Interview: Dr. Francis Loth

Historically, research into Chiari and syringomyelia has been dominated by neurosurgeons. However there is a small, but growing, group of researchers looking at the problem from a different point of view and with different tools and ideas. Bioengineers are beginning to study how the CSF system works and develop ideas on Chiari and syrinx formation.

So what can the engineers bring to the table? Can they solve the problems of why syrinxes form and improve treatment techniques?

Frank Loth has a Ph.D. in Mechanical Engineering, is an Associate Professor and the Undergraduate Director of Mechanical & Industrial Engineering at the University of Illinois-Chicago. He is also the Director of the Biofluids Laboratory there and has been studying the CSF system, Chiari, and syringomyelia for several years.

We put Dr. Loth In the Spotlight to see if we could shed some light on what to expect from the bioengineers:

What is bioengineering? L: Bioengineering is pretty much what it sounds like, its a combination of biology and engineering. Bioengineering is using scientific ideas - like physics, fluid dynamics, structural mechanics - and incorporating them into problems of biology and perhaps more importantly medical questions. Trying to understand diseases and how the body functions.

In general, what can an engineering perspective bring to the table when dealing with a medical condition? L: By nature of the engineering training, the goal of an engineer is to take complex phenomenon and try to break down that complex phenomenon into something that's predictable or at least understandable through equations or experiments. In other words, simplify the problem. If you can recreate the major aspects of the complex function with a simple model, maybe you can come up with ideas to change or optimize the complex system.

Is there much resistance among doctors and neurosurgeons to engineers working in their space? L: There's definitely resistance. I think its becoming much less in the last decade. It's natural, the way an engineer thinks is different than the way a medical doctor is trained. It's completely understandable...trying to understand how everything works is not something a medical doctor has time to do. They're working on tried and true methods that have been tested by other doctors over the years...It's two different ways to approach the problem and probably neither one is sufficient by itself to solve major problems, you need a combination of approaches.

How did you become interested in bioengineering over other types of engineering? L: I had several friends in Med school when I was in grad school for engineering and I really thought I should become a medical doctor. So, I started getting really interested in that and volunteering, but then I found I was a little bit squeamish, so I started looking at other options to get involved. It turns out bioengineering allowed me to use my engineering skills and still have an impact on something very important, medical care here and around the world.

What is one of the major successes bioengineering has had as a field? L: Ultrasound in medicine is a great example of bioengineering in medicine. When it first came out, doctors thought it was just a bunch of pretty pictures. They were skeptical of what it could do. Then as time went along, they showed the pictures could quantify something but they had errors that went with it. Then the bioengineers presented the data in such a way that it would be useful for doctors to make certain decisions. Then the technology advanced and today it is used for all kinds of things. Twenty-five years ago, some doctors were saying its a toy and they'll never use it.

Could you describe your current research? L: My research is directed towards understanding the flow of cerebrospinal fluid out of the cranium into the spinal canal and back again in an effort to understand these diseases. Basically, what we're doing is trying to understand it from an engineering perspective; looking at pressures and flows and trying to quantify what is normal for healthy subjects, what is typical for Chiari, and how it changes before and after surgery and can we do a good job of quantifying those things with MRI on a consistent basis.

What kind of process are you using to understand this? L: The main thing we're looking at is trying to understand how much resistance exists from the fluid going from the cranium into the spinal canal when there is a malformation and without. We try to estimate the pressure change when the fluid goes from the cranium to the spinal canal. Because of the nature of the system, we can't use classical definitions of resistance. The CSF motion is pulsatile and changes with the frequency of the heart rate, every second the fluid goes down and comes back up, so what we use is called Longitudinal Impedance.

Where do you get the data for this analysis? L: We get the data from MRI, we work closely with Dr. Oshinski at Emory University who takes measurements of flow rate using phase contrast MRI and he also takes careful measurements of the geometry [of the spinal canal]. We take that geometry and make a mathematical model that simulates the environment.

You are also building a physical model of the spinal system? L: We are. The model building is trying to get

Definitions

bioengineering - using engineering principles to understand and solve problems in biology and medicine

central canal - center tube shaped part of the spinal cord

cerebrospinal fluid (CSF) - clear liquid in the brain and spinal cord, acts as a shock absorber

Chiari malformation - condition where the cerebellar tonsils are displaced out of the skull area into the spinal area, causing compression of brain tissue and disruption of CSF flow

cranium - the skull

flow - movement of a fluid like blood or CSF

fluid dynamics - the study of how liquids (or fluids) move through different types of containers; often uses mathematical modeling to simulate the motion

hydrodynamic - relating to the movement of a liquid

ml - milliliter, small unit of volume, equal to .0338 fluid ounces

MRI - Magnetic Resonance Imaging, non-invasive, diagnostic test which uses a magnetic field to create internal images of a person

phase contrast MRI - type of MRI which can record velocities of fluids - like CSF - in the body

pressure - measure of force per unit area

pulsatile - not steady; vibrating or beating

syringomyelia - neurological condition where a fluid filled cyst forms in the spinal cord

syrinx - fluid filled cyst in the spinal cord

ultrasound - diagnostic device which uses sound waves to create internal images of the body

some basic understanding of how the pressure environment is involved in syrinx formation. We have a physical model that we made out of a plastic material called Sylgard. The model is based on a geometry from the MRI. There is a cavity simulating the brain area and we use a pump to pump fluid into the spinal area and simulate the motion inside a person. We can then take pressure measurements throughout the system to see what is going on.

What do you hope to accomplish with this research? L: Two ultimate goals. One is fundamental understanding and documenting what we measure so that it can be useful for us or someone else. The second is to obtain a clinical pararmeter - like resistance - that would be useful for surgical planning and evaluation. If we could come up with a parameter that is predictive of the blockage level of the malformation that would be important for surgeons. The 3-D shape of the malformation is much more complicated than just the level of descent.

Any early results from your work? L: We've measured three cases pre and post surgery, and completed the analysis on two of them. In the two cases we've looked at, the resistance parameter went down after surgery and all the parameters for patients with Chiari, both before and after surgery, were higher than healthy cases. So they seem to make sense, but we need to evaluate many more cases.

How much fluid is actually in a typical syrinx? L: The total amount of fluid in the system is around 150ml. In the subarachnoid space its about 75ml. So if its maybe 3mm diameter and extending 10 cm, it will only contain about 1ml of fluid which is less than a teaspoon. A very large syrinx obviously will have more fluid.

So a syrinx may not contain that much fluid, yet can cause tremendous amounts of damage? L: Yes, that's right.

Over the years, there have been several theories on syrinx formation. One of the original thoughts was that CSF enters the central canal from the top, through the obex. Has this pretty much been discounted at this point? L: It's been discounted in being a major reason for syrinx formation. It's been shown that many syrinxes are non-communicating - there is no direct path through the central canal to the brain. So it's essentially been disproven, but it's not completely clear the central canal doesn't play some role, but not a major one.

One current popular theory is the "piston" theory, where the malformation drives down with every heartbeat and creates a pressure wave which somehow forms a syrinx. What are your thoughts on that? L: I think this is a very interesting theory. It's certainly plausible. The problem is that it is difficult to prove. I do know of some research going on to look at these pressure waves and how a pressure wave going along a flexible tube might force fluid to go inside. But currently, these are just theories, they're not proven at all.

So does it take you aback when you read publications treating this as a given? L: As an engineer, I have difficulty with some of the theories presented. Not that they're incorrect, but there isn't enough data to prove one theory over another. Right now, they're in that area where there's lots of ideas. But its difficult to get measurements inside this space so its difficult to prove one theory over another. I think the biggest problem stems from the fact that a fluid filled cavity should have greater pressure outside to fill the cavity. But, since its a flexible cavity, that pressure would be transmitted to the inside and you would expect the pressure to be higher inside the syrinx. So there's some type of special process where the fluid gets pumped inside the syrinx which isn't obvious.

How much money would it take to really understand what is going on? L: Let's put it this way. If an agency were able to give $100 million, I have great confidence the problem would be solved in 4-5 years. But, the problem may actually be solved with less than that. It's a statistical question. The point is to get good researchers interested in the problem and motivated. One we need awareness for scientists to get interested in the problem - and I think this is happening. Second, if funding is provided, that interest will stay and keep going.

In five years, say the problem is completely understood, do you think it is likely that would change the treatment options for patients, or is it likely to still be a surgical solution? L: Depends on the results. If the pressure environment turns out to be important, then a surgeon may be able to determine if decompression will work or not.

Is it possible there is more than one cause of syrinx formation? L: It is very likely. Probably three reasons for syrinx formation, not just one or two.

Do you think it will turn out that some people are more prone to developing syrinxes than others due to their biology? L: Yes. I don't know if we'll be able to tell who is more likely to develop. As an engineer, I believe the geometry, the size of an individual, the amount of CSF that goes back and forth varies a lot. If we understand what causes it, we do have a better chance of saying who is at risk.

Do we know why surgery stops and sometimes reverses syrinx progression? L: An excellent question. Depends on what level of understanding you mean. I don't feel we know in detail why it works.

On a scale from 1-10? L: If we compare it to something like hip replacement surgery. I would put hip replacement at about an 8 and decompression surgery at a 2 or 3. But this doesn't mean it can't help patients.

At the end of your career, what will you have accomplished that will make you say, "Yeah, I did it"? L: I would be happy if we found an improved method to evaluate the geometric extent of brain herniation for a patient based on its full three-dimensional shape. I would be thrilled if we could develop a method to determine a measure of hydrodynamic importance of a patient's brain herniation that correlated with clinical symptoms. I would say "yeah, WE did it..." if we could develop a method that could explain why a patient's syrinx has formed, what procedures would likely eliminate it, AND what procedures would have no effect. I say "WE" since I think it is unlikely that any one person will figure these things out alone. Most important, new techniques will ultimately come from the neurosurgeon (and not an engineer) since the neurosurgeon will test the methods and direct the development with their insight and intuition. I feel that if engineers and doctors work together and share their ideas, we may realize these ambitious goals in the near future.

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Qualifications:

- Director, Biofluids Lab, UIC
- Member 2003 NASA Biofluids Panel
- Reviewer for several bioengineering journals

Education:

- M.S., Ph.D., Mechanical Engineering, Georgia Institute of Technology, 1990, 1993
- M.S. Aerospace Engineering, University of Cincinnati, 1988
- B.S. Aerospace Engineering, West Virginia University, 1984

Research Interests:

- Fluid dynamics of CSF
- Effects of Chiari and syringomyelia on CSF system
- Fluid dynamics of blood and its relationship to disease

Selected Publications:

- F. Loth, M.A. Yardimci, N. Alperin, **"Dynamics of cerebrospinal fluid in the spinal cavity,"** Journal of Biomechanical Engineering, Vol. 123, No. 1, pp. 71-79, Feb. 2001.
- N. Alperin, K. Kulkarni, F. Loth, B. Roitberg, M. Foroohar, M.F. Mafee, T. Lichtor, **"Analysis of magnetic resonance imaging-based blood and cerebrospinal fluid flow measurements in patients with Chiari I malformation: A system approach,"** Neurosurgical Focus, Vol. 11, No. 1, Article 6, pp. 1-10, July 2001.

Selected Talks:

- **"Engineering Perspective on Diseases Related to CSF Motion,"** University of Chicago in the Department of Neurosurgery (Grand Rounds), June 6th, 2003.
- **"Numerical simulation of cerebrospinal fluid motion within a healthy and diseased spinal canal,"** Fourth World Congress of Biomechanics, August 4-9, 2002, Calgary, Canada.

Editor's Note: In addition to his own research, Dr. Loth has been instrumental in highlighting this problem to other researchers and recruiting them to work in this area.