Interview with Graeme Lowe

[RB] Is it that we live in a world of electrical impulses, governed by structures of physics and facilitated by chemicals, or, are chemical reactions converted into electrical responses?

[GL] Both. These ideas are interchangeable. From the point of view of neurophysiology, you could 'boil down' the workings of the brain to a bunch of electrical impulses that are being exchanged between neurons, but that's a pretty low level way of looking at it.

[RB] Now your world is really about the interface between the cognitive processes and the stimulus. Somewhere there's 'magic' in there that I don't understand.

[GL] Well, I started off studying the very first stage of transduction, where chemicals would come into the nose, bind with the receptors, and then get converted into an electrical impulse. Then I moved to the next level of the cell, that's in the olfactory bulb, where that impulse is received, asking the question, "What happens from then on?"

[RB] So, it's really in this gap where this conversion happens, so it's coming in as chemical stimuli and continuing on as electrical impulse.

[GL] Yes. So it's the very first step. Since everything that we know about the universe comes through our senses. SO, for a while I was focused on what the first step in that process was. Now I'm looking at what the second step is. So, even by going from step one to step two things have become exponentially more complicated. But, it's a basic, low-level coding question; "What's the strategy of the brain as a collection of neurons?" "How does it represent or code that information?"

[RB] And this is an area that we still know very little about, isn't it? I mean, the actual molecular construction and how it carries the information?

[GL] Well, we have a good model now. You may know that the Nobel Prize was given to Richard Axel and Linda Buck for discovering the receptors that are responsible for that initial coding step.

[RB] And they used a sort of DNA fishing technique, didn't they?

[GL] Yes. So, we know now that there are a finite number of receptors, a fairly large family of them that are all different. And that in itself is quite remarkable because you have one particular receptor that is being re-engineered over and over again to produce many variants; hundreds of them in humans and thousands of them in mice and rats.

[RB] How come they get so many more? Are they that much more attuned to that sort of sensory response? I read that the ant has a remarkable capacity for olfactory reception. What can these differences be understood?

[GL] Well, the ant is a very different creature. It does have an olfactory system but its brain is somewhat underwhelming.

There are commonalities between the ant and the human, in fact. If you look at its brain you see something called an antennal lobe – that's the functional homolog of the olfactory bulb – and the overall architecture is amazingly similar. So, the insect has a specific set of receptors for binding odours, just like we do, albeit, it's a smaller family. So, while the actual details of the wiring of the brain is different, the whole strategy of segmenting the chemical world into different channels of information using receptors that's utilised in the insect and in the human.

[RB] So, is that where we are at? Are we trying to find the strategies of how this information is interpreted by the brain? And then reinterpret that strategy in the different contexts of our respective biology?

[GL] Philosophically, I guess that the only way to do it is to have a range of receptors, because only then can you detect a range of different chemicals.

[RB] In 'Electrical Signalling in the Olfactory Bulb', you use the phrase, "The universe of input-output relationships of the underlying neural hardware…" This was interesting for me. Is this how you perceive the work that you are doing? A universe that's hidden from sight?

[GL] Well, there is a particular way that things work and the goal is to find out what that is. So, the bulb codes information a certain way – we don't know what it is exactly. We have a lot of theories and ideas about how to test those theories. So, the Holy Grail is to find that coding mechanism. It's like trying to figure out how your computer works, what's the software behind it.

[RB] So, what drives you is this discovery. Exploring something that has not yet been done.

[GL] Right. But when I wrote that I was really describing the bottom-up strategy of approaching this problem. We don't know what the coding is that is happening in this complex circuit but let's take a close look at it, look at what the components are, see how they are connected together, how they talk to each other, what are the dynamics of that conversation, how many cells talk to how many other cells, how many receptor information channels are cross-linked to other ones, potentially through synapses, and maybe we can look at those specific physiological properties and deduce something about what could be the higher-level function of this device. Because it's not random, it has a very specific architecture.

[RB] You mention artificial chemical sensors; where are we at in this technology? I was reading, ' Calcium permeable amparecеptors and autoreceptors in external tuft cells of the rat olfactory bulb', and you said that "we speculate that this may constitute an avalanche mode of neural transmissions that may be advantageous in controlling the sensitivity and gain…" Is this similar to creating a stereo amplifier, where we are able to 'tweak' the various settings? Where are we at with this technology?

[GL] If you look at the olfactory bulb and the way that it responds to odour input you find a lot of feedback loops, and a lot of those feedback loops are positive feedback loops that amplify. So, the analogy of a stereo amplifier finds a lot of similar principles in olfaction. In an amplifier, if you start to get too much feedback then you begin to get oscillation, there's a lot of that underlying engineering in the circuits of the bulb to amplify and to make the brain more responsive, or sensitive, to be able to detect incoming signals. But, also to filter them in such a way as to format the code in a certain way so that it can be transferred to the next stage in the process.

[RB] So, what might some of the real-world applications of a synthetic nose be?

[GL] There are companies that are making artificial noses but they are still struggling with the detection process; I.e. how do you detect odours using a silicon device? And how do you take those signals that you get and process them in a way that would do even a little bit as well as we do? It's like comparing a digital camera to a human eye. There's a long way to go to get that kind of versatility.

[RB] We seem to be pretty good, once we get the basics down, at turning it that technology into something more useful. So, what would they use a synthetic nose for?

[GL] Sniffing out explosives, mine detection, IEDs, quality control of food products, disease detection (I.e. cancer detection). You can train dogs to detect cancer – there is something that is being emitted by the body that can be, theoretically, detected for diagnosis.

[RB] In the world of food there is, at the moment, a lot of talk about flavour pairing. And the way that they're approaching this is by searching for compatible volatiles; so, odorants with similar composition will 'taste' better together. Is there any merit to that idea? What's your take on that sort of thing?

[GL] This is an area of research that is still embryonic. This is something that I am interested in and working on some aspects of, that is, what happens when you give mixtures of odours. So, we have a lot of information learned from various physiological imaging technologies to know how chemically pure odour is coded by patterns of receptors. A lot of work has been published on this information. Much less information is available on what happens if you take two or more of these chemically pure odorants and mix them together and then present them to the olfactory system; so, what's the code for the mixture and is that mixture going to smell very different, or create a novel sensation that didn't exist with each pure odour? Or, can we still smell each component in that mixture and then recognise them?

[RB] My understanding was that, in this sense we are not like colour, where if you take two colours and mix them together then you get a different third property which is somehow individual, but that in olfaction it still maintains elements of the original. Is that so?

[GL] Well, if you mix two colours then you are no longer able to see the component colours. In olfaction, it depends very much on memory and experience. If you present a new mixture that's never been experienced before then it may be possible to pick out the components. If you train detection of that mixture for a while then the brain can integrate the components; so, your ability to detect the components changes over time depending on …

[RB] So it begins as being all of the variables that you're able to perceive and then it becomes the sum of the parts. So, we recall 'bacon' rather than ham + frying…

[GL} Yes, yes. There are actually synapses, or circuitry downstream from the olfactory bulb in the olfactory cortex (piriform cortex)…well the organisation of neurons in the piriform cortex looks a lot like the kinds of models that people have proposed for associative memory neural networks, so, you can imagine that the synaptic connections in the cortex could be very plastic to create new connections that would represent a holistic new odour object that's being created from the sum of the parts.

[RB] So, it's really a flexible system – we have all of these structures in place but it's so responsive to all of the different input and it's constantly re-evaluating what it perceives.

[GL] I don't know if you can draw much of an analogy to sight, where we have more of a problematic approach to analysing a scene, but with olfaction it's more of a synthetic sense. I suppose that the visual system can still synthesise – so, if you look at that rat, for example, you can say – 'well that's the rat' but now we can break it down to the rat's ears, nose, eyes, feet, etc. Whereas, with olfaction we couldn't do that directly in some cases with odour mixtures.

[RB] I often read references to early human olfactory and taste reception – looking at the primitive man. And you also stated in one of your papers, "An experience dependant modulation of olfactory nerve ET synaptic strength might be part of an early olfactory learning mechanism that regulates the activity of specific glomeruli to odorant stimuli."

What's the difference between the early days of mankind and how they perceived things and that of man now? I was speaking with Daniele Reed and she was explaining junk DNA and the 600 receptors that we don't use anymore, so it seems as though there is a filtering process that happens inside of the human body that determines what is relevant for the world that we live in now. Is this constantly being negotiated? In the next several hundred years are we going to see a different capacity for sensory perception than we have now? Is it going to be directed by the environment that we shape for ourselves?

[GL] My reference to the term 'early' in that paper was not in reference to time, but rather, early in the sensory pathway. But the question is still interesting.

You would have to argue that the hardware, or the wetware, of the brain itself could evolve in such a short time, which I doubt (several hundred years). You could argue that a mutation where you lose a bit of reception (such as to bitter) would be maladaptive, because you would expose you to toxins in nature. But, since we live in an FDA regulated environment, then that's no longer the case. And therefore, you might expect to see more people in the population that couldn't taste bitter anymore because those genes would not be selected out …

[RB] One of the criticisms against the senses of Taste and Smell in aesthetic literature is that it lacks principles of order. Principles of order in aesthetic terms refers to notions like harmony, scale, proportion, shape. This is written by an aesthetic philosopher who probably didn't study much science, so I wanted to come to this side of the table and ask if you think that there are principles of order in taste and smell? In my opinion, some of those ideas are contrived, however, as in the case of harmony, they are not. If such principles of order exists for olfaction, what might those be?

[GL] In olfaction you certainly have this huge family of receptors, hundreds or thousands of them, so why couldn't we impose or create some sort of order out of that huge diversity of chemical receptors. We have classifications of odours already, like fruity, floral, putrid – those are rather broad categories, but I guess that the professional perfumer who is trained to recognise subtle distinctions between different floral fragrances [could narrow this down].

[RB] Could one use a term like harmony to describe certain flavour pairings?

[GL] Returning to the ideas of mixtures, if you mixed something that was congruent with the quality that was represented by each component … [then that might be described as harmony].

[RB] I guess that this is going back to the idea of pairing compatible volatiles. It doesn't seem that we are very good at it yet, but maybe we're starting to get the hang of what makes volatiles compatible.

[GL] Another idea may be that, because the olfactory system is so plastic and malleable in terms of experience and learning and associational memory, it may be difficult to create some sort of a universal order, because it's such a personal experience. Whereas, vision and hearing – I think that we can all agree that middle C is middle C.

[RB] So there may be nothing like that [principles of order]; so he was right to make his assertion.

[GL] I wouldn't say that there is no order. I think that it's more difficult to have a clear universal ordering in the olfactory sense. But then again, there are a lot of universalities, like we all probably have some innate recognition of a bad odour and want to avoid it just because of the biological implications of putrid odours (we don't want to eat decaying matter).

[RB] So, in this sense, is there an ideal smell? We have 20/20 vision, we have acute hearing, but is there something similar in olfaction?

[GL] You're talking about acuity. The receptors in your nose determine sensitivity, but actually those, it seems, can actually be quite plastic and you can induce expression of certain receptors by exposing your nose to a particular odour over and over again. So, you can sensitise, or you can desensitise. So, at the end, it would seem as though there is the lack of an absolute.

[RB] I'm always thinking that, if the gold standard in art is visual art then what can the senses of taste and smell tell us about the world that we live in.

[GL] If you look at the way that taste and smell go into the brain, they go more directly into the emotional centres of the brain or the brain stem, whereas the visual and auditory senses are going more through a relay to the higher senses. So, it could be that it's intrinsically easier to communicate intellectual or political messages through visual and auditory channels. Whereas, when you go through lower brain stem, emotional centres, it's more of a 'gut feeling'. Maybe you're setting yourself up into a conflict situation where you're try and use these chemical senses to evoke higher rational processing. Because they're kind of working against each other.

[RB] I understand what you're saying. So, on one side, perhaps we're undervaluing the emotional nature of ourselves, by forcing those senses into 'a corner' and saying that those senses can only tell us about ourselves as individuals; which I don't feel is entirely true, because I do think that we can learn things about our world through intuition and emotions.

[GL] There's some interplay there, but could you really enjoy the pleasures of an ice cream Sunday while having some political discourse? You are not really enjoying the pleasure of the taste/flavour of the ice cream because you are being distracted from the task by the political discourse. And if you're really focussed on the ice cream Sunday then you're not going to be thinking about the political discourse.

[RB] I think that there's a third dimension to this in that art itself, the medium of art, the way that the tools that shape the message also can add value to it. [I give example of roasted chicken flavoured origami project as an illustration.]

[GL] You could think of the smell as being a sort of exclamation mark or underscore that fires a particular concept into your memory or argument that you're trying to make through the sensory channels.

[RB] Right. It's a provocation, really, and it's raising questions – which is what I believe art is particularly good at.

[GL] The sense of smell is very strongly linked to memory. A lot of people say that the most profound childhood memories are brought back by smelling some odour that they haven't smelled for dozens of years, but as soon as they pick up that odour the brain instantly reaches into the memory banks and pulls out this memory that they had forgotten for decades.

So, that brings with it the potential to use it as a tool for some sort of a conversation in art.

[RB] Yes, assuming that there are enough people that share the same memory. This is why I used the example of the dentist's chair in my talk this morning, because most people in our society will have been able to relate to the horrors of being in the dentist as a child with the candied-flavoured fluoride associated to it. For other people, such as many in India (where I live), may not relate to that experience. But that's ok, art is placed into a cultural context and that's not a

problem. One person who has not had such an experience might see an artwork and ask, "Why? I don't get it." Which creates an opportunity for somebody else to explain that experience to them, so a dialogue can then take place.

[GL] But you're talking about using those sensory qualities to trigger an emotional response, or shared emotional response, based on shared experience. But what I'm saying is that maybe you can use these going forward – so that everybody in the room that you are trying to send this particular message to smells this odour, and therefore, this creates the shared experiment. Going forward, rather than retrospectively.

[RB] And especially if it was an odour that hadn't existed before.

[GL] A novel fragrance that could be associated with a particular visual stimulus or thought or argument.

[RB] I'm thinking about the rats that I saw here yesterday that had to associate the odours to one of three visual images before they received a reward. I'm thinking that you could do a sort of play on that with humans where they would have to have their 90 correct hits before they are allowed to leave the room (as with the rats).