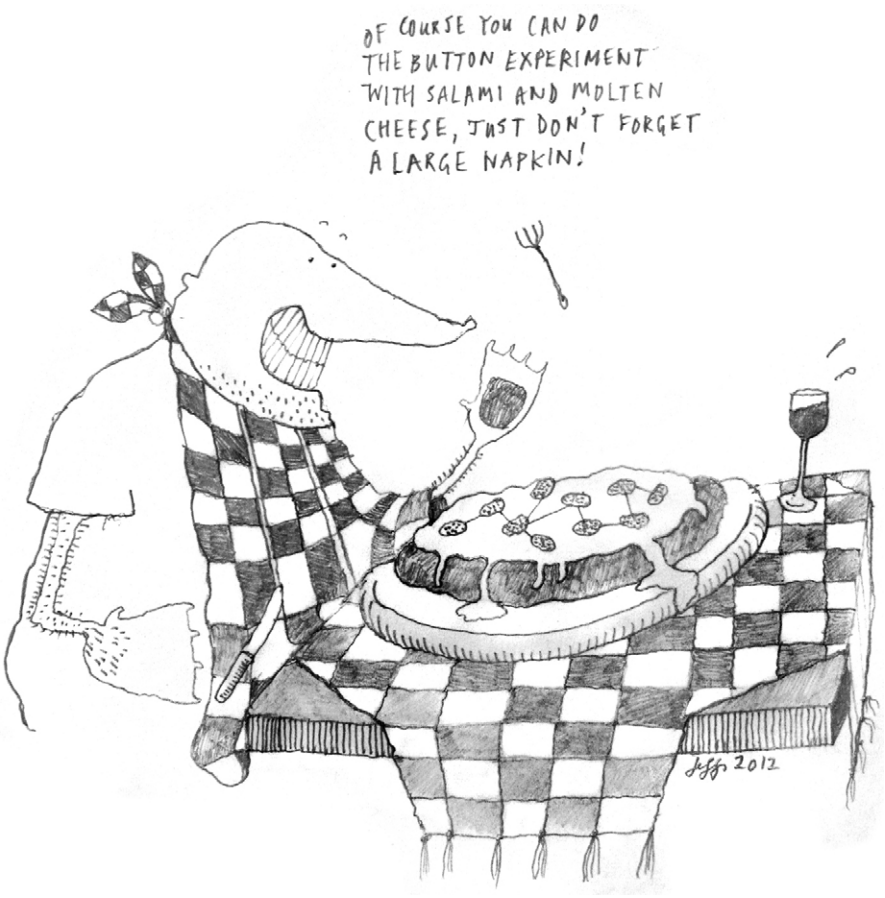
Journal of Cell Science

An occasional column, in which Mole and other characters share their views on various aspects of life-science research. Correspondence for Mole and his friends can be sent to mole@biologists.com, and may be published in forthcoming issues.



My total fave

Buono Sera! Here I am in one of my favorite places, Roma, doing one of my favorite things (attending a good meeting – okay I'm a bit of a geek) but actually really I'm sitting in a park among the antiquities, as the sessions have ended. Oh, and some of my favorite friends are here too: Rabbit and Vole and old Badger among them. Alas, Weasel is not here, but I'll certainly mention him in a bit (so he is here in spirit at least). And soon we'll all have dinner together, *alora*!

Something you start to notice when you hear talks over time, is how some of our colleagues can stay focused on one molecule for years, even decades. We hear how it was discovered (perhaps by the same scientist we are listening to), what they thought it did, what they think now, who it interacts with, how it is modified, what happens if there's more of it, or less of it, or none of it. Their total fave – best molecule forever. Their BMF.

Please don't get me wrong – there's nothing necessarily bad here. Indeed, some molecules are enormously important and the more we learn, the more important we realize they may be. In fact, my dear friend Weasel (ah, I *told* you he'd pop up, in spirit) has spent his career studying a very important molecule, and I'm sure he will continue to do so. Once he said, "the formal definition of an interesting molecule is that I work on it, and therefore *this* one is the *most* interesting of all. By definition." Yes, Weasel has a BMF, and you know I regard him as an extraordinary scientist. Other friends each have their BMFs, and they do fantastic work, often working together if they find that their BMFs interact in interesting ways. Yes, some molecules are awfully important, and it makes sense that we may choose to focus on one of these, maybe for our whole careers. Besides, it makes it pretty easy to remember what we work on. "What does Wombat study again? Oh right, *that* molecule!"

But we also know that there are scientists who focus on a molecule that we may not immediately find compelling or important – we might even find it pretty dull. We might wonder if the focus by this investigator on that BMF is entirely because they actually found it – and often that's true. Many years ago, I had a colleague, Professor Panda,

who was looking for a receptor we thought was important for understanding a class of diseases. What he pulled out, though, was something completely different, unrelated to the problem at hand. So rather than going back to find the receptor, he changed his program, and ever since he has been an expert on his new BMF, trying to figure out what it might do.

So, is every BMF actually *worth* studying? Could be (I bet you thought I was going to say "no", didn't you?). If, for whatever reason, a certain molecule becomes your own BMF, and you can think of some good questions to ask, you may well find your way into some fundamental biology. The reason comes from one of my favorite concepts, illustrated by Stuart Kauffman's wonderful 'button experiment'. Here's how it works: cover a table with a lot of buttons, say a few hundred or more. Choose two buttons at random, tie a piece of thread between them, and drop them back on the table. Now choose any one button out of all of them, pick it up, and count how many buttons you've lifted as a group. Very probably only one (unless you cheated). Now return your button(s) to the table, and choose another two random buttons, tie them together, repeat the random lifting of a button, and record your score again. Keep going (and going) tying more buttons together (even if they are already tied to another) and choosing another random button. Eventually, you will start to lift buttons that are tied to the one you pick, and the score begins to very slowly rise above one.

But if you continue, suddenly you start lifting more and more buttons with each go, and the slope of the scores changes dramatically, until it eventually levels off at nearly all the buttons being lifted with each random choice. That change from very few to very many buttons is essentially a 'phase change' going rapidly from one state of low connectivity to another of high connectivity. And when does this phase change start (that is, when does the curve become dramatically steeper)? The answer is, when the number of threads equals about half the number of buttons.

This is real – of course it isn't something you'll want to do with real buttons and threads unless you have a *lot* of time on your hands, but it's pretty easy to model *in silico*. (Hey, I'm in Roma among the antiquities, so it's fun to slip into pseudo Latin.) Go ahead, look up the button experiment (http://complexityworkshop.com/cw/tutorial/RePast/). I'll wait here in the park.

Back? I've been enjoying the changing light on the trees as evening comes on. Okay, so what's the point of this? Well, suppose 'buttons' are the molecules in a cell. Let's say just the proteins for now. Cells express lots of these buttons, and the 'threads' are the interactions with other proteins. And if the number of threads approaches the number of buttons, we are well into the phase change where almost *any* button is connected to at least very many of the others.

Of course, we know that *every* protein interacts in some way with at *least* one other protein, so the button experiment tells us that our BMF is *very* likely to connect to a large part of the biology of the cell in some way. Our BMF, then, is most probably as good a starting point as any for exploring the complexity represented by the varieties of buttons that come along when we tug on our favorite.

This is not a guarantee that fiddling with any protein is necessarily going to be interesting to other scientists, or even that you are going to discover something new and hopefully exciting (new and exciting are not the same thing – I hope you know that). But you might, especially if you are clever about *how* you tug at your BMF. So go ahead, choose a BMF and play with it, if that is an approach that appeals to you.

And don't forget, there are *lots* of buttons that aren't proteins encoded by our genomes. There are metabolites and stressors and ions. There are viruses and bacteria and other parasites or symbionts that bring along their own collections of buttons to mix with our own. Maybe your BMF is one of these. That's okay too.

Me, I don't have a BMF, I'm afraid. I'm more into processes, the ways in which different types of buttons and threads influence certain aspects of biology. I guess I'm more into the design (and how it came to be without an actual designer), than the components, but that's just me. And the downside of my approach is that it isn't quite so easy to identify me with a BMF: "What does Mole work on? Oh, right, um, stuff." *Alora*!

If you have a BMF, don't apologize, but wear it proudly, and if some of us don't appreciate how special it is, *show* us. Hey, it's *your* total fave. Just please don't be upset with me if it isn't mine.

Anyway, I've got to get ready for dinner and a night on the town. The restaurant is one of my favorites! So, *ciao*, for now.

Mole

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