

felt so proud of some of those sections, but in hindsight I see that they were not necessary. She also mellowed my anger. Once, a senior editor of a journal advised me: “Why don’t you run your letter of complaint by Margrit before I send it on to the reviewers?” Third, I had the great fortune to have had outstanding people in my lab, specifically graduate students and technicians. Their contributions are unique and have led to the character and reputation my lab has.

Is research more competitive than it was 30 years ago? This is difficult for me to answer but I know that everyone has an opinion about this issue. Clearly, the research fields have become more crowded, systems more complicated, labs bigger and now several labs often collaborate on the same project. This makes it more difficult for a young scientist after a post-doc to establish his or her lab. Furthermore, for young assistant professors, long-term funding is difficult to obtain and they may get three or four years of funding. This can pressure them to continue their post-doc work on a smaller scale. Thus, today’s environment does not allow young scientists the necessary time to develop their own identity. This was possible 30 years ago. Let me illustrate this with an example from the 1970s. Christiane Nüsslein-Volhard and Eric Wieschaus, as young investigators, set out their genetic screen to find *Drosophila* segmentation genes. It took them several years before they were ready to publish their first paper in the journal *Nature* and to complete subsequent work for which they won the Nobel Prize. I cannot imagine that today’s environment would allow such a long-term funding commitment. I would like to speculate that today our research is more restricted and that funding generally does not reward risky but innovative proposals.

What incident(s) can stifle a specific research field? I think it is usually a combination of several factors. It is most often the result

of bad research, but other factors, such as a failure of progress because of technical limitations, or a lack of creativity, can stall certain avenues of research. Furthermore, in scientific communities there are always people with strong opinions who can elevate or discredit specific fields of research.

Do you know of a specific example? Yes, this happened with studies on regeneration. In the late 1970s and early 1980s research on regeneration was very active and was studied in many organisms, including *Drosophila*. But most, if not all of these studies were rather descriptive. For example, a piece of limb was removed and the reoccurrence of the missing part was described. On the basis of the final product of regeneration, models were developed. To attend regeneration meetings in the 1980s was rather painful because colleagues argued about almost everything. Strong disagreements were expressed about the data and their interpretation. It was argued whether a model is really a model or a description of the data, and if it was just a description then it could not be tested. The unfriendly tone at those meetings was even reported in the public press. In 1980 I was on sabbatical leave in England. It was at the time when compartments in *Drosophila* were studied and the entire cell lineage in *C. elegans* was worked out. My work on regeneration was criticized because it was argued that nothing could be learned about normal development. Granting agencies also curtailed or stopped supporting studies on regeneration and many scientists left the field.

It is interesting to see a reactivation of research in this field today, with studies on planaria, mice, and others. New approaches, tools and techniques have become available now and allow new and exciting research on regeneration.

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Quick guide

The vomeronasal system and pheromones

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What is a pheromone? Do vertebrates use them?

Pheromones are molecules used for communication between animals within a species, and the response in the receiver can be behavioural or physiological. The word ‘pheromone’ was coined by Karlson and Lüscher and comes from the Greek words *pherein*, meaning to carry or transfer, and *horman*, to excite. Pheromones are used by almost all animals: more communication is through pheromones than any other kind of signal. It appears that pheromones often evolve from non-signal compounds — for example, steroid hormone metabolites leak from female goldfish, and males respond to these compounds as pheromones, causing both attraction and stimulation of sperm production.

Vertebrates use chemical signals for mate attraction, dominance, territorial marking, alarm signals, trail-following, sex ratio manipulation and probably many other functions yet to be discovered. It appears that all vertebrate taxa use pheromones, although the evidence in birds is still somewhat circumstantial. The compounds used are as varied as those of invertebrates — but can sometimes be the same. For example, (Z)-7-dodecen-1-yl acetate is a pheromone in Asian elephants as well as in many moths. As in moths, mixtures of compounds often serve as pheromones in vertebrates. Vertebrate pheromones can be large molecules, like the peptides used by some aquatic vertebrates, or small, although the latter may frequently be

associated with larger carrier proteins.

In addition to pheromones, vertebrates have individual or 'fingerprint odours' that partly reflect genetic factors, such as the MHC type, as well as diet, hormonal state, and bacterial flora: when dogs sniff each other they learn a lot.

What is the vomeronasal system? The vomeronasal system is an accessory olfactory system that is present in most amphibians, reptiles, and mammals. The vomeronasal (Jacobson's) organ contains a sensory epithelium that contains different cell types than olfactory epithelium, and the two epithelia use different transduction mechanisms. The neurons of the vomeronasal and olfactory epithelia project to different parts of the central nervous system through several synapses, suggesting that the two systems have different functions.

Although separate olfactory and vomeronasal systems are present only in tetrapod vertebrates, the 'olfactory system' of teleost fishes may really be more like a combination of an olfactory and vomeronasal system. Neurons in the olfactory epithelium that look like mammalian vomeronasal and olfactory receptor neurons express vomeronasal- and olfactory-type transduction molecules, respectively, and the neurons expressing the different elements project to different parts of the brain.

What is the connection between the vomeronasal system and pheromones?

Although the vomeronasal system is often portrayed as being specialized for detection of pheromones, this idea is contradicted by a substantial amount of data. While it is true that some pheromones are detected via the vomeronasal system, the system also responds to some chemicals that are not pheromones, and some pheromone effects are mediated by the olfactory system.

For example, female mice reach puberty faster when exposed to male odours and will abort developing foetuses if exposed to cues from an unfamiliar male, and both of these effects are dependent on vomeronasal input. On the other hand, oestrous female pigs will adopt a mating posture when exposed to male pheromones, a pheromone response dependent solely on olfactory input.

Similarly, rabbit pups, which nurse in very quick bouts during brief maternal visits to the nest, find nipples using an olfactory-mediated pheromone.

Furthermore, the vomeronasal system is involved in finding food in salamanders, snakes and opossums, so obviously the vomeronasal system responds to more than just pheromones.

So then what does the vomeronasal system do? It is really not clear. Some have suggested that the vomeronasal system responds to non-volatile molecules that are too large to reach the dorsally located olfactory epithelium, and that the olfactory system detects lighter, more volatile molecules. This hypothesis has been hard to test in part because we do not know enough about how chemical stimuli move around and gain access to the various organs, and in part because we do not know enough about the roles of large carrier and transport proteins in urine and mucus. Another idea is that the vomeronasal system mediates unlearned responses to odorants, and that the olfactory system mediates learned responses. Unfortunately, this intriguing idea has received little experimental attention.

Do humans have a vomeronasal system? No.

Embryological studies demonstrate that the vomeronasal organ begins to develop in humans, but dissolves along with the cartilage encapsulating it well before birth. Adults lack a vomeronasal organ, along with functional genes coding for the vomeronasal receptor proteins and

transduction elements. Our nearest relatives, the other apes, also appear to lack a vomeronasal system. The loss of the vomeronasal system in apes is not particularly unusual, as the system has been lost independently several times in bats, as well as in birds, crocodilians, whales and dolphins, and some salamanders.

Do humans have pheromones?

As indicated by the examples from pigs and rabbits, we do not need to have a vomeronasal system to detect pheromones. Sadly, there is no evidence that any smell — free or expensive — can act as an attraction pheromone, making us irresistible.

But there is strong evidence for one human pheromonal effect: when women live in close proximity, their menstrual cycles start to synchronise. This phenomenon can be mimicked by taking swabs from the armpit of one woman and transferring the chemicals to the upper lip of another. The odourless pheromone(s) involved have not yet been identified, but the search is on, as the chemicals involved could offer a route to a new kind of contraceptive.

Where can I find out more?

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