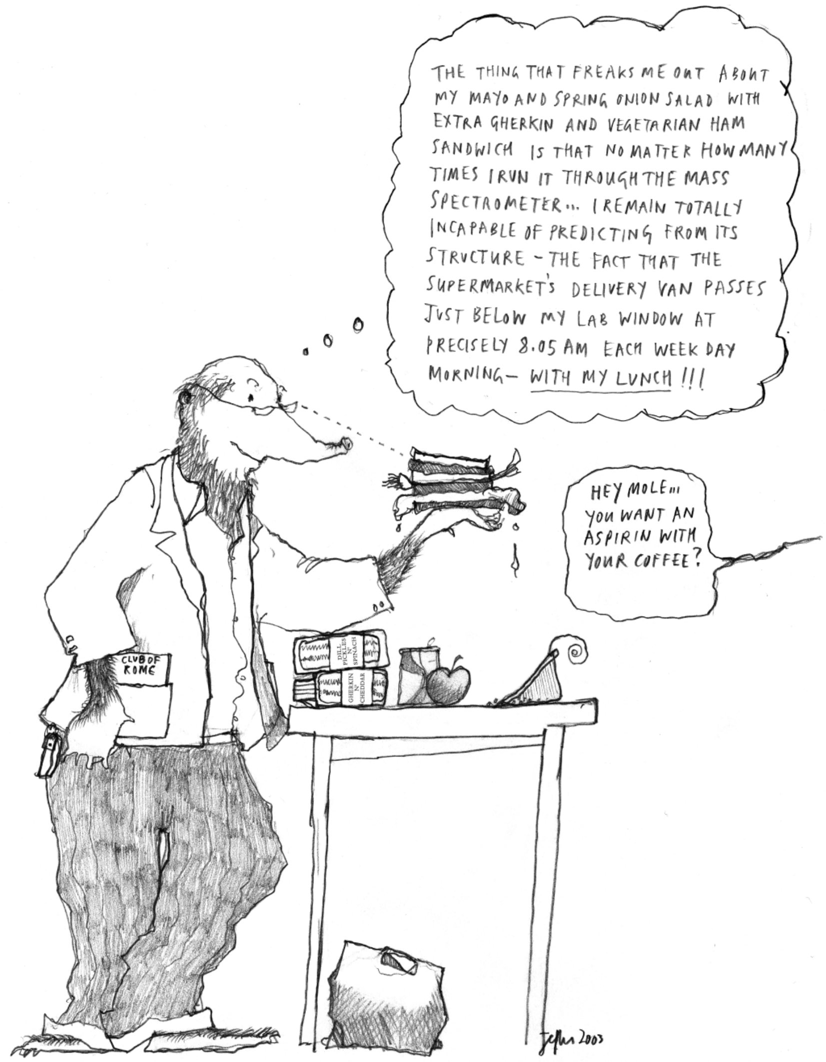
An occasional column, in which Caveman and other troglodytes involved in cell science emerge to share their views on various aspects of life-science research. Messages for Mole can be left at **mole@biologists.com**. Any correspondence may be published in forthcoming issues.



No free lunches

One of the fundamental laws of the universe, without which, apparently, we could not have a universe, is essentially indistinguishable from what we (most of us) learn at a fairly early age: there is no such thing as a free lunch. But before you plunge ahead of me, o astute reader, and presage my discussion of thermodynamics and Carnot engines with a nod and a wink ("I've a friend who for all intents and purposes is almost perpetually in motion", you snicker), I want to derail your thinking path and state from the outset that that isn't what I want to talk about.

I want to talk about lunch.

The fact that I'm sitting on board an airliner that is delayed on the runway well past lunchtime has nothing to do with it. Okay, maybe a little. And the chairman of the department I'm visiting, who was to take me to dinner, informed me in advance that late arrival means no din-din; this also does not figure into this. But perhaps it influenced my thought processes a bit.

Most people, faced with the prospect of lunch, do one of three things: they buy it; they make it; or they convince or coerce someone else to make it for them. This, in a nutshell is the basis of civilization. We are all buying, making or coercing lunch. So much for sociology, economics, anthropology and geopolitical theory.

But scientists, I'm afraid, are a whole different species. We need to know what lunch consists of, what *defines* a lunch. When is it no longer breakfast, and not quite supper? How does a lunch differ from a brunch? Is it still lunch if we don't actually eat it?

What would happen if the molecules in our lunch were not digested but instead simply integrated into our being? Stuart Kauffman, the theoretical biologist, poses this as his "Noah Experiment", asking what impact molecules from other living entities (is it still lunch if it was never living?) would have on our molecular makeup. Alternatively, if we were simply to assemble a sufficiently complex set of molecules, would they spontaneously assemble into lunch? Manfred Eigen, the biological theorist, poses this as his hypercycle and suggests that, yes, this would indeed be lunch, but he can't guarantee that it would be served hot. And would it taste good? Richard Dawkins, the biological biologist, says that any lunch will evolve to taste good or, conversely, we will evolve to experience it as good, which Albert Einstein, the theoretical theorist, asserts is the same thing.

Meanwhile, some of us are exploring the intricacies of lunch, reducing it to our intellectually preferred level of understanding. The physical biochemistry of toasting (why does the bread turn brown rather than some other color, say aquamarine?); the physiology of water homeostasis in lettuce, and how to keep it from wilting; the molecular biology of casein digestion by bacteria (and what makes cheese taste so good); and innumerable studies on pastrami and its relatives.

This is, in short, why science is so hard. We ask so many hard questions, at so many different levels. And that's less than half of it.

There is a notion that is shared not only by informed lay persons (defined as "anyone who has the sense not to do science for a living but still can't help thinking about it, to their never ending detriment") but also by most scientists (same definition but without the "sense") that the business of science is about reductionism. We envision a chain of virtual knowledge (knowledge that might not but in theory *can* exist) that extends from our sandwich to the very fabric of reality, and beyond. No, really. Take a bite (I'd join you, but we're still on the runway – think of me though) and chew it. Now, (in) which reductionistic direction would you like to move (in)? Biochemical metabolism: watch as the various protein, carbohydrate, fat and other molecules are digested, converted, reconverted, inverted, extraverted, and reverted into energy and waste – and trace each hydrogen, carbon and oxygen until they either become us or leave us forever (and good riddance). Or cognitive neurobiology: we chew and receptors on our tongues and in our noses transmit well-defined signals (we can head in the electro-chemico-physiological direction if you wish, but let's not) to the proper regions of the brain to analyze the taste and compare it with a partly learned and partly inherited 'yummy' template, which in turn elicits programmed, innate and more complex responses to signal conspecifics about the state of our lunch ("mmm, but the service is still terrible …"). And the reductionist paradigm implies that in each direction, if we dig more deeply, we can work things out at the chemical, physical, and ultimately mathematical level. We can reduce lunch to an equation – probably a very big equation, but an equation. It could even predict how much it will cost.

The philospher and physicist Michael Polyani challenged this view. Not only isn't this sort of reductionism reasonable, he says, but in many cases it isn't even possible. He pointed out that no amount of dissection of a typewriter would ever reveal what the machine is actually *for*. And for those of you who don't actually know what a typewriter is, substitute toaster. He proposed that there are boundary conditions around levels of study that are defined not by what we *can* do but by what *we want to learn*, and beyond these the information ceases to inform us in a meaningful way. The function of a tyrosine kinase may be critically important in the behavior of cells that present influenza antigens to T lymphocytes, but it probably won't inform us about the patterns of flu epidemics, and no amount of studying that kinase is going to change that.

The staggeringly ingenious medical doctor and writer Stanislaw Lem wrote a staggeringly ingenious and entertaining novel that is translated from Polish to Molish as "The Investigation." In it, a statistician is engaged to figure out why dead people seem to be getting up and walking around a bit before lying down again (it's fiction). I don't want to ruin the ending for those of you who might want to have a look, but in the conclusion he solves the problem – purely from a statistical viewpoint. What Lem shows us (and so terrifically) is that the problem *is* indeed solved, but at the same time isn't solved at all – it all depends on the level at which we want to understand things. Even more intriguingly (or perhaps disturbingly), he goes on to show that the scientific approach may be completely useless in some matters of explanation. But we don't want to go there just yet.

Is there a point here? Oh my yes! It's all about how we do science. Look how many people have contributed to our study of lunch, and none of them comes up on a PubMed search for "lunch". (I sincerely hope that regular readers are fully aware that I have indeed done a PubMed search of "lunch".) Where do you want *your* lunch investigation to take you? When will you be satisfied that you've reached an understanding of your lunch question? Do you *have* a lunch question? And how are you going to answer it?

Okay, so this isn't really about lunch. It's about any sort of phenomenon at all about which we can ask questions. And as scientists many of us assume (at least, those who think about it) that we can ask questions about anything – at any level. But do we? Do we look at the world around us and ask questions? Or do we choose a field and focus our attentions on pleasing mentors, and then supervisors, and then colleagues and editors and reviewers, and work on getting papers published and grants funded and positions appointed and promoted and tenured and retired from? Do we ever worry, in the end, if we've explained anything? Even something as simple as lunch?

Stay with me. Lunch isn't free, but it can be the best part of the day.

Mole

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