My blue whale: Seeking order in a chaotic world.
An autobiographical reflection.

By *Tamar Schlick*[1] January 20, 2020

FIGURE 1. A photograph of my blue whale.

DEDICATION

I dedicate this essay to my mother, Dr. Shalmith Schlick, who passed away on Jan. 15, 2020. Her dedication to science, pursuit for perfection, and intellectual curiousity have been an inspiration.

Abstract. This autobiographical reflection originated in an assignment for a Science Communication Workshop offered to ten selected science faculty at NYU last fall taught by science writer Stephen Hall. We were asked to write on the beginning of our journey in science. In my story, I recall my emerging interests in seeking order and patterns since I was a toddler growing up in Haifa, Israel. This journey eventually took me to the United States, where I earned degrees in Applied Mathematics and pursued research work in mathematical biology and computational biophysics. This research, described in my Keynote lecture on folding genes at the 7th International Conference on Algorithms and Computational Biology (AlCoB 2020) in Missoula, Montana in April, blends computational mathematics, biology, chemistry, physics, computer science, and engineering in a creative way.

[1]Department of Chemistry and Courant Institute of Mathematical Sciences, New York University, 251 Mercer Street, New York, New York 1001

LEVIATAN

I'm not sure exactly when I decided to become a scientist but, looking back, a desire to seek pattern and order was there since I was a toddler, growing up in the seaside town of Haifa, Israel.

When I was three years old, my parents gave me a big blue plastic fish on yellow wheels. It had a string at the mouth and a cover that opened, so I could fill the fish's belly. I coined this toy my "whale" ("Leviatan" in Hebrew), as its size was overwhelming. I promptly started a habit that intrigued my puzzled parents. I would load Leviatan with my all my treasures: wooden blocks, lego pieces, small dolls, and coloring set, and noisily wheel my whale along the main corridor of our apartment — from bathroom to front door. Arriving at the front door, I would unload all my loot, line up the pieces like wooden soldiers and, only when satisfied, dismantle my workmanship, load my Leviatan again, and proceed back to the bathroom. I repeated these journeys without tiring for hours.

As soon as I started to attend elementary school, I wanted to emulate the teaching experience at home, but with the roles reversed. In my little bedroom, I would line up all my dolls and beloved teddy bear (still with me today) in three neat lines, assign numbers and names to my students, and proceed to teach them arithmetic and reading/writing in front of my closet, using a long ruler as my pointer. My father, relieved that the whale migrations were on hold, decided to indulge my teaching fantasy by painting my closet with blackboard paint. He also gave me a set of colored chalks to complete the mission. As soon as I came back from school, I would rush to line up my diligent students on the floor in their assigned seats and proceed to lecture them on whatever I learned in school that day. When my father would open the door and enter my room to call me for dinner, I would turn to him with great embarrassment and say quietly, so that my students wouldn't hear: "Dad, can't you see that we are in the middle of class"?

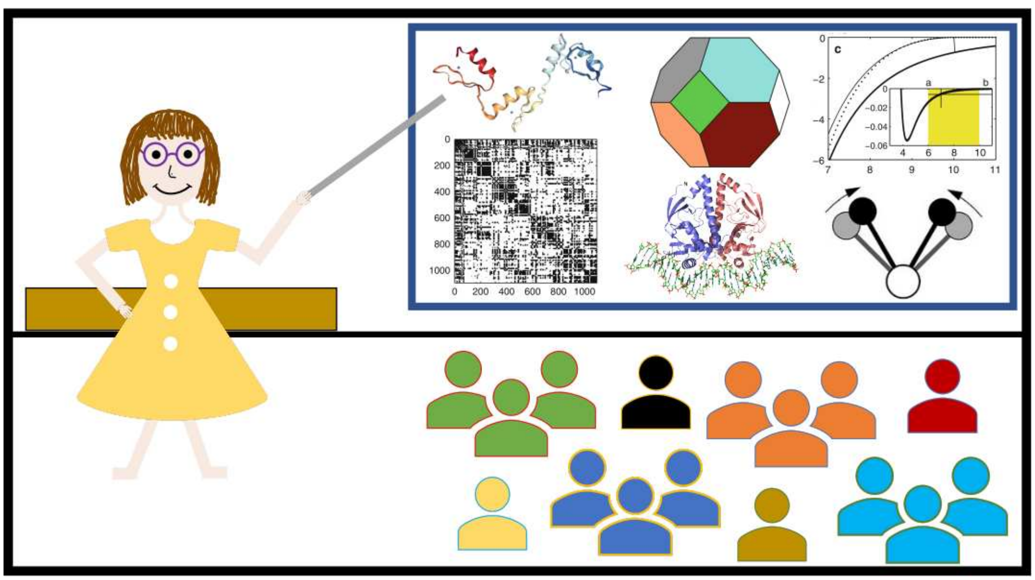

FIGURE 2. Teacher in training.

ANNE FRANK'S STORY

A year later, my parents took me to the play "The Diary of Anne Frank" at the Technion Institute of Technology theatre, which presented many children's educational programs. Although Anne's plight was remote from my comfortable life in the sleepy city of Haifa, far in those days from bustling Tel Aviv, growing up in Israel instilled a feeling of fear and uncertainty about the world, where enemies are real and war preparedness is part of life. I was so shaken and inspired by the story of Anne and her family in Holland during World War II that I decided on the spot to start writing a diary. I now have three meters of diaries since that day, as I haven't stopped writing since. As I read and re-read my entries and look at the large collection of drawings, charts, photos, and article scraps I have amassed in these volumes, many events and memories come alive that have long escaped me.

Data Collection and Analysis

From my first simple notebook which I covered with the red diamond shelf-liner paper I found in our kitchen, I loved to illustrate my writings with maps, calculations, photos, newspaper cutouts, and precise tidbits of information. In one of the first entries, I discuss the high price of entry to the private swimming pool near our home where I learned to swim. This was the beautiful outdoor pool of the Dan Carmel hotel, a sister to the well known five-star King David hotel in Jerusalem. I reported in my diary the prices of entry (in the lira currency of those days) for adults and children, on weekdays and on holidays; I then compared the total cost for our family to that required for swimming at a nearby public pool. These habits of finding value and efficiency still resonate for me today.

Whenever I received report cards, I prepared tables in my diary, recorded the grades and comments I received from teachers, and then compared these to the older sets. As those lists got longer and more complicated, I found ways of recording that information in new ways: by changing the page orientation, taping added pages to widen the margins, and finding more compact ways to label and tabulate the data. This excitement about data collection and comparative analysis rings true today as I pursue my research in biophysical modeling.

My parents, a scientist and an engineer, were very busy during my school years, proving themselves at their jobs and working hard to support our growing family. Yet they sent me to an excellent private school and made sure to enroll me in many extracurricular classes, from swimming to piano lessons. I inherited from them many math books and tools. I loved to play with these gadgets, like protractor, triangular rulers, and ellipse drawing instruments of all shapes and sizes. These studies of patterns and connections are not unlike the search for chromosome rearrangements and folding that occupy my research group today.

Puzzles and Patterns

I liked solving puzzles and building objects. I had subscriptions to magazines with puzzles and challenges and solved every one in order. I liked story problems that most of my classmates despised, as they preferred numerical calculations. A special event for me was a bimonthly radio show for adults called the "Island of Treasure." In this contest, a variety of clues were provided, and contestants had to decipher and manipulate them to arrive at a specific location in Israel where the prize was hidden. The radio show often extended late into the night, and I would lie in bed curled up with my small transistor radio and follow the treasure hunt, trying to piece together the difficult historical and geographical clues.

In middle school, I especially loved studying maps in geography class, drawing routes and paths from our small country to far away places, and learning about the weather, landscape, and culture across the world. No wonder I became fascinated by graph theory to study biological systems decades later! We use graph theory extensively now in my group to represent, analyze, and design novel RNA molecules.

When we were assigned a research project on a country of our choice, I chose Canada and wrote to the Canadian embassy in Israel as well as to my uncle in Montreal. I poured over the beautiful colorful maps and pictures I soon received, excited to see pretty snow and peaceful landscapes, so foreign and distant from my chaotic homeland, where war and death were well known to children. Despite the sheltering by my parents to many realities, the volatility of the political climate penetrated my life, where fathers, uncles, and brothers went to war and where army draft awaited us all immediately after high school. There was always a sense that we have to live life to the fullest, seizing every moment, before it may be too late. I still live with that missive, trying to make every minute productive.

Proving Hypotheses

In high school, I chose a math/physics track because a teacher recommended it. I loved all subjects, without much discrimination. Whether determining the answer of a mathematical puzzle or finding the origin of a lost tribe, I found the process of establishing knowledge fascinating.

Although I had good rapport with many of my high-school teachers, one of them infuriated me because he seemed to grade our homework without rhyme or reason. I developed a hypothesis, which I shared with my classmates, that this teacher gave all the pretty girls who smiled at him an A grade, while the rest of us received a B or lower depending on our gender and level of our enthusiasm for his teaching style and content, both of which I despised. Determined to prove my conjecture, I organized the class to submit homework assignments where half a dozen of us had filled the pages with nonsensical content, namely repetition of the sentence "The cow chewed green grass in the pastures." Sadly, my hypothesis was quickly proven to be true, as the teacher had not even noticed the garbage content and awarded us the usual grades. My complaint, which I promptly took to the principal with the evidence, eventually resulted in this teacher being expelled due to this and other incriminating incidents. This hypothesis-driven proof energized my righteous spirit and emboldened my interest in scientific research.

Fortunately, when my high-school physics teacher became interested in my progress, I started to think more seriously about what I wanted to study. He suggested that I learn as much science and math as possible and continue an academic rather than professional track. Numbers and patterns had a special resonance to me, and I decided to pursue my interest in data collection/analysis and problem solving more systematically.

Applied Math and Theoretical Chemistry Research

Soon, after a combination of world events and personal family circumstances, my family immiggrated to the United States and settled in a Michigan suburb north of Detroit. With a four-year Merit scholarship to attend Wayne State University, I connected with a small group of honor students who were almost exclusively set on a pre-med academic track. For a while, I entertained going into medicine as well. However, at the wise advice of a counselor, I promptly found a summer job at a local hospital and was soon turned off by the vials of blood and loud, cluttered environment. The organized and quiet world of numbers and theorems, with concepts and logical deductions that I could explore on my own seemed much more appealing and suitable to my personality. Chemistry Professor Bill Hase gave me the opportunity to work as a researcher in his lab, allowing me to gain invaluable experience in computer modeling and theoretical chemistry research. I enjoyed this research experience throughout my undergraduate years.

In tandem with the lab research experience, I took as many math classes as possible, solving hard homework problems and take-home exams with my fellow students, mostly men. I saw myself as one of them and so did they. As I enjoyed more advanced math courses, notably group theory and real analysis, I realized how little the public knows about math. Many people associate mathematics with arithmetic, with tasks like calculating compound interest rates or adjusting recipe quantities. Higher-order math, however, is about abstract thought and ideas, concepts to organize numbers and algorithms, and discovery of new paths and patterns by deduction and resourcefulness. Such logic and creativity excited me. From real to complex variables, graph theory to number theory, numerical analysis to computational mathematics, I found applied math infinitely wondrous. Rather than seek exact solutions to made-up problems, applied mathematicians solve real-world problems approximately. These imperfectly phrased but relevant problems are solved by creative theoretical analysis and computer modeling.

Mathematical Biology and Chemical Physics

My love for applied math soon took me through graduate school at NYU's Courant Institute of Mathematical Sciences, working with Professors Charles Peskin from Mathematics, Michael Overton from Computer Science, and Suse Broyde from Biology. I chose for my thesis topic modeling the DNA molecule and recruited these advisors to guide me in this difficult task. Solving biological problems using mathematical tools and computer modeling seemed like a perfect marriage. This research combined my interest in both life and mathematical sciences with creative problem solving and scientific discovery.

Upon graduation with a doctoral degree in applied mathematics, my academic path swiveled back to Israel on a postdoctoral fellowship at the Weizmann Institute of Science. There I learned from a grand pioneer in chemical physics, the late Shneior Lifson, more about modeling and molecular mechanics. These combined interdisciplinary experiences eventually led me back to New York City, where I work on modeling and simulating biological systems like DNA and educating a future generation of computational biologists.

Computational Biophysics and Genome Organization

In this exciting multidisciplinary field, we decipher biological phenomena by computer modeling and simulation. In the subfield of genome organization on which my group focuses, we seek to understand how the molecular agent of heredity, DNA (deoxyribose nucleic acid), folds and unfolds in our cells to regulate basic processes of life. These processes include DNA replication, expression of genetic traits, and disease progression. Human DNA is organized in our cell nuclei as chromosomes in the shape of long spaghetti-like string called the chromatin fiber. This spaghetti adopts different shapes and separates into various compartments in our cells depending on the state of the cell. Understanding these shapes and patterns is key to understanding regulation of the basic processes of life. While the first order of biological information is encoded in our DNA through the DNA (primary base) composition (those A,C,G,T components), another level of regulation distinct from the sequence is expressed through the chromatin fiber structure. This "*epigenetic regulation*" — through changes in the structure of this spaghetti-like string — is now believed to hold part of the key for understanding human disease. Our models for the chromatin fiber are revealing folding patterns encoded in the chromatin fiber that direct the folding of genes, thereby determining when genes are silenced (not expressed) or when they are switched on (expressed). Knowing how to control this switch can help halt the progression of events that lead to abnormal cell growth in cancer. Such an understanding has immediate applications to disease diagnostics and therapy. On a technical level, the work involves developing innovative models and algorithms for simulating the structures and motions of these complex biological systems, merging mathematics, biology, chemistry, physics, computer science, and engineering ideas.

Whether I'm writing papers on chromosome folding or teaching at a summer school on cancer genomics, I still feel like that toddler, shuffling objects and ideas from place to place, trying to establish pattern and order and make discoveries to comprehend this complex and chaotic world. My Leviatan is alive and well, occupying a prime spot in our Greenwich Village apartment, having weathered the years a bit better than me. His reassuring presence reminds me of the far away sea and vast knowledge still awaiting discovery.

Tamar Schlick is Professor of Chemistry, Mathematics, and Computer Science at New York University. Her research focuses on computational biophysics, specifically chromosome folding and gene regulation. She has authored more than 200 research articles and is the author of an interdisciplinary textbook on molecular modeling (Springer-Verlag, Second Edition, 2010).

ACKNOWLEDGMENTS

I thank my family for making my journey in life and science a happy one. I thank my mentors and mentees for making this wonderful life in science possible. Current research is made possible through an NIH MIRA Award from the National Institute of General Medical Sciences R35GM122562. I thank Stephanie Portillo-Ledesma for assistance with two figures.

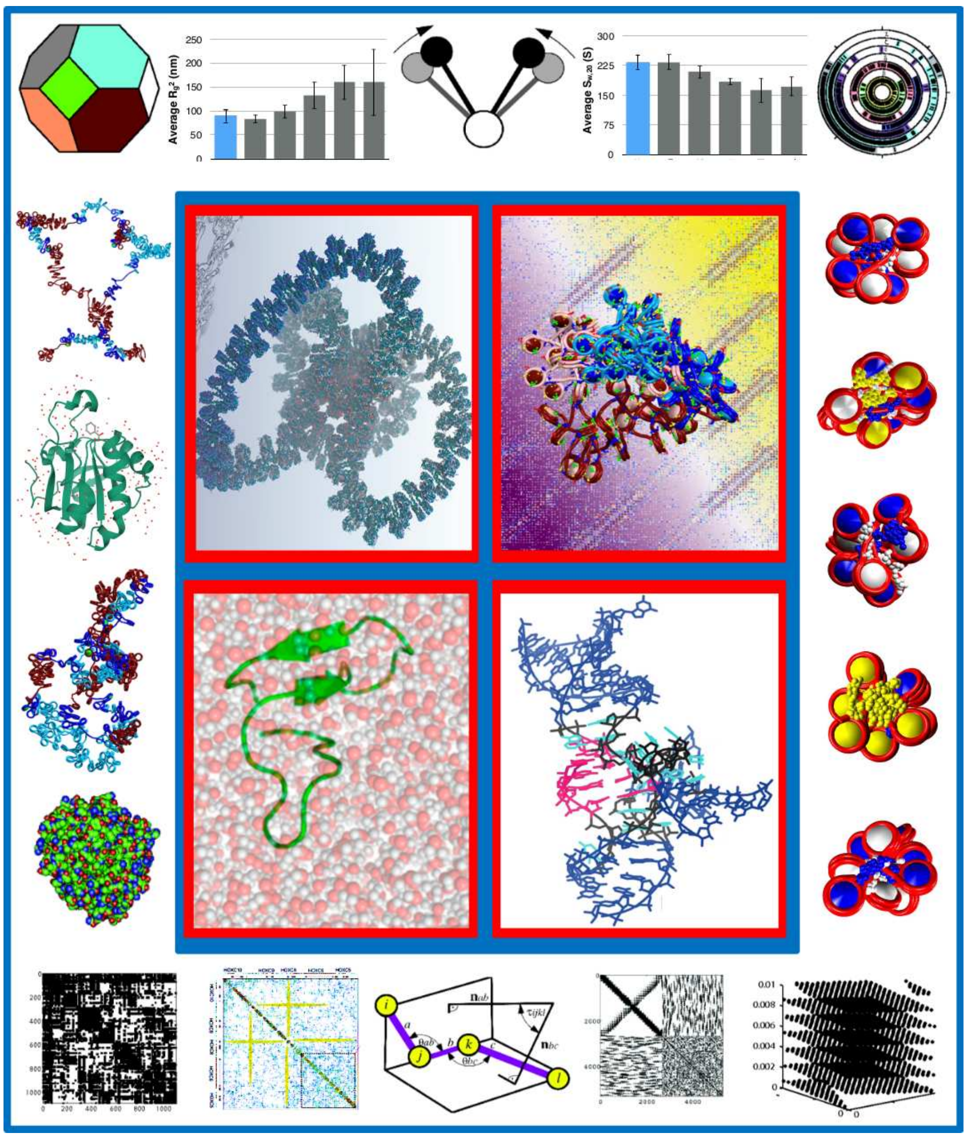

FIGURE 3. A collage of various plots, analyses, and images required in computational biophysics to study biological molecules and simulate their structures and motions to infer biological activity.