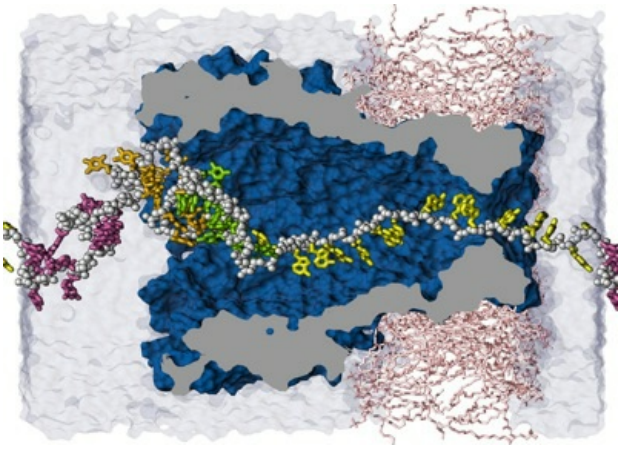
Aleksei Aksimentiev makes medicine personal with supercomputers

Jorge Salazar

Aleksei Aksimentiev is developing an inexpensive way to sequence a person's DNA. In other words, this computational physicist from the University of Illinois is learning how to determine the precise ordering of the bases (A,T,G,C) from which DNA – the famous double helix molecule that transfers genetic characteristics from each parent to each child – is composed. He's using some of the world's fastest computers, such as the AMD Opteron-powered Ranger computer at the Texas Advanced Computing Center. His goal is to create what's called personalized medicine. Dr. Aksimentiev spoke with EarthSky's Jorge Salazar.



Give us your take on personalized medicine and how your work with supercomputers is making a difference in advancing the science.

The goal of personalized medicine is to make medical procedures more effective by tailoring them to the genetic and biochemical makeup of individuals.

As you know, all humans are slightly different partly because of the program that is written in our DNA. So figuring out what is written in my, your, and other people's DNA is the first step towards making personalized medicine a reality. Here at the University of Illinois, we are using supercomputers to discover new ways to sequence DNA to make this procedure faster and less expensive so it can be used as a routine medical procedure.

What is sequencing, and why is that important in understanding DNA?

DNA is a very, very long molecule. You can think of it as a very long word made of just four letters, A, C, G, and T.

And *sequencing* is determining the exact sequence of these letters in this very long word. It's needed because we'd like to know why some people get sick and some people don't – why some drugs work for some people and some drugs don't. Understanding genetic sequencing will give us a more general picture of why we are all somewhat different.

Figuring out a way to determine the sequence cheaply is essential because right now it's a very costly procedure.

Would you give us some numbers here?

This is a very interesting story because 10 years back, the costs of personal genome sequencing were astronomical. It was a billion dollars [to sequence a person's DNA]. Five years back, it was ten million dollars. Current sequencing costs are about fifty thousand dollars.

Tell us about your project to create machines for personal genome sequencing that will be less expensive and so more accessible to hospitals. How does this all work?

The basic idea is that we take a DNA molecule and thread it through a very tiny pore – a *nanopore* – in a very thin

membrane.

Click here to view a video illustration. (Requires QuickTime player, available here.)

And as the molecule passes through this pore, we record electrical signals that result from DNA interactions with the nanopore. And thereby we record the DNA sequence just directly off of the molecule.

What is a nanopore, and how is it able to read these DNA codes?

First of all a nanopore is a pore one nanometer – one billionth of a meter – in diameter, along with a very thin membrane. Just to give you an idea of how thin the membrane is, it's about 1,000 times thinner than the foil we use to wrap our groceries. And the pore itself is about 10,000 times smaller in diameter than a human hair.

Now, this size is comparable to the size of a person's DNA. So, when DNA is confined to this pore, you really localize a very tiny fraction of the DNA, just a few letters.

So these nanopores are tiny holes, incredibly small like the pores of our skin, and computers are able to create realistic simulations of DNA actually going through these tiny holes?

That's correct. We can simulate in atomic detail the process of DNA transfers through these nanometer pores. And we can directly compare the result of the simulation with experiments, which gives us confidence that our computational model is correct.

How does this technology change medicine? How does it improve people's health and well-being?

First of all, it's really an ultimate diagnostic tool to determine all kinds of genetic disorders. Secondly, it will be crucial to developing cures for cancer. That's because, as you know, cancer is a disease of DNA. And the most direct way to find out what kind of cancer it is – and possibly learn what drugs would affect the cancer – is to sequence the genome.

Would you give us an example of how personalized medicine can be employed to help a patient from preventative care to diagnosis to treatment?

The main idea is that when a patient comes to hospital, he or she would give blood. And in real time, maybe in less than an hour, the physician would get access to the patient's DNA sequence. Then the physician would see which diseases could be associated with the genetic makeup of the individual and prescribe drugs that would be most effective.

At what stage is the research right now?

This is a very good question. I must say that it's still in basic research. Researchers have been able to sequence, so far, only very short fragments of DNA. But, it's conceivable that within a two-year frame we might see an experimental demonstration of DNA sequencing using nanopores.

And after that, it would probably be another two years before a first commercial device is available on the market.

After that, it could make its way into a hospital near you. But that really would depend on the market forces, patent law, and other factors that are beyond science.

But supercomputers do allow us to develop new technologies to improve human health, one of which is personalized medicine. One thing about personalized medicine that I really like to say is that *it's coming*.

What general impact do you think supercomputers are making in understanding human genetics?

Supercomputers – and the way they have been developing over the past 10 years – are offering a completely new

perspective. Supercomputers are making it possible for us to understand the intricate machinery of a biological cell.

So in my field, biological physics, the biggest question is, really, what is life? How does the collection of proteins, water, salt, and lipids that make up our cells come to be alive?

And there are several ways people try to address this question. Some experimentally would like to combine and make a synthetic cell by putting together different compounds. Others would take a living cell and trim down the genome to make a minimal cell.

I think the answer would also come from our ability to simulate a cell in a computer. Then we can really pinpoint what is life and what is not.

How close do you think scientists are to being able to do that?

We're still far from that. My estimate is that the earliest would be in at least 10 years – probably 20 years – from now. But computer development has really exceeded my expectations and everybody's expectations.