Tom Baden wins the 2017 Eppendorf Award for Young European Investigators

Tom Baden, University of Sussex

Julie Gould: Congratulations! How does it feel to have won this award?

Tom Baden: It's very nice. I'm very humbled by this situation. Of course, it represents a team effort, especially the work on the mouse.

JG: Your research concerns the retina of the mouse. Tell us about that.

TB: In the retina of vertebrates, what we have is a layered structure. On one side, the light hits photoreceptors. These pick up the light signal and transduce it to electrical potential. On the other side are ganglion cells, which are the connections to the brain. In between, are bipolar cells.

In our research, we used optical imaging to record the responses of each element in that retinal network to a set of visual stimuli. This allowed us to follow how visual patterns are filtered through the retinal network. At the input stage you take a set of neurons that respond to a very broad set of things, and then you filter that through multiple layers of neurons until you have neurons that only respond to specific things.

JG: How is a specific stimulus filtered through the retina of the mouse?

TB: The simplest stimulus to use would be a flash of light. You are in the dark and you switch a light on and quickly off. In the mouse you have two types of cone photoreceptor, and both of these will decrease their activity when the light goes on.

In the next layer are bipolar cells. Different types of bipolar cell will transform the stimulus in different ways. The 'off' bipolar cells basically copy the photoreceptor signal and decrease their activity when the light goes on. The 'on' cells flip that signal. So they will increase their activity when the light comes on. Going from photoreceptor to bipolar cells, you've split the signal into the on and off pathway. In each of these groups, the ons and the offs, there might be differences, for example, in the speed at which they respond. So you might have a fast or a slow on cell. You might also have differences in spectral preference; they might prefer green or blue light, or not mind.

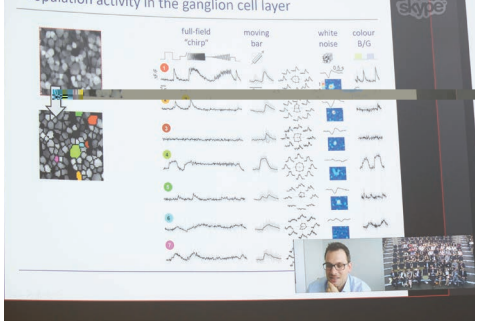
This set of information, not 2 but 14 streams, gets sent into the next layer in the retina: the ganglion cells. And if you count up the ganglion cells, we're not quite sure on the numbers yet, but it's certainly more than 30, they will be much more specific. You will still have some cells, which are just on or off cells, with a certain speed. But those will be in the minority now. Other cells with much more refined stimulus-response characteristics will come in, things like direction-selective ganglion cells (cells that will only respond if the signal is moving in a particular direction). Or you've got orientation-selective ganglion cells that need the stimulus to be orientated on a particular axis, usually vertical or horizontal.

This is how the retina parallelizes the stimulus. And then ultimately, rather than having just 2 representations, there are 30 or more representations of the image sent to the brain. On the basis of those parallel channels, the brain reconstructs the image.

JG: Tell us how you went about your research.

TB: We looked at the output synapses of the photoreceptors and presented them with different patterns of light, measuring how they responded to light in a systematic way.

We looked at different regions of the eye, for example, the upper and lower halves,



Baden presents his research at the Eppendorf Award ceremony in Heidelberg, Germany.
PHOTOS: EMBL PHOTOLAB, HEIDELBERG, GERMANY.

and saw that they responded differently. Specifically, the cones and synapses that looked up responded better to dark contrasts on a bright sky, so like a bird in the sky.

JG: **And it's important for a mouse to be able to see that!**

TB: Yes, exactly. It seems that the mouse has biased the retinal network that looks at the sky at the input stage to be particularly good at seeing dark shapes.

Afterwards, we concentrated on the next synaptic layer, the inner plexiform layer, which is where the bipolar cells provide inputs for the ganglion cells. We used pattern light simulation to characterize how different types of bipolar cells (which are positioned in different depths of this synaptic layer) responded to a defined set of stimuli. The punch line here was that these differences weren't very pronounced if you used a spatially restricted stimulus.

JG: **What is that? A small flash of light?**

TB: One that would roughly cover about ten photoreceptors, which would be the input to a bipolar cell. But then if you take a stimulus that is much bigger, one that would hit maybe 100 photoreceptors, which also hits neighbouring bipolar cells and circuits, then the differences that we saw between bipolar cell outputs, between the different types, were much more pronounced.

That led us to conclude that the size of the stimulus is very important, but also that the specific size at which this happens particularly well is also the size at which the ganglion cells respond well. It seems that the bipolar cells are tuned to a size regime, which is appropriate for the next layer down. Quite neat, I thought.

JG: **And now you are working on the retina of the zebrafish?**

TB: One of the things that is nice about zebrafish is their colour vision. Humans are trichromats: we have three different cone-type photoreceptors that pick up red, green and blue light. The fish are tetrachromats, so they have four of them: they also see ultraviolet light. Now you've got a retina network with the same players as the mouse, but it needs to deal with four colours, not two. This means, presumably, that the network needs to be either more efficient at dealing with colour, or it will become more complex. This is something that we are looking at now. We're looking at different layers of neurons in the retina and the brain of the zebrafish, and seeing how they process colour.

JG: **What species are you looking at next?**

TB: For me, I'm interested in how neurons achieve computation, the species is secondary to the behavioural task that the animal is trying to achieve. So if you've got an animal that uses it's eyes for an interesting, unique thing, then the retina will be uniquely adapted to do that thing.

Take an archerfish, for example. These are fish that spit water at insects above the water's surface, the insect falls in, and the fish eats them. For that you need to be good at seeing the insect and turning that into a set of command instructions that lets you spit in the right direction. That's a complex behavioural task, and if we look at the retina of this fish, presumably, we would find regions that are specialized for that behaviour. And if we can look at the functional level of what the computations are that are implemented, I think that would get us a bit closer to learning how neurons achieve specific things.