Discussion

Taekjip Ha

Q: What is possible application of your imaging technique for molecular movement?
A: Generally, it's very far from using this kind of cure technologies to cure disease at the moment, but better fundamental understanding of the mechanisms of these molecules will be useful at least in sustaining some diseases such as cancer.

Q: I think if you can apply these systems, especially *in vivo* system, it's more powerful for finding out different effects of some anti-cancer drugs, those for example targeting DNA helicase, and therefore good for drug design or discovery.
A: Thank you. I think that's a really good point.

Q: How do you know that it's not just another protein coming when the first one disassociates?
A: We know that because we do the measurement at very low concentration of the protein. So, individual protein finding is a singular event that can be well separated from the binding of another protein.

Q: You coupled molecular movement with force measurements, and do you have an idea of how much energy in each event? Can you bug out efficiency for these linear motors?
A: For motors that move on actin and microtubules, people have estimated the efficiency of chemical energy into mechanical work is about 30 or 40 percent—perhaps somebody in the audience may know better than that. But I believe that Dr. Noji will show us data that show that this rotational motor can have close to 100-percent efficiency.

Q: For the human walking, gravity is very important point. Is there any effect of that kind of force in this mechanism?
A: Well, I think the gravity has a very small, probably negligible effect, because the solution is a highly viscous environment. So, before the gravity can move the molecule by any substantial distance, then you come to a stop.

Hiroyuki Noji

Q: I'm interested in your relationship between the amount of spin and the amount of ATP you have in there. And when ATP is consumed, does it give off byproducts that's still in that little volume? Does ATP readily get to the molecule?
A: Actually, you have many, many mitochondria synthesizing ATP in your single cell. And actually, Brownian motion of small molecule is very rapid, within 1 micron. So you don't care about the shortage of ATP. As for your concern on byproducts, we only put in the solution ATP and phosphate as substrates. So, possible artificial product is, if it would be produced, very small.

Q: When you use magnetic effects to rotate F1 motor in the direction of ATP consumption, what's happen?
A: Actually, it's our ongoing topic, so I cannot answer precisely, but the artificial force enhance the reaction, so speed up, increase, the velocity of ATP hydrolysis when you push the motor using magnetic forces.

Q: There is analogy between the electromotor we usually use and your molecular motor. Electromotor works as each direction, while your molecule decided the directions. Why the molecule can decide the rotation direction?
A: It's good and fundamental and difficult question to answer. Asymmetry of the molecule might be very important to decide a direction. Thus, the protein decides its conformation in one state, not so flexible.

Q: You mentioned that in order to make a bigger move, multiple units need to work together at one time. Then what are the factors that make them synchronize?
A: Synchronization is, I think, caused by mechanical stress.

Steven Conolly

Q: The resonant frequency depends on the intensity. At the view point of patients, 2 minutes for scanning is too long. So, is it possible to reduce the time, increasing the magnetic field?

A: We are not going to be limited in what you would call “imaging bandwidth” by virtue of being too low a frequency. We’re actually moving up in center of frequency so we can go a little bit faster. So we should be very comparable to normal MRI scanners in speed.

Q: What these devices might be used for if they were very well-cost and very easily available.
A: That’s very difficult to predict. But it would be used for knee imaging, and then, perhaps after that, some version of neural imaging. In case of breast imaging, X-ray mammography has a lot of bad aspects; it’s not very sensitive or specific, and the images are not all that good quality. However, the cost structure is an-order-of-magnitude different; it’s about $100 for a mammogram and it’s about $1,000 for an MRI scanner. So, if the cost for our MRI, which is more sensitive than using a conventional MRI, would be order-of-magnitude less costly, it would be used widely.

Q: It might make more sense to do the price comparison with genetic testing than with the mammography, which is comparable in cost.
A: That’s true. And I think that it’ll wind up being somewhat complementary, because if you do have one of the breast cancer genes, BRCA-1 or BRCA-2, then I think you’re extremely motivated to get MRIs. And then you can actually maybe justify the cost of the current MRI scanner in that market, because it is a much smaller population.

Q: I think the MRI has the risk against metal. So, do you think these kind of small MRIs are safer than bigger MRI system?
A: If you have a pacemaker, you’re not even supposed to go in the room. But there’s actually not very high risk. The primary problem is not danger. You need very large precision in the magnetic field or the susceptibility of the metal, to make it good enough. So, titanium is not too bad; copper would be perfect, but it’s too soft. So, titanium you can actually make a pretty good image now. But most of the stainless steel stuff produces large artifacts.

Q: You talked about a number of different innovations that are making MRIs cheaper, better, faster, mostly in the hardware domain. Is there anything in the software domain that is moving things in the same directions?
A: I’d say about 99 percent of all of the work in MRI is done on the acquisitions in

software. And the group I come from in Stanford is actually like that. And that's mostly where the university work has been, and most of the innovation, honestly, on the hardware side has really been in the companies.

Hiroshi Kanai

Q: Can you predict the rapture of the plaque in the blood vessels by your imaging?
A: Unfortunately, we cannot evaluate the estimation of the rapture of the plaque because we have no experience to image the rapture occurring in the patient.

Q: From the practical side of your discovery, how easy and how much influence you're going to have on the way you're going to actually put the probe on the patient, and how, from the practical side, it should be done from non-medical doctors?
A: For the arterial walls we measure such cross-sectional image by using the very minute change in thickness from the skin surface by attaching the probe here. And it is not easy for the normal medical doctors, not because this cross-sectional imaging is difficult, but because the measurement of minute change in thickness of several micrometers from the skin surface is not so easy. But in the commercial side, the device realizing this method will be developed in 2005.

Q: Can you comment on the difficulties or challenges on making sure that you're actually seeing the same point from image to image?
A: To do that, we set such ultrasonic beams and many match points from the intima side to adventitia side. Then, for each point we obtain such velocity signals, so that we obtain the change in thickness between some combination of the point.

Q: Can you explain more about electronic staining?
A: The term "electronic stain" means ultrasonic-based non-invasive staining here.

Q: Where in the body your method can be applicable?
A: Besides the common carotid arteries and femoral arteries, which I mentioned, the brachial arteries can be applicable, if we use the 10 megahertz or higher frequencies of the ultrasound.