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Figure 1 | *Drosophila sechellia* feeds and breeds solely on the noni fruit. Auer *et al.*[8] explore the neural and genetic mechanisms that underlie this unusual behaviour.

Neuroscience

Engineering a picky eater

Jessica L. Zung & Carolyn S. McBride

Neurogenetic tools commonly used in model organisms have now been adapted to investigate feeding behaviour in the fly *Drosophila sechellia*. The experiments shed light on why this fly is such a fussy eater. **See p.402**

Even closely related animals can behave in strikingly different ways. For example, the fly *Drosophila sechellia* feeds exclusively on the toxic noni fruit (*Morinda citrifolia*), whereas its closest relatives reject noni in favour of more-conventional options[1]. In these flies[2–4], and in other animals[5–7], researchers have observed intriguing neural differences between close relatives that might explain their differing behaviours. But until recently, it has been impossible to test these neural–behavioural correlations directly. On page 402, Auer *et al.*[8] adapt genome-editing approaches for use in *D. sechellia*. This allows them to probe the neural and genetic changes underlying the fly's dietary preference.

Our story begins with the arrival of *D. sechellia*'s ancestors on the Seychelles archipelago in the Indian Ocean, probably a few hundred thousand years ago[9]. Although at first glance a tropical paradise, the islands probably offered a harsh welcome. The noni fruit — nicknamed the vomit fruit for its pungent smell — might have been one of the only food sources consistently available to the ancient castaways[10]. At first, noni would have been unappealing and even deadly to the flies, but over time they evolved to tolerate the toxins and love the smell[10]. Present-day *D. sechellia* feed on the fruit exclusively[1] (Fig. 1). By contrast, *D. sechellia*'s sibling species *Drosophila simulans* and more distant cousin, *Drosophila melanogaster*, retain their dislike for noni[8].

What makes *D. sechellia* such a picky eater compared with its cosmopolitan, generalist relatives? In 2003, scientists studying the sense of smell in this group of flies uncovered an intriguing clue[2]. One class of sensory

neuron that expresses the protein odorant receptor 22a (Or22a) was more abundant in *D. sechellia* than in any other fly species they analysed. And in both *D. sechellia* and *D. simulans*, these neurons were attuned to a class of compound prevalent in noni odour. Subsequent work revealed similar changes in further sets of noni-sensitive neurons[3,4]. Could these olfactory alterations underlie the specialists' appetite for the smelly fruit? It seemed likely, but an inability to precisely manipulate *D. sechellia*'s olfactory system prevented scientists from moving beyond correlational evidence.

Now, Auer *et al.* have finally cracked the case using the genome-editing tool CRISPR–Cas9. This technology is commonly used in model organisms such as *D. melanogaster* and the mouse, *Mus musculus*, to manipulate genes at will. However, importing the technique into other species is not always straightforward. Other animals might take poorly to life in the laboratory, or it could be difficult to obtain enough viable embryos during the crucial time frame when genome editing takes place. The authors cleared these obstacles, thus gaining the precise genetic control necessary to begin rigorous causality testing.

Auer *et al.* focused on how changes in Or22a contribute to *D. sechellia*'s selective diet. Inactivating the *Or22a* gene left the fly almost completely unable to locate its favourite fruit from just under one metre away. This result confirmed that neurons expressing Or22a process cues that help *D. sechellia* to target noni. But removing a receptor completely is a drastic manipulation — more extreme than the receptor 'tuning' that occurred as Or22a evolved greater sensitivity to noni compounds. It is similar to asking whether you can still perform a concerto on a violin missing a string. The missing string is clearly important, but you cannot tell how its tuning would have affected your performance.

The authors therefore sought to explicitly test how tuning changes in Or22a affect noni-seeking behaviour. They substituted Or22a in *D. melanogaster* with the version of the receptor from *D. sechellia*, and vice versa. The two species' receptors are nearly identical, harbouring just a few changes in amino-acid residues that tweak sensitivity to different compounds. To continue the musical analogy, we might compare this experiment to swapping strings between a violin and a viola and asking how the mismatched, differently tuned strings on each instrument affect the recital. Remarkably, the receptor swap gave *D. melanogaster* a slight taste for noni and diminished *D. sechellia*'s attraction to the fruit. This definitive test, made possible by the group's cutting-edge toolkit, clearly showed that changes in Or22a tuning contribute to *D. sechellia*'s partiality for noni.

Of course, evolution of Or22a tuning is only part of the story. One of the most interesting aspects of Auer and colleagues' study is just how many evolutionary changes might contribute to this apparently simple behavioural shift. The authors confirmed[2] that, besides tinkering with Or22a's tuning, evolution has amplified its ability to trigger downstream signalling in *D. sechellia* by doubling or tripling the number of Or22a neurons. Further receptor-deletion experiments strongly suggested that previously documented changes[3,4] in two other key classes of sensory neuron are also involved. And remodelling of downstream circuits might play a part, too: Auer *et al.* discovered a structural branch on neurons deep in *D. sechellia*'s brain that could alter how the fly processes information about noni odour.

Unfortunately, it remains difficult to directly test causality for many of these evolutionary changes. We can cleanly manipulate the activity of sensory neurons by altering the receptors they express, and can even modify the activity of neurons deeper in the brain — as demonstrated by recent work on the evolution of central brain circuits in two other non-model *Drosophila* species[11,12]. However, it is difficult, if not impossible, to precisely manipulate structural features such as the number of neurons in a circuit or the connections between them. This wiring is established early in an animal's development, and has a genetic basis that is not yet well enough understood to allow custom manipulation. As our neurogenetic toolkits expand, it will be exciting to continue piecing together the puzzle of *D. sechellia*.

We are entering an era in which genetic tools are available to alter precise targets in the nervous systems of diverse organisms. At the same time, we have countless observations of variations in animal behaviour at our disposal, gathered over the past century and more. By combining these two resources, as Auer *et al.* have done in *D. sechellia*, we can finally begin to test long-standing hypotheses about behavioural evolution across a diverse range of organisms. Even humble flies that love stinky fruit can provide powerful insight into how brains evolve to shape complex behaviours.

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Flow chemistry

Automated synthesis on a hub-and-spoke system

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Organic compounds can be synthesized in a continuous flow of solutions, but the need to balance mass flow across multiple reactors complicates the development of such systems. A new platform for flow chemistry addresses this issue. **See p.379**

The desire to perform chemical synthesis quickly and without tedious manual manipulations has long driven the development of automated chemical synthesizers. On page 379, Chatterjee and colleagues[1] report an automated approach that they describe as radial synthesis. In their system, individually accessible compartments for performing reactions are arranged around a central hub that coordinates reagent delivery, product sampling and chemical analysis, and the temporary storage of compounds produced as intermediates. The authors' approach not only promises to reduce manual manipulation, but also eliminates the need to customize a synthesizer for each target molecule.

The synthesis of structurally complex organic molecules is the first task in the discovery of functional compounds needed for new technologies, including those in medicine and flexible electronics. Starting with relatively simple, purchasable reactants, the process