

It's Not Magic, It's Biology:
a guided tour through
your molecular world

by

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with illustrations by

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ISBN# XXXXXXXXXXXXXXXXXXXX

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Dedication:

Of all the people that might be recognized here, it is my sister, Jenny Leaser, to whom this book is dedicated. As I wrote the book, I kept asking myself if my non-scientist sister would understand what I was trying to say. If the answer was “no”, I tried again. Hopefully, these chapters will help you think about molecular biology and how it applies to your world.

I also want to thank Warren J. Hagestuen, who was my first biology teacher in 7th grade, for starting me down this path in the first place.

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Preface

As a professional molecular biologist, one of the most difficult questions I get asked when I meet a new person is “what do you do for a living?” Here is how the conversation usually goes:

“Good to meet you Allan, what do you do for a living?”

“I am a professor at Boise State University. I teach classes in cell biology and molecular genetics and run a research lab.”

“That sounds fascinating, what do you work on in your lab?”

“I study a cell communication pathway called Notch. It’s basically a way that two cells can use proteins on their cell surfaces to make contact and communicate with each other about what they are doing.”

Head nodding politely. “Oh, that sounds interesting. Done any fishing lately?”

After years of having this conversation, and of immediately losing my audience, I’ve realized that many people don’t care to talk about how cells, much less how molecules, work. It could be that they don’t find it interesting, but more often I think it’s that they have no reference points from which they can construct an understanding of what happens in my lab. Or maybe they think it’s so confusing there is no point in talking about it. This isn’t surprising since molecular biology is rarely discussed, even in popular science. Myriad great science articles about fascinating

topics are published every day. Many of them could easily introduce and discuss some simple molecular mechanisms, yet the vast majority of popular science articles only vaguely hint at the fascinating molecular biology that is just under the surface.

I have also noted that there are very few resources designed to teach non-scientists about how molecules work in living systems. Almost every molecular biology book I have ever seen, with the exception of *The Manga Guide to Molecular Biology* and maybe some of Larry Gonick's *Cartoon Guide* books, have been written for upper level college students in advanced biology classes. This is unfortunate. Molecular interactions are the foundation of our everyday life; individual molecules shape and govern how we perceive every single experience we have, even though we cannot even see them. And yet, most people don't understand the simplest principles of molecular behaviors.

I think this lack of understanding is unnecessary. While molecular interactions can become very complex, I assure you that you don't have to be a professional molecular biologist to appreciate the simple elegance of what molecules do and how they do it. I think that a very fundamental understanding of molecular biology can enrich anyone's life, and should be accessible to everyone!

So I decided to try to fix the problem in the way that most professors do, which is to say, I wrote a book. **The goal of this book is to help people understand how biology works at a molecular level and to help them appreciate the molecular world.**

It may sound funny, but I am indebted to electric eels since

these creatures gave me the idea that sparked this book. As I taught students about electric eels, I thought to myself, “how could anybody **not** be interested in knowing and understanding how an electric eel produces several hundred volts of electrical energy and uses it to communicate and capture food?!” If you don’t understand it, it might seem like magic. But here is the really cool thing, if you **do** understand how eels generate this voltage, it’s even **more** amazing than magic. These “magical” abilities that living things have are built on very simple, yet highly effective, systems that nearly everyone can understand. My challenge, of course, is to help you really appreciate how amazing that eel is, even if you don’t have a background in cell and molecular biology.

Appreciation of an idea or a phenomenon is a real gift. My wife is a professional musician and has tried to get me to **really** appreciate what she calls Bach’s *cosmic music*. I don’t have a music degree. My playlists are filled with heavy metal music. I acknowledge that Bach sounds nice, but it’s difficult to realize the true beauty of Bach’s work since I don’t have the knowledge that would allow me to fully appreciate his achievement. With a little bit of handholding by a professional who can help me see the music from a trained perspective; I have gained some level of appreciation for what’s happening with the music without needing to go back to college again. This appreciation opens up and deepens my understanding of the world. That’s what I wanted to do with this book; to give non-scientists an appreciation for what’s going on in the molecular world and how that world works. So, let me hold your hand and try to show you that the molecular world is not magic, it’s just biology.

And also, for the record, the fishing has been great lately.

Introduction

Who cares about molecular biology?

In my opinion, the first and best reason to understand at least a little molecular biology is that it will change the way you look at the world. It will give you a better appreciation for all life. Even murder hornets. The second reason is that, whether you know it or not, you depend on molecular biology to get through every single day and having a little understanding will help you to navigate your world.

Don't believe me that molecular biology impacts your everyday life? Here is an obvious example from 2020: the COVID-19 pandemic. How can this little invisible virus do so much harm to so many people and to the global economy? The simple answer is rooted in molecular biology. Viruses are super elegant, compact packages of minimalist molecular biology that have only one mission in "life": to make more viruses just like them. But the virus needs a host, and in order to get inside that host, the virus needs something in the host that it can stick to. The SARS-CoV-2 virus uses a sticky protein on its surface, aptly named the *spike protein*, that tightly sticks to the *Ace-2 protein*, which is produced in your body and presented on the outside of some of your cells. The interaction is akin to molecular Velcro. When the spike protein binds to Ace-2, the binding interaction fools your own cell into pulling the virus inside of itself where the virus can complete its mission. **This simple interaction between two proteins based on matching shapes and chemistries is one of the most fundamental ideas in molecular biology and is arguably the root of all the devastation of the viral pandemic.**

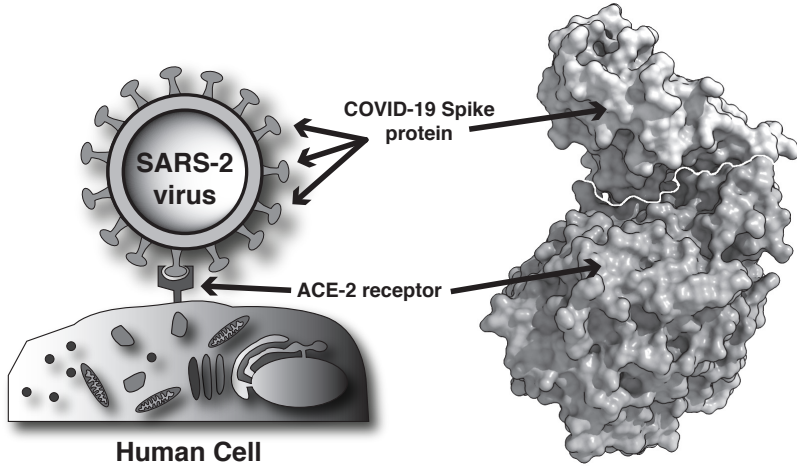


Figure 1: Sars-2 spike protein binding to its receptor, ACE2. The SARS-CoV-2 spike protein binds to the ACE-2 receptor on the surface of cells in your lungs and blood vessels. The figure on the right shows the actual interaction between the spike protein and its receptor. this interaction is only possible because of the perfectly matched shapes and chemistries of these two proteins. This is a fundamental concept in molecular biology. Image on the right is taken from open access paper [1].

What about the new vaccines that have been approved to prevent the spread of COVID-19? The first vaccines are called mRNA vaccines and they work through molecular mechanisms that are shared by all life on Earth. These mRNA vaccines are different than traditional vaccines. When the mRNA vaccine is injected into your arm, your cells read the mRNA code, produce the same spike protein that the virus uses to attach to cells, and presents that spike protein to your immune system. Your immune system recognizes that the spike protein is a “foreign protein” that is not supposed to be in the body and starts making antibodies, which will attack any other spike proteins they encounter. We only know how this works because of all

the effort of molecular biologists, and we only learned how to make and use these mRNA vaccines after many years of studying these basic biological mechanisms.

Finally, what about all the new SARS-CoV-2 variants that began popping up in early 2021? These variants are new SARS-CoV-2 mutants that have evolved as the virus has spread through the human population. Some of these mutants have subtle changes in their spike proteins that could possibly make them resistant to our new vaccines, although this does not seem to be the case, yet.

So why do **you** need to understand molecular biology? Because it makes you prepared to understand the world around you. You will be less dependent on what other people tell you, and more empowered to make up your own mind about what is true or what is just somebody's online opinion. We are bombarded by information every day and having some basic skills to sort the truth from the "fake news" has never been more important than it is right now. For instance, a question that you will undoubtedly face is whether or not you are going to take the COVID-19 vaccine. Whether you do or don't take the vaccine is your choice, but if you understand a little about how the molecular biology of the vaccine works, you will be in a better position (with your doctor's advice of course) to confidently make the choice that is right for you.

I could go on and on describing how molecular biology impacts your every day. I don't think you want that though. You already picked up this book so I have to assume you are ready and eager to learn, and that you don't need me to try to convince you that you should! So, let's get to it!

Molecular Biology 101

In the first day of your first high school biology class, your teacher probably taught you that “bio” means life and that “ology” is the study of something. Putting this together then, biology is the study of life. Okay then, what is molecular biology? It’s the study of the molecules that all life depends on. The study of the molecules of life. No doubt you have heard of these molecules already even if you didn’t appreciate them as molecules of life. They are proteins, carbohydrates, fats or lipids, and the nucleic acids, DNA and RNA. Molecular biology seeks to understand all the complexities of how these molecules work.

Let’s talk specifically about proteins for a minute since the vast majority of the examples I describe in the book are proteins. First, what are proteins? In a simple sense, proteins are the main molecules in cells that makes things happen. Proteins are sometimes called the "workhorses" of the cell. Whenever something happens in a cell, you can bet that proteins are probably making it happen.

Where do proteins come from? You probably remember that the information for how to make a protein is stored in genes within the DNA, and that DNA is copied to make an RNA that serves as blueprint for the protein. A simple way to think about this is to imagine a recipe for your moms favorite dish that is written on one of those 3X5 notecards that used to be so popular. The note card is like the DNA and stores the information but you can make a copy of the recipe with a copy machine. Think of the new paper copy as the RNA. The cell uses the recipe/information in the RNA copy to make the dish. In the case of a protein, the dish is going to be a yummy chain of amino acids.

The amino acids are the ingredients for the dish and they are connected end to end according to the directions in the RNA, resulting in a protein. Sometimes, several individual proteins can be combined together to make a single larger protein with multiple subunits. Many of the proteins we will be looking at consist of four or more identical subunits. Overall, this process of DNA \rightarrow RNA \rightarrow Protein is called the “Central Dogma” of molecular biology.

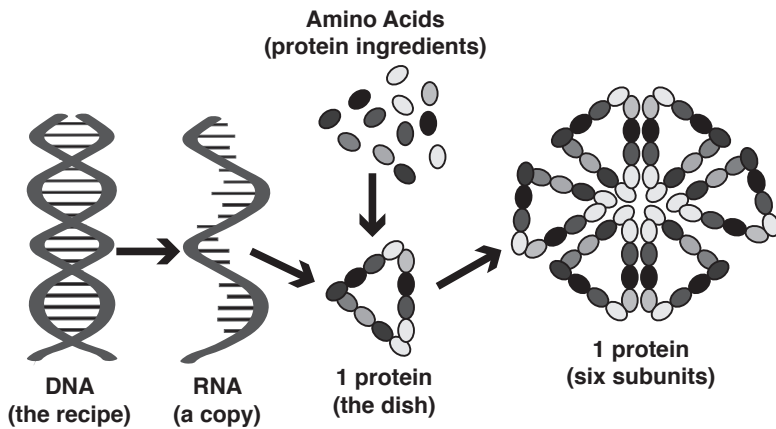


Figure 2: The Central Dogma of molecular biology.

This may be the technical description of what proteins are, but when most people hear the word “protein”, images of steak and eggs appear in their head. This isn’t wrong, but it’s not exactly correct either. Steak is animal muscle, and that muscle is made of cells that have lots and lots of individual proteins inside. Most of the proteins in those muscle cells are “molecular machines” that are dedicated to giving muscle cells the ability to move. But these proteins are just a few kinds of proteins. We don’t know the exact number, but most scientists accept that humans can make a few hundred thousand individual and different kinds of proteins. Each of these many proteins has an individual function and working together, they give cells special

functions. Some proteins produce energy from the food we eat, some proteins enable cells to communicate with each other, some proteins form long fibers that give cells shapes, and some proteins allow cells and muscles to move. There is a nearly endless variety of functions that your proteins perform in your body. Understanding how these proteins function is a major part of what it means to study molecular biology.

One of the most challenging things about molecular biology is that, while there are only four basic kinds of molecules of life, there are almost limitless variations of each type. Proteins, for instance, have a mind-boggling diversity. As a wild guess, I'd have no trouble believing that there are trillions of different kinds of proteins on Earth, and this is probably a gross underestimation. No individual, no matter what their IQ is, could possibly know and understand the molecular details of all these proteins. Because of this, many of the world's most dedicated molecular biologists choose to learn everything they can about just one protein. But these molecules don't give up their secrets easily. Some people spend their entire scientific career studying how a single protein works. Through decades of research by thousands of individuals, we have gathered enough of this deep knowledge to make some generalizations about how molecules work. The good news for non-scientists is that by studying these generalizations, even an inexperienced person can get a pretty good conceptual understanding of how molecules work.

The intent of this book is simple; to help people tap into the generalizations of molecular biology that we have discovered over the years. To translate these generalizations into plain language so that we can all appreciate the elegance of molecular mechanisms. The people who I think will really benefit from this

book are those who lack (but want) a conceptual understanding of biology, and their world, at a fundamental level. People who don't even know where to begin. I'm thinking of people who were interested by biology and chemistry, or even physics, in high school, but didn't have the opportunity to go to college, or maybe did go to college but majored in a different field. People who have tried to learn some molecular biology but have found it really difficult because there are no translations from deep science into common English. That's what this book is. A translation between the "geek-speak" of modern molecular biology into the common tongue we all speak in our kitchens. Or, maybe you're a person who has a biology degree and has a decent understanding of molecular biology but finds the topics of these chapter titles interesting and exciting! I'm definitively in this last category. Despite having many years of investigating and teaching these subjects under my belt, I immensely enjoyed the process of researching and writing that went into this book. I learned quite a bit myself. If you get even half as much enjoyment from reading this book as I got from writing it, you are in for a treat.

Since I am writing this book in a time where knowledge is immediately accessible on the internet, I highly recommend that you read this book with a smart phone or an internet-enabled device of some kind nearby. Most of the topics I introduce are easily searchable, and there are some real gems of videos and well-written science articles about some of them. I have pointed out a few searches that are worth your time, and I encourage you to come on this journey with me but to take whatever detours capture your interest. If you don't have an internet-enabled device – don't worry. I have tried to provide complete explanations, and my talented daughter has contributed many

original illustrations that I think are both enjoyable to look at and effective at explaining difficult concepts.

As a final note before we get started, when I sat down to begin writing in the spring of 2020, during the COVID-19 pandemic, I started off by writing about electric eels. As I mentioned, eels were my initial inspiration for this project. I quickly realized that I couldn't jump right in with the eel, though, since understanding eels requires a basic understanding of topics like basic receptor-ligand interactions. I even started to worry that some readers might not remember basic chemistry or maybe what a cell is. I really struggled with balancing what introductory information to provide. I even wondered for a while if I should go way back to the beginning and discuss what atoms are. In the end I decided that, in order to keep this book short and sweet, I should assume that readers have taken, and remember at least a little, high school biology and chemistry. My goal was that anybody with that background should be able to understand and appreciate this book.

Hopefully I succeeded, and you enjoy this ride through the molecular world. By the time you reach the end, I hope you look around at your world with different eyes. I hope you come to appreciate that even the most common organisms and experiences you encounter every day are actually phenomenally elegant and amazing. I hope that you start to think about the molecular biology that is going on, in, and around you, every millisecond of every day.