FeaturedLab

BY KRISTIN COBB, PhD

The Institute for Systems Biology

The Institute for Systems Biology (ISB) was founded in Seattle, Washington, in 2000 by **Leroy Hood, MD, PhD, Alan Aderem, PhD**, and **Reudi Aebersold, PhD**. Five years later, they are pursuing the frontiers of systems biology in an interdisciplinary, non-academic enviroment with 170 staff members and a 65,000 square foot building.

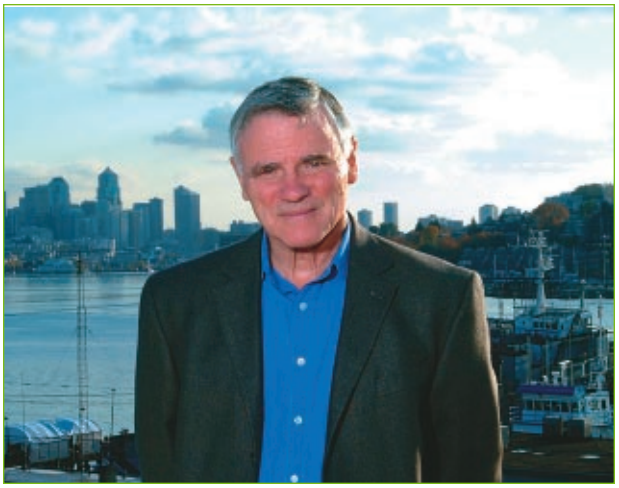
Biomedical Computation Review spoke to Leroy Hood, president of ISB.

Q: How do you define systems biology?

A: Systems biology is the window by which biological circuitry can be deciphered. If you broke a radio into its parts, this would not give you insight into how the radio works. Rather, you would have to develop techniques for seeing how the parts connect together into circuits and how these circuits interact to convert radio waves into sound. Living organisms also operate by virtue of networks that function together. You need systems approaches to define the networks and understand how the networks interact to carry out biological functions. You have to look at the whole system and see what it's doing as you tweak it in various ways. The old fashioned approach of studying one gene and one protein at a time is inadequate.

Q: What was the motivation for setting up the Institute for Systems Biology?

A: The institute was set up to learn how to do systems approaches to biology. It was set up in a cross-disciplinary environment because we are convinced that biology needs to drive technology and computation. None of the tools we have today are adequate to the task. It's critical that you not just practice the biology but you invent the future with the new technology.



Leroy Hood, MD, PhD, president of ISB. Courtesy: ISB

Q: What was the rationale for moving outside of academia?

A: The bureaucracy of classic academia was getting in the way. We needed to create the cross-disciplinary environment, high-throughput facilities, and computational infrastructure. We needed the flexibility to negotiate strategic partnerships quickly and effectively. We've been responsible in one way or another for the spin-off of nine companies in five years, and we've started a big K-12 science program. Those are things we could not have done at a university.

A lab meeting in one of the Institute's many shared spaces that encourages cross-disiplinary interactions. Courtesy: ISB

Q: Can you give an example of systems biology at work in your lab?

A: The halobacterium project, led by **Nitin Baliga**, is very interesting. Halobacterium is a simple organism with 2400 genes and only about 125 transcription factors. We perturb some of its most interesting circuits and see what it does: it's resistant to radiation, so we give it radiation; it deals with metals very well, so we give it large doses of metals; it shifts how it makes its ATP when oxygen is low, so we put it in a low-oxygen environment. From these experiments,

we've gotten this first glimpse of the interconnected networks that exist. And we've been forced to develop new computational approaches to integrate these data. These tools will all be extended up to the higher organisms. The simpler organisms drive—if not an understanding of the higher organisms—the technology that will enable us to understand them.

The Institute, near Lake Union. Courtesy: ISB

Q: What is some of the work that you've done in prostate cancer?

A: Up until recently, we've done very nice work to show unequivocally that prostate cancer is a genetically heterogeneous disease. Now we are taking tumors and their normal counterpart tissue and looking at DNA arrays to see how the patterns of gene expression have changed. We've compared prostate cancer tissue at an early stage, an intermediate stage, a late stage, and a metastatic stage with normal tissue. Really recently we've begun to delineate the prostate-specific secreted molecules that we believe will constitute molecular fingerprints for telling us the exact state of the prostate: Is it normal? Is it inflamed? Is it hypertrophied? If it has cancer, which of the four or five types of cancer does it have? The idea is that the blood is going to be a window into health and disease.

Q: How far along are we in being able to use molecular fingerprints in the blood to diagnose disease?

A: We are at the very beginning. That's the vision. The vision is that we can computationally make predictions about the molecular fingerprints that will exist for each of the different organs. We've now set up a company (Homestead Clinical Corporation) that is beginning to search for these molecular fingerprints. I think within a year we'll have three to five markers for prostate cancer and three to five for ovarian cancer. We're also starting to do blood molecular fingerprinting analysis in brain cancers. Glioblastomas are an irreversible death sentence, but that's only because they're detected so late. If you can detect them early, you actually can cure them. So we'll see if we can do early detection and save people's lives.

Q: What advice do you have for young scientists?

A: I think anybody who doesn't want to be left behind is going to be forced to move toward systems biology. And I think a lot of this will come from younger people, who recognize what the future is. So my advice to them is, first, it's really important for young scientists to learn to think in a more global way. We have many lab meetings where I will come in and say: "Here's an idea we're going to talk about." And everybody will have to say what they think about that idea. It's important to have your focus and do your thing but it's also important to think in a big way. Second, it's really important to enjoy what you are doing. Passion is what makes science fun. Finally, I think this is the most exciting time in science in the 40 years of my career. In some ways I wish I were young again so I could start all over. On the other hand, I'm happy where I am now. Maybe I wouldn't do as well the second time around. □

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ISB QUICK FACTS

What: Non-profit research institute
Where: Seattle, Washington
Faculty: 11 members
Staff: 170 members
Facility: 65,000 square feet
Funding sources: 80% federal grants & contracts; 20% grants from foundations, industry, individuals
Annual symposium: every spring