic sciences and engineering schools. Not surprisingly, the PRC had members from chemistry, chemical engineering, civil engineering, and physics, thus creating a truly multidisciplinary environment.

Is that interdisciplinary culture typical of other Turkish universities?

I don't know about other universities, but it was not the case in ITU. I was in chemistry all the time, and only in chemistry. When I first came to the University of Pittsburgh, I experienced some resistance to my plan to launch a joint program between the U of Pittsburgh and Carnegie Mellon University. The University of Pittsburgh is strong in biological and medical sciences and chemistry. In contrast, Carnegie Mellon is strong in computer science and physics, and joining force would be the most natural thing to benefit both universities. But it took a lot of work to let academicians in both institutions understand there was no harm in joining forces across disciplines. Some colleagues thought we were invading their area as newcomers, but that was not true. We were just proposing to join forces, to communicate better, which is crucial for research, especially in multidisciplinary research. I wanted my students to be comfortable speaking to people from different disciplines, from chemists to clinicians. This was all about establishing a common language and peer-learning as often people from other fields talk about the same concepts using different terminology. Indeed, the joint program became a success, which is to day one of the best doctoral programs in this field.

Did you contribute to science education to attract the young generation to choose a career in science?

Yes, I believe I did, especially women in Türkiye. Not surprisingly, my first five Ph.D. students were all women who had successful careers, and since then, I mentored many women students, and I felt I served as a role model. I was very young when I became a professor and was promoted at a young age, which was presumably inspiring to young female students. That's my perception, and that's also what they told me later. They could see that even though they were very young and there was always some hierarchy, if not prejudices, it was possible to break all those barriers and achieve.

I believe that my election to the US National Academy of Sciences as the first female Turkish scientist also inspired many young students and future researchers. It has been a pleasure to give talks at many 'career' meetings, especially during COVID time via Zoom. I had the opportunity to chat with high school and even middle school students in Türkiye, who ask brilliant and stimulating questions. The middle school students, aged 10-12, were prepared to ask so many intelligent questions -naive but intelligent questions. The more trivial interactions were the regular university talks/seminars we give all the time. However, I particularly enjoyed interacting with the high school and middle school students.

I have also attended career planning meetings, such as those organized by the Biophysical Society, to share my experience. I met with many young scientists, especially those from underrepresented groups, such as women and third-world countries. I always encourage them to dream, think big, pursue their dreams, and not give up despite the barriers at the early stages.

Is there any advice you can give young female scientists in their early careers on what to do and what not to do?

My "not to do" advice is not to get distracted by some prejudiced norms and to consistently pursue your dreams. First, you need to dream and think big. Then, consistency and perseverance are essential. This is the most standard thing to say, but it is crucial. It is not enough to be intelligent; it is important to be persistent. That's what I keep telling anybody who wants to listen. They all can make it if they are ready to invest enough time and effort and not get affected by all the hardships on the way.

"It is a long, sometime tedious path to be a scientist. It is important to enjoy it, sometime to take a step back, look from another perspective, and come back with a fresh mind, which is often possible with a balanced life."

Another thing I always try to emphasize with my students is the importance of being well-rounded in balancing personal/family life and professional life. Having a good family life helps you do better in your profession. Besides, it is a long, sometime tedious path to be a scientist. It is important to enjoy it, sometime to take a step back, look from another perspective, and come back with a fresh mind, which is often possible with a balanced life.

Finally, I would also recommend them to be open to making changes in their careers, taking bold steps to follow their aspirations, and doing research in areas in which they are most passionate and curious about. The area may be, and is likely to be, different from their undergraduate or PhD areas, but the foundations they received will serve as a good ammunition in the new area. I moved from chemistry and chemical engineering to polymer science, to structural biophysics, computational biology, and systems biology and computer-aided drug discovery, each time bringing a new perspective to the new area, and I am still learning about neurobiology, infectious diseases, cancer biology and immunology.

Is the academic environment in Türkiye open and accepting regarding gender equality?

Yes, I think so. I don't know about the private industry or government service, but girls and women may climb up the scale and succeed in academia, in principle. I know that it is possible. But unfortunately, many women or underrepresented groups stay at lower levels of the pyramid. Their numbers gradually decrease at higher levels, and especially top positions, not because of professional reasons but because of cultural norms that expect women to take more responsibility in the family, and they do so. Gender inequality starts in the family with the way children are brought up and is eventually reflected in women's carrier. It takes a certain state of mind, to refute social norms, to stand firm and be determined to keep climbing up the scale. There are no rules/policies or academic traditions that stop women in Türkiye from competing effectively for top positions in academia; so, it is possible to get promoted and take on leadership roles. Of course, some support from senior academicians may go a long way, especially from women who have somewhat achieved.

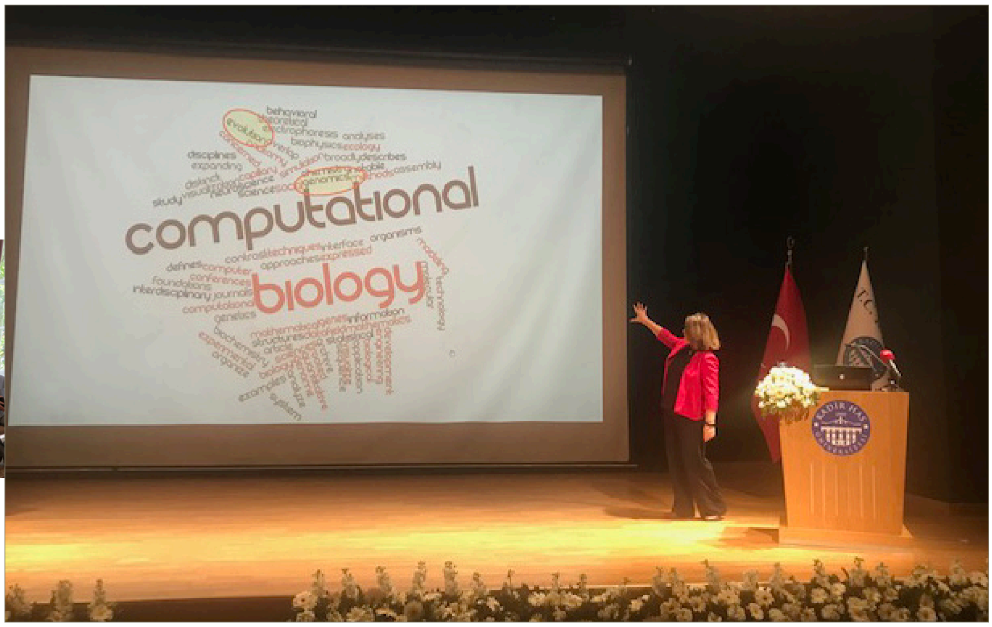
Can you relate to the Turkish brain drain, brain gain, or brain recycling, as Yuan Tseh Lee defined?

I don't know about brain recycling in Türkiye. Unfortunately, the country still experiences brain drain. The government and some universities in Türkiye try to attract those people back home. But passionate or ambitious scientists would like to work in an environment where they can realize their dreams; and they want to be in an environment where their efforts are appreciated. Since science has no boundaries, regardless of nationality, gender, or background you're coming from, you can contribute to science, if you have the suitable environment and conditions to achieve your goals. If the goal is to impact and make a difference in the scientific world, talented individuals will tend to go wherever they find better opportunities to do so. That's universal; this is an unavoidable trend everywhere.

Can you share some details about your personal life and family?

I am married and have two sons. My husband is an independent scholar. My two sons were born and raised in Türkiye. They both studied economics and business administration and live in the US. They are in their early 40s. One of them is married to his high school sweetheart from Türkiye, currently an academician at Washington University, and the other to an American girl highly successful in her career. Our family is interfaith and international. I am the happy grandmother of a 4.5-year-old grandson. I benefited from a balanced family and professional life. Finally, I'd like to acknowledge the constant support of my husband, which was essential to pursue my dreams, and I'd like to gratefully acknowledge that I completed in Türkiye all my training (BS, MS and PhD) as well as the first 15 years of my academic career (1986-2001), which laid the foundations of my current research.

Ivet with her first four (former) PhD students from Bogazici University Chemical Engineering Department and PRC, gathered to celebrate Ivet's prize awarded by Kadir Has University in 2019. All four (former students) are currently internationally recognized scientists and Professors at universities in Türkiye. From left to right: Canan Atılgan (Sabancı U), Türkan Haliloğlu (Boğaziçi U), Ivet Bahar, and Özlem Keskin (Koc U).



Ivet Bahar at the ceremony organized at Kadir Has University, Istanbul (Türkiye), as the recipient of the Kadir Has Outstanding Achievement Prize in 2019.