DOUGLAS HEALEY/AP/PA

Thomas Arthur Steitz

Lunchtime science

Biophysicist at Yale University in New Haven, Connecticut. Shared 2009 Nobel Prize in Chemistry for knowledge of the structure and function of the ribosome — the intracellular machine that builds proteins from instructions carried by RNA. Born in Milwaukee, Wisconsin in 1940. The oldest of five children, Steitz has admitted to being an average student in high school, until motivated to compete against his youngest brother who was getting better grades. Steitz was a keen musician and chorister, and considered a career in music before finally choosing to pursue science.

In Lindau, you said that eating lunch alone in your office is bad for doing good science — do you always think and act scientifically?
The reason it's important to have lunch with colleagues, students, postdocs, faculty etc., is so you can talk about ideas and experiments and science. It's a great opportunity to connect with others. See what they are doing, tell them what you're doing.

I picked this up from my years at the Laboratory of Molecular Biology in Cambridge, UK. Everybody would have coffee in the morning, lunch and tea together in the afternoon. They would always gather around tables and exchange ideas. It helps to stimulate thinking, to give ideas about new experiments; or you might realize that an experiment you wanted to do is perhaps not the best idea. It goes both ways.

Here [at Yale University] we often have lunch with faculty from other departments, such as geology, chemistry or physics. Obviously you can't talk about your experiments in as much detail with these colleagues, but I have still learned a lot of interesting things, for example about global warming — erosion of salt marshes and rising sea levels.

The view that scientists are insular, quiet and uncommunicative is not correct. I've had some students like that in my lab, but they're not the best scientists. I can't exclude the possibility that it's field dependent: theoretical physics might be one scientific discipline where it's more important to think through your own thoughts. But certainly in biological sciences, which are so complex with lots of bits of information to piece together, having conversations and learning things is very useful in solving puzzles.

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Has winning the Nobel prize changed the way you eat lunch?
I'm not able to eat with colleagues as often as previously. But then again I'm also able to have lunch in many more places in the world, such as China.

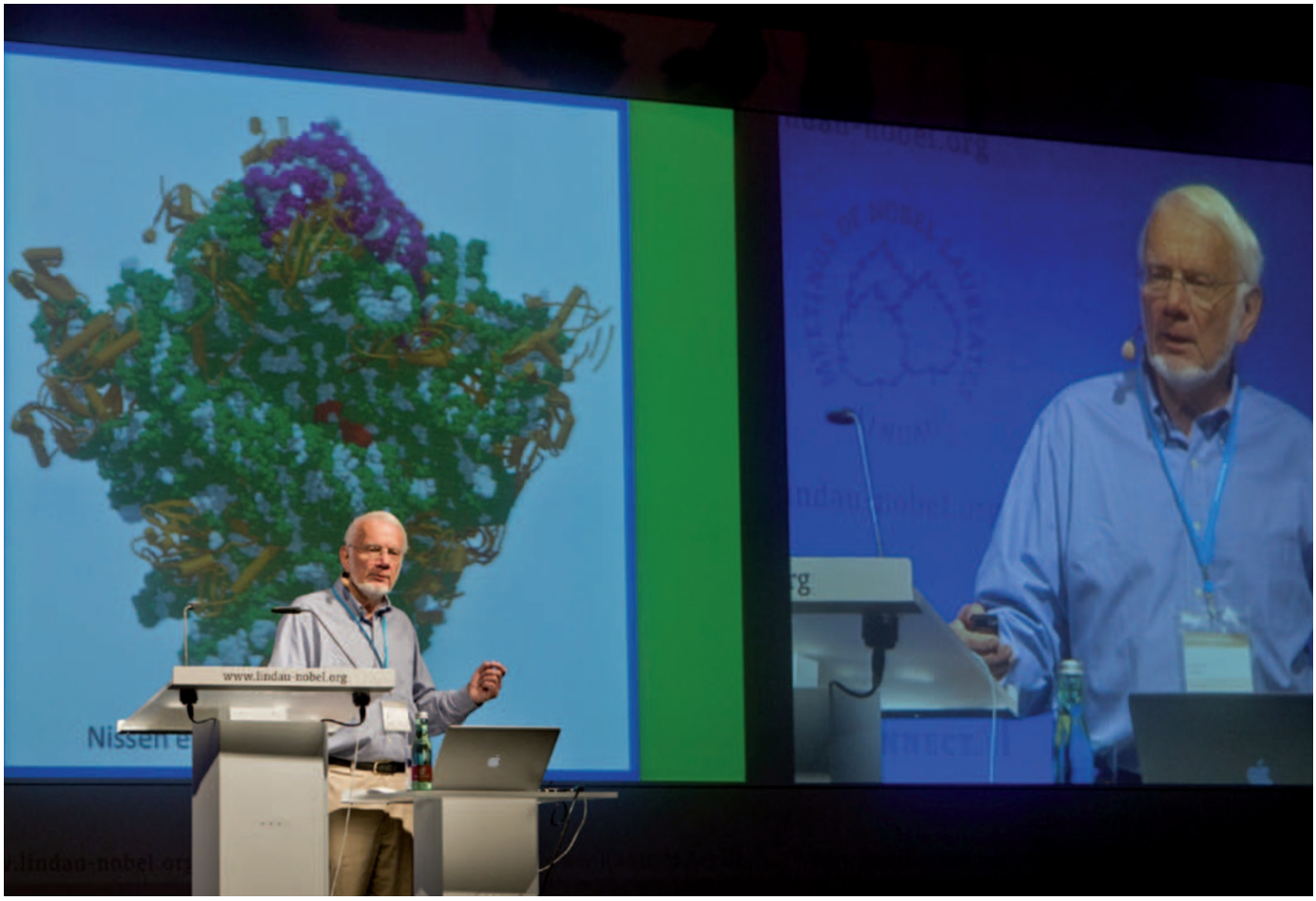
What most motivated you in your work: the Nobel prize, being published, enthusiasm, curiosity or a desire to be of service to mankind?
I was never motivated by the Nobel prize; I think that's the wrong goal. I'm just curious, and everybody I know who does well in science is very curious. You have questions and you want to know the answers, and you get excited when you find things out. You are the kind of person who wants to turn over the rock and see what's underneath. This curiosity is also driven by the adrenaline rush that hits you when you find the answer to a question you have been asking.

Of course, when it comes to being of service to mankind — this is important when considering which questions to ask in the first place. Some problems have more practical impact than others. For example, in the late 1980s, several postdocs came into my office saying that we should do something about HIV, as it was becoming clear it was a big problem. I decided that we should work on HIV reverse transcriptase. That made sense to us because we had been studying DNA polymerases involved in replication, so we could then ask about the differences between reverse transcriptase and DNA polymerase — and, by the way, we'll study it in complex with a non-nucleotide inhibitor so we can also help with drug design. That way we could kill two birds with one stone: furthering our research into these types of enzymes and also into HIV proteins that can assist in developing drugs against it. So it's a combination of following your own nose and doing something that will be helpful.

We also solved the first structure of synthetase and transfer RNA (tRNA) in 1989. We went on to solve the structure of synthetase and tRNA in complex with an antibiotic to see if we could design new antibiotics. You have to look for opportunities that achieve a number of goals.

My major goal is not to design pharmaceuticals, important and exciting as that is to people in the pharmaceutical industry, but I'm not opposed to doing that if it fits in with other objectives.

CH. FLEMMING/NOBEL LAUREATE MEETINGS



Steitz's lecture at the Lindau meeting in 2011 discussed a broad range of topics from the structure of the ribosome to the better design of antibiotics.

As a recent laureate, what impact do you hope your Nobel prize will have?
I frankly think that just because I'm good at structural biology and uncovering the mysteries of how molecules work, I'm no expert on peace. I have opinions, but they should not be any more highly regarded than any others.

That said, people pay more attention to what laureates say — more than they should — and you should take advantage of the opportunity when it comes. However, that's not my objective at the moment. I get letters from various organizations wanting us to sign letters for this or against that, and I'll sign if I agree with it. But in terms of going on a campaign — that's not on my list of things to do.

Do you think bacterial antibiotic resistance is as big a threat as the media makes out?
I think it's gargantuan. About 100,000 people die each year of methicillin-resistant Staphylococcus aureus (MRSA). More people die of MRSA infection than from AIDS. It is very important to have more antibacterial drug development.

Fungal infections are even more difficult to treat. Bacteria are prokaryotes, but fungi are eukaryotes like us, so we need drugs that can target the fungus but not the host.

Together with a few colleagues, I founded Rib-X Pharmaceuticals about ten years ago. The idea was to use the structure of the bacterial 50S ribosomal subunit in complex with existing antibiotics, to see where they bind and what the reactions are, in order to design new antibiotics. We use computational chemistry (initially from Jorgensen's Lab at Yale) to design new compounds that will be effective against bacteria. One compound (radezolid, a next-generation oxazolidinone) is through phase II clinical trials and appears to be effective against all strains of MRSA. Another set of compounds are designed completely de novo, based on knowledge of the target site. These compounds appear to be effective against both Gram-negative and Gram-positive bacteria.

Will medicines move away from being chemical to being more biological?
I think biological medicines are useful in many diseases, but not as antibacterials. I don't see anything on the horizon. There is the challenge of delivering the drug: it has to be stable and soluble in the host skin or bloodstream. And then it has to be able to get inside bacterial cells. Nucleic acids are not easy to get in — or cheap.

Antibacterials are really part of a microbial biological warfare. Bacteria have been fighting with each other for millions of years; they use these chemicals to try to kill other species. That is where antibiotics initially came from, they were all isolated from species of bacteria or fungi. Nature figures out how to do it, and we're just following nature.

Will we be fighting this war forever?
Bacteria have learnt to overcome everything we have thrown at them so far. It goes to show that evolution trumps intelligent design. ■

I would prefer if Nobel prizewinners said that they were most motivated by observing the suffering of mankind, or motivated by love and kindness. But I am really happy that they have given an honest response.

K.L. Senarath Dayathilake, psychologist, Human Well-being Science Program, Kotte, Sri Lanka, who posed the original question on lindau.nature.com.