Cognitive Science Online

A journal published by the Department of Cognitive Science, UCSD

Vol 1, Issue 2. 2003

about this column

Column: Interview with Anders Dale

Anders Dale was one of the first graduates of the UCSD Cognitive Science department. While a graduate student, he pioneered methods to localize brain activity by combining EEG, MEG, and MRI measures. He also did ground-breaking work in surface-based MRI data analysis and mapping of visual cortex. Since then he has continued to further the development of non-invasive imaging technologies and our understanding of their physiological underpinnings. His current work ranges from the optical imaging of rat barrel cortex to the use of structural MRI to diagnose neurological disorders.

Anders is currently an associate professor of Radiology at Harvard Medical School and is Associate Director of the Massachusetts General Hospital/Harvard Medical School/ Massachusetts Institute of Technology Athinoula A. Martinos Center for Biomedical Imaging. Anders also works in the private sector as the Chief Scientific Advisor and co-founder of the neuroimaging company CorTechs Labs Incorporated.

The following interview was conducted by **David Groppe**, **Hsin-Hao Yu**, and **Christopher Lovett**.

Cognitive Science Online: What is your education background? And how did you join the UCSD Cognitive Science department?

Anders Dale: I got my undergraduate degree in Computer Science at the University of Hawaii, served in the Air Force, and then I started a little control systems consulting company. After a year or two, I got a Fulbright Fellowship and went to Harvard and MIT for a Masters in Engineering Science. Then one day Marty Sereno called me up and asked if I wanted to come down here. I said, "Yeah, that sounds like a fun plan."

CSO: What research were you planning to do?

AD: I've always been interested in using quantitative modeling methods and simulations to answer biological questions. At the time, I was interested in approaching connectionist neural networks from a more biological angle. Marty was one of the few people who took this work seriously. After I came to UCSD, my interest shifted to learning how to test models of how the brain works. Ideally you'd like to test your models not in anesthetized animals and brain slices, but by measuring brain activity in humans non-invasively. I wanted to study normal people doing normal tasks. That was what brought me to imaging. My goal was to see what kind of things we can measure non-invasively that can be quantitatively related to the models we want to build. It was kind of a megalomaniac project, but I think that was a good thing. While you're a student you have to be allowed to be unrealistic. If you are completely realistic you will probably never get into any of this stuff in the first place.[all laugh]

So that's how I got into imaging here. I worked with Marta Kutas on EEG. I wanted to know what exactly we are measuring, how can you model it, and how can you relate the signal to what is going on in the brain physiologically...at a level that say you could measure invasively and that you could relate to parameters of quantitative models.

My thesis work was on the EEG and MEG forward and inverse problems, and how to use anatomical information to constrain the solutions. It is clear that if you only use EEG or MEG measures, the spatial precision is not good enough to make inferences at a scale that's most useful to neuroscience. That led us into trying to use information with higher spatial resolution to constrain or bias our estimations of the signal sources in the brain.

Toward the end of my graduate work and during my post doc work here, Marty and I got into MRI and fMRI. The field had just gotten started. We tried to use cortical surface reconstruction from MRI to constrain the localization of EEG and MEG signals. We also used those geometrical representations of the cortex, combined with functional MRI, to look for maps in the visual cortex. Steve Engel at Stanford had just developed the phase-encoded stimulus paradigm. He showed that if you present subjects with expanding annulus and rotating wedges, you can apply Fourier analysis to fMRI signals on a voxel-by-voxel basis, and obtain a delay map, or an estimate of the retinotopic representation. We thought up the idea of looking at these maps on the cortical surface, because the maps are actually two-dimensional. Although the topology of these maps is simple, their folding makes them complex in volume. In order to visualize and analyze the patterns of brain activity, you really need to take into account the individual geometry of the cortex. So we decided to do an experiment. We went to Massachusetts General Hospital, and tried our little experiment on a weekend. We collected two data sets, first on Marty and then on myself after I made a little modification to the stimuli. It worked very well and the results got into *Science*.

CSO: As an alumnus of our department, what do you think are the advantages and disadvantages of getting your degree from an interdisciplinary department like ours?

AD: I'm very happy with the education I received here and how it prepared me for a subsequent research career. The department really provides a great opportunity for someone who wants to put together a custom program. There are some excellent people here from different disciplines and they really work together. And it's not just the department, I think UCSD in general is very encouraging of interdepartmental collaborations. For someone who is motivated and kind of knows what he wants to do, I think it's a great environment. The danger however, would be that somebody could fall through the cracks, since there is no agreed upon core of things we need to know.

CSO: What are you working on now?

AD: Several things. One avenue of research is to find ways to design experiments that you could use for EEG, MEG, and fMRI. The most common experimental design for fMRI is a block design where you go back and forth between having *n* seconds of one stimulus and resting for a few seconds. This is a fine and powerful design for fMRI, but nobody in their right mind would use it for EEG and MEG and behavioral experiments. So I've worked on developing event-related fMRI methods...trying to figure out how to analyze the data and how to optimize the experimental design if you want to present stimuli at a reasonable rate. A number of researchers had argued that you couldn't do such a thing, that the fastest you could present stimuli was about once every 5 seconds. But these arguments were based on assuming things like a fixed rate of presentation. My collaborators and I showed that if you randomly jitter the interstimulus interval the right way, you can present multiple stimuli per second and still pull out the event-related response you want. This part of my research is actually built on some work I've been doing with Marta Kutas on overlap correction for EEG/MEG.

More recently, I've gotten much more into animal work. I'm part of a big collaborative project involving Amiram Grinvald of the Weizmann Institute in Israel and a group at Los Alamos. Part of the project is developing high-field MR technologies that would allow you to get very high spatial resolution with a high signal to noise ratio. Another part of the project involves developing simultaneous optical imaging and electrophysiological recording techniques. In addition to this instrumental component, there is a modeling component. We make all these measurements at the same time with a stimulus paradigm that would allow us to quantitatively identify the coupling between the electrophysiological activity and the hemodynamic response: changes in blood oxygenation, flow, volume...stuff that underlies the fMRI signal. And we're using event related designs that we'd want to use in real experiments. If you look at the stuff Grinvald and those guys have done, it's beautiful work but the stimulus paradigms that they use aren't all that relevant for standard electrophysiological or behavioral experiments. In some cases, I think the lessons from such work are misleading. You want to look at what the impulse response of the system is, and not have to do all this work in the steady state regime. We have some recent results from this project on the barrel cortex of rats.

Another aspect of my work is clinical applications of anatomical data analysis. I am working on optimizing the image acquisition protocols and post-processing techniques that would help doctors to find anomalies in anatomical images and to detect diseases. Clinically, it is important to detect differences in before-and-after images. For example, you may want to know if a tumor has grown or not. Usually the changes need to be rather large, because you have confounding factors, such as slices being in different positions. With computers, it is possible to automatically look for features in the images, to align them correctly, and to make the diagnosis more quantitative. A spin-off company, CorTechs Labs Inc. was started a few years ago to package and commercialize these technologies for the medical industry. We just got a contract from Siemens for our image registration software.

CSO: What advice do you have for graduate students interested in doing fMRI research?

AD: Go to a place where it's working. [all laugh] Seriously, there are so many things that can go wrong. It's amazing how many things can break when you're doing imaging. Especially if you're doing multi-modality stuff. And these things, they can take such a long time to get working. So that's just a practical issue. But it looks like things are happening here, and that's a good thing! You've got a great team here in San Diego. Other than that, enjoy it while you can - it's a good life.

CSO: What are the most common abuses of neuroimaging techniques that you see?

AD: Abuses?

CSO: Yeah, you know, bad imaging experiments, etc?

AD: Well, there is this tendency to want to look at imaging as a black box...a tendency to just pick up something like statistical parametric mapping, and to just crank data through without looking at it. I think that's the most common abuse. And actually, the quality of a lot of the stuff that's being presented at conferences has kind of gone down as imaging has become perceived as more and more turnkey. People are just not aware, I think, of the pitfalls because they're hidden behind all kinds of smoothing. If you actually sit down and look at the data, you might be horrified...you've got drop-offs, you've got distortions. If you want to relate your measurements to anatomy and physiology in a robust way, the level of complexity of what you have to do in the analysis is just an order of magnitude higher. You have to actually have an understanding of what the hell you're doing. But if you're just kind of using it as a black-box tool, which I think is more and more often the case, you can be fooled into thinking everything's hunky-dory -- you always get some blobs lighting up. I think the reliance on black-box programs is a little scary. I think people have this perception that the field is more mature than it actually is.

CSO: What kind of background do you think best prepares someone to do research in your area?

AD: A solid quantitative background. It's very hard to pick that up late in life. So you want to have, as early as you can, some sort of physics, engineering, math, and computer science background. You have to have a healthy helping of that as early as you can in your career. It's like learning a language. I don't think there's a critical period for it. [all laugh] But practically, it's very hard to take a sufficient amount of time off to learn it.

CSO: The 1990's have been christened the "decade of the brain," in large part due to advances in non-invasive brain imaging. What are some important lessons these new imaging techniques have provided? And what questions do you think still need to be tackled by our current techniques?

AD: Lessons so far? I think it's much more of a promise, a work in progress. The technology's evolving very, very rapidly, but what fundamental insight has neuroimaging led to? Hmm...I don't know if I can really point to a concrete, great revelation so far.

CSO: It seems like it's driven home the point that the brain is a distributed processor that lots of different parts of the brain are involved in a single task, and particular areas can be involved in a wide range of tasks.

AD: Yeah, certainly it's falsified a lot of theories. [all laugh] That's a very good point. If you look at any of these imaging data sets for some kind of cognitive task, what is fundamentally clear to me--especially if you look at the spatial-temporal stuff--is that it doesn't look like any neat boxes and arrows theory that is testable by reaction times. I don't see how you can reconcile those with the data. On the other hand, to say that it's a distributed network is vacuous. It's like saying "nonlinear" or "complex."

It's very clear that the brain's not a feedforward system. It's much more complex than that, but do we have a language to actually describe it? No, I don't think that we do. You can look at these movies of brain activity and say "oh, the activity's going back and forth," but for the life of me I couldn't tell from that how the brain works. Potentially the brain is a very powerful constraint on our models. But it's very clear that we need a much more powerful language to describe how it works. That's the challenge I think. The measurement methods provide us with a very rich way to constrain models, but I think the actual models...the very language we use to build them with needs to be developed.

CSO: So you agree with the characterization of neuroscience as being "data rich" but "theory poor?"

AD: Absolutely. Certainly at the cognitive neuroscience level.

CSO: But it seems like we're still very data poor. We're far from having the non-invasive data that we want.

AD: Yeah, but what I find encouraging from the developments of the 1990's and what's going on now is that it's becoming possible to collect data that is vastly more rich than was possible in the past. Now I think the challenge is to build testable hypotheses, to express your models of cognitive phenomenon in a language that actually makes strong predictions about what you can measure. We need to phrase our hypothesis about cognitive neuroscience in a way that is directly relatable to the animal work and biophysics. Otherwise, it's just rhetorical exercises. But I wouldn't say that we have a lot of examples of that yet.

CSO: Do any come to mind?

AD: Immodestly, I guess the work that Marty and I did on retinotopy. It's not language...it's more modest in this regard, but it's one of the few cases I can think of, where what you're estimating can be directly related to something like magnification factors and questions like: "Is the map angle-preserving? Is it conformal?". Those are questions that have been around in the neuroscience community for a long time and it was possible for the first time--I think--to use imaging to get answers to those questions. Maybe they weren't great answers [laugh], but they're answers. For that field, I think that's a modest first example. I'm sure there are others but they don't come to mind. Can you think of anything?

CSO: That's why we asked you.[all laugh] How about attentional effects on V1? Again it's modest but...

AD: That's true. But immediately the question is: "When is it happening?" It's a work in progress. Without the timing information I think it's much harder to interpret. Is it a feedforward early filtering type of thing or is it some kind of later process? That has huge implications I think on the appropriate models.

CSO: Where do you think brain imaging is going? What do you think the next advances will be?

AD: Optical imaging is very interesting. I've been putting a lot of activity in to that these days. It gives you another window, even transcranially, and has potentially very fast temporal resolution. It's got its own inverse problem, which is almost as hairy as the MEG/EEG one. I think that's a very interesting area. I don't think it's going to revolutionize anything, but I think it can provide very useful, complementary information to other modalities. Are you familiar with any of this stuff?

CSO: No.

AD: It's called "diffuse optical tomography."

CSO: Is it a hemodynamic measure?

AD: Yes, but there's also a component to it that's very, very rapid. It's not clear what exactly it is, and part of what my collaborators and I are doing is to look at this fast response. So that's one area I'm interested in from a methodological point of view.I think the instrumentation is reasonably mature at this point. I don't think there's going to be like a 14 Tesla scanner. We have a 7 Tesla, but I do my work on a 3T because it's a nice stable system. There's no qualitative difference between the two and it's just a pain in the ass to go to super high fields. You have to have them to be a player, but if I had to choose, I would actually stick with a lower field strength and tweak a lot of things.

Hmm...I think it's the appropriate modeling of the signals...understanding what the hell we're

actually measuring...that's the open challenge I think. You asked what I think the future of imaging is, and I think that's the area where there's the most room and most critical need for improvement. It's not higher field strength. That stuff is fun and it poses interesting engineering challenges. But if we had it today it wouldn't make any difference in our ability to answer the scientific questions we're interested in.

---

back to top

In this section of *Cognitive Science Online*, we will feature interviews with cognitive scientists. If you have suggestions for future issues please **contact the editors**. Please also feel free to interview your favorite scientists and help out with this section of the journal!