More Fun Than Fun: The Fly in The Room

27th April 2022

*The common house fly (*Musca domestica*). Photo: USDAgov, CC BY 2.0*

RAGHAVENDRA GADAGKAR

This article is part of the 'More Fun Than Fun' column by Prof Raghavendra Gadagkar. He will explore interesting research papers or books and, while placing them in context, make them accessible to a wide readership.

- *Unlike the proverbial elephant in the room, we do not ignore the fly because it is a well-known but uncomfortable truth.*
- *People usually ignore the fly because they do not appreciate its myriad mysteries. To change this is the challenge and the joy of science writing.*
- *Vincent Dethier did this best in his 1962 classic,* To Know A Fly, *in a mere 124 pages with wisdom, wry humour and artful prose.*

> "A fly is just as much in the scheme of things as man… To know the fly is to share a bit in the sublimity of knowledge. That is the challenge and the joy of science."

With these words, Vincent Dethier closed his little classic *To Know A Fly* (1962).

Unlike the proverbial elephant in the room, we do not ignore the fly because it is a well-known but uncomfortable truth. People usually ignore it because they do not appreciate its myriad mysteries. To change this is the challenge and the joy of science writing.

Vincent Dethier

No one could conceivably do this better than Dethier. By all accounts, Vincent Dethier (1915-1993) was a remarkable man. I never had the pleasure of meeting him in person, but in a recent interview, my friend Cynthia Moss who was lucky to have him as her undergraduate advisor, said:

> "Vincent Dethier … was a modest man who made profound scientific discoveries, displayed an extraordinary ability to communicate science to the public … appreciated the arts, wrote novels, … and showed mindful consideration for everyone in his lab, from the washer of glassware to new students and senior postdocs."

In their biographical memoir, his colleagues Alan Gelperin, John Hildebrand and Thomas Eisner had this to say:

> "Vincent Dethier was a man of many facets—scientist, writer, musician, historian, explorer, and paragon of civility. His interests and activities ranged broadly, from the biophysics of chemosensation and the comparative architecture of renaissance cathedrals, to the ecology of natural populations and the tonal structures of baroque cantatas. Just as it takes a village to raise a child, it took a university—nay, several universities—to provide the depth and diversity of colleagues and coworkers to engage fully Vince's varied interests in science and the arts."

Vincent Dethier (1915-1993). Source: University of Massachusetts Amherst, fair use

Yet, the life-long muse of such a man was the humble fly. And with very good reason. Flies may be familiar enough – house flies, mosquitoes, fruit flies, tsetse flies, black flies, carriers of disease and famous for their nuisance value – but that's not the same as appreciating their intricate design, elegant flight, enormous diversity, ancient history or their role as pollinators and as model systems for the scientific study of animal and human life.

Taxonomically, flies belong to the insect order Diptera, a Greek word that reminds us that they possess two wings rather than four, which is more common among insects. In the flies, the hind pair of wings are modified into balancing organs called halteres, and we will return to them.

Flies evolved 140 million years ago. In their long stay on Earth, flies have diversified into hundreds of thousands of distinct species; some 150,000 species have been catalogued.

Among the insects, the ratio of known to unknown species is of the order of 1:10, which may be even higher for flies. It is estimated that there may be some 17 million individual flies on earth for every human being! We often associate flies with disease. Mosquitoes, for example, are best known for spreading malaria, yellow fever, dengue, chikungunya and more. But there is much more to flies.

The blow fly

Dethier chose to study the blow fly (*Phormia regina*), or rather, the blowfly chose him – one particular "egg-burdened female" which flew in through the open lab window (open to beat the heat because the university administration denied him an air conditioner) and deposited her eggs on a liverwurst sandwich that someone had left on the windowsill, as he recounts in *To Know a Fly*.

Blow flies are common metallic blue-green flies, about the size of the common house fly. While the adults feed on nectar, they usually lay their eggs on rotting meat or carcasses. That is why that particular *Phormia regina* female was attracted to the liverwurst sandwich in Dethier's lab and made her species famous. In forensic entomology, blow fly maggots, especially those of *P. regina,* are widely used to determine the time elapsed since the victim's death.

Naturally, Dethier had to grow a large number of blow flies in his lab for his experiments. He says, in his inimitable style,

> "It was both expensive and impractical to continue raising flies on liverwurst sandwiches. And for sanitary and esthetic reasons, it was desirable to find some substitute for the fly's normal diet in nature… For the past eight years or so, they have been breeding happily on a

mixture of powdered milk, brewer's yeast, and agar. Aside from a moderately strong ammonia odor, the cultures are not especially objectionable."

The hungry fly

Dethier and his students focused on the feeding behaviour of the flies. How did the flies know what, when and how much to drink?

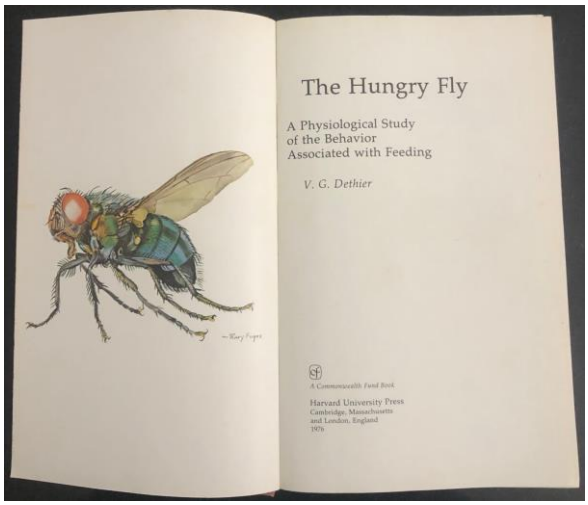
Flies have a rich supply of taste receptors on their foot pads, so they can literally taste with their feet. They will walk around, and whenever they taste something they like, they will extend their proboscis and suck it up. Through simple and elegant experiments, Dethier and his students showed that a hungry fly is ten million times more sensitive to sugar than we are. With simple tricks they learned how to measure the exact quantity of each kind of food the flies drank, which helped them answer many more interesting questions.

The flies drink more if the sugar concentration is high and maximise sugar intake with minimum effort and volume. When the females develop their eggs, their preference shifts temporarily from sugar to protein. These simple facts raise intriguing questions about the mechanisms by which the flies make these decisions.

Answering such questions and exploring the role of different chemoreceptors and the involvement of various muscles and nerves kept the Dethier lab busy and entertained for decades.

The experiment in which they fed the flies with non-metabolisable sugar starkly illustrated the mechanical nature of the fly's behaviour; after drinking some of which, they stopped feeding anymore even though the flies were "metabolically hungry", but were "behaviourally satiated".

Some of their experiments were so intricate that they required great skill; merely technology would not do. They developed painstaking techniques for "transfusing blood, loading the gut, feeding rectally, ligating and removing various regions of the gut, making parabiotic flies, and analysing blood sugar levels," all in these tiny flies. A fascinating discovery concerned how the flies knew when to stop feeding. After eliminating several other possibilities, they zeroed in on feedback from the foregut. Cutting off the nerve connected to the foregut, they "were able to gaze in awe at the bursting hyperphagic flies that [they] had produced".



In 1976, Dethier summarised over 20 years of their research in his magnum opus, evocatively titled *The Hungry Fly*. One can glean a good summary of their research just by browsing the equally evocative chapter titles: 'Appetitive Behavior', 'To Each His Taste', 'The Etiquette of Eating', 'Detecting the Unpalatable', 'The Sweet Tooth', 'The Flavor of Things', 'Avoiding the Temptation of Gluttony', 'Food For the Next Generation'.

Dethier the writer

Dethier was as much a writer as a doer. His biographers tell us that "After a brief appointment as a junior faculty member at John Carroll University in Cleveland, Ohio, Vince joined the Army Air Corps in the Africa-Middle East theater of operations during World War II. Turning adversity into opportunity, he wrote his first book … in the bomb bay of a B-25 using a captured Italian typewriter."

Dethier wrote many books in several genres, textbooks (*Animal Behaviour*, 1961, with Eliot Stellar; *Biological principles and processes, 1971*, with Claude Alvin Villee), monographs (*Chemical Insect attractants and Repellents*, 1947; *The physiology of insect senses*, 1963; *Man's plague?: Insects and agriculture*, 1976), natural history (*To Know a Fly*, 1976; *The Tent Makers* (1980); *The Ecology of a Summer House* (1962); *Crickets and Katydids, Concerts and Solos* (1992)), children's books (*Fairweather Duck*, 1970; *Newberry, The Life and Times of a Maine Clam*, 1981), satires (B*uy Me a*

Volcano, 1972*; The Ant Heap,* 1979), And short stories (*Haboob*, 1960; *The Moth and the Primrose*, 1980).

Dethier took his career as a writer no less seriously than his career as a scientist. In an autobiographical essay, he recalls a phase in his life:

> "Having now taught Introductory Biology (and a potpourri of other courses) for thirty-seven years, with a four-year hiatus during World War II, and having had my tum at the chairmanship at Princeton, I decided upon an early retirement to our home in Maine. Here, so I dreamed, I would pursue my avocation of writing fiction.
>
> In this pursuit I had been moderately successful. I had published two novels, a book of children's stories, and nine short stories. One of the latter was anthologized in the Best of the Kenyon Review and another in the Best American Short Stories of 1981. But it was not to be. Children still in college and the national economy dictated otherwise. I accepted a research professorship at the University of Massachusetts where for the first time I was essentially a totally free spirit."

To Know A Fly

But Dethier's best-known book is surely *To Know A Fly*. In a mere 124 pages, he describes the best in science, but more importantly, he lays bare its process. And he does so with wisdom, wry humour and artful prose, always relating the topic at hand to what his readers might already be familiar with. Wonderfully illustrated too, *To Know a Fly* can and should be read by all, and scientists will do well to read it once a year.

Every paragraph is a gem, but if I have to vote for my best, I will choose the second paragraph (split in three for ease of reading):

> "It is believed in some quarters that to become a successful modern biologist requires a college education and a substantial grant from the Federal Government. The college education not infrequently is as useful for acquiring proficiency in the game of Grantsmanship as it is for understanding biology.
>
> No self-respecting modern biologist can go to work without money for a secretary, a research associate, two laboratory assistants, permanent equipment, consumable supplies, travel, a station wagon for field collecting, photographic supplies, books, animals, animal cages, somebody to care for the animals, postage, telephone calls, reprints, and last, but by no means least, a substantial sum (called overhead) to the university to pay for all the stenographers hired to handle all the papers and money transactions that so big a grant requires.
>
> The grant, of course, must be big in the first place to allow for the overhead. Thus equipped, the biologist retires into his automated electronic laboratory. He may never see a live animal or plant. He has come a long way since the days when he pulled off the wings of flies."

But then he clarifies that this need not be the case. "Anyone with a genuine love of nature, an insatiable curiosity about life, a soaring imagination, devilish ingenuity, the patience of Job, and the ability to read has the basic ingredients and most of the necessary accoutrements to become a first-class biologist."

Through his writings, and especially through *To Know A Fly*, Dethier has not only imparted scientific knowledge but has also inspired his readers to become scientists themselves, reminding me of the philosopher Daniel Dennett's aphorism: "A scholar is just a library's way of making another library." Dethier has made many libraries by inspiring many a scholar. Let me introduce one of them here.

Sanjay Sane

My friend and colleague Sanjay Sane told me recently in an email:

> "I like that the book [*To Know A Fly*] infuses its reader with exactly the right spirit: it presents research as a curiosity-driven, often serendipitous, and joy-filled endeavour. It does not shy away from presenting the difficulties, but stops well short of treating them as problems. Each time [a] student returns my old weather-beaten copy of the book, I spend some time thumbing through the pages and reminding myself of what a precious little treasure I acquired from a used book store."

Sanjay Sane now heads a research group studying "The Physics, Neurobiology and Ecophysiology of Insect Flight" at the National Centre for Biological Sciences in Bengaluru, India. Educated in St. Stephens College in Delhi and the University of Poona, Sane studied physics, was charmed by mathematics and wanted to study astrophysics to detect gravitational waves and ultimately applied his interest in fluid mechanics to the study of insect flight!

Often the most successful scientists, and the happiest ones, are those that reach their topic of study by circuitous path, the simple reason being that they have gathered a lot of knowledge and wisdom as they hovered over and rejected vast landscapes of knowledge, in search of their true calling.

Left panel: Sanjay Sane and Tanvi Deora. Right panel, top: Amit Kumar Singh; bottom: Siddharth Sane

Sane was even more unusual in that he had found his true calling even before his PhD, which he pursued at the University of California, Berkely. He studied how insects generated the aerodynamic force needed to fly using a mechanical model of the fruit fly (*Drosophila melanogaster*).

Not content with the so-called "Robofly", Sane moved to the University of Washington as a postdoc to study the mechanosensory control of insect flight. In one of many fascinating pieces of work, he showed that four-winged insects such as moths that lack the balancing organs called halteres (modified hind wings) maintain flight stability using their antennae instead.

Return to India

The next major event in Sane's career was the decision to return to India to continue to pursue his calling, often a challenging transition for those abroad for graduate studies and a few mandatory years of postdoctoral training.

In my experience, most people have a hard landing. They are suddenly thrown into a new situation almost always suboptimal compared to their previous experience – in terms of the state-of-the-art technology, funding, academic freedom, and above all, in terms of a critical mass of like-minded scientists pursuing similar or parallel interests with whom they can readily share ideas and experience.

We also unnecessarily add to their difficulty by demanding a rapid accumulation of peer-reviewed publications in so-called high-profile journals. The easiest way to deal with this situation is to

continue working on a problem they have already been working on abroad, preferably collaborating with their PhD or postdoc mentors.

Such a course has an unfortunate consequence. They forego the opportunity to assess their new situation at home and choose scientific problems that, while interesting to them, allow them to capitalise on their strengths and duck their weaknesses.

Sane is made of more potent stuff, and he has made as good an example of a soft landing as I am aware. When asked why he went back to India, he said the reasons were personal: his parents wished it, and he and his spouse desired their two boys to grow up with their extended family. Despite having returned for personal reasons, he was quick to identify the professional advantages and disadvantages of working in India and steer his career trajectory to capitalise on his situation.

Sane has had the wisdom to realise that our rich biodiversity is one of our great strengths, and he has dared to work on locally available non-model organisms with the clear motivation that it would allow him to take his research back and forth between lab and field. It is easy to imagine Dethier's wry remark, that "Thus equipped, the biologist retires into his automated electronic laboratory. He may never see a live animal or plant", played a role in this decision.

Sane also realised that another strength is our human capital – "wonderful students who are hungry to learn" – and he has therefore trained an unusually large number of them. But he also realised that maintaining a large research group comes with loads of administration, especially in India, but he has had the sagacity to accept this "recalling the Urdu saying *kisi ko muqammal jahan nahi milta*" ('nobody gets a readymade world'.

As I already mentioned, the hind wings of flies are modified into balancing organs called halteres. But how do the halteres balance the fly during complex aerodynamic manoeuvres?

It is known that the wings and the halteres oscillate at the same frequency but in opposite phases. What is the nature of the feedback between the wings and the halteres? How do the wings and halters know each other's phase? Sane and his students set about investigating this question using the so-called soldier fly (*Hermetia illucens*).

Tanvi Deora, took up the challenge because she loved neuroscience. A reasonable hypothesis was that neurons mediated the coordination between the wings and the halteres. However reasonable, we should first see if we can falsify a hypothesis.

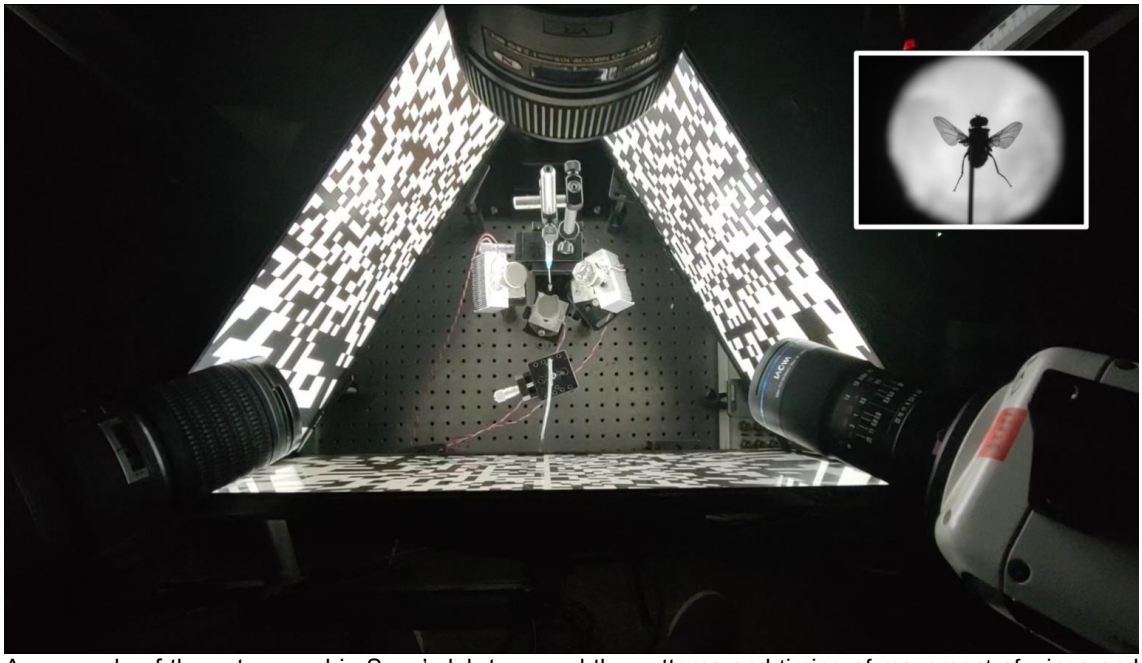
The 'reasonable' hypothesis was categorically falsified because the wing-halter coordination was intact in dead flies! Clearly, the answer to their question was not to be found in the neurons but in some mechanical properties of the wings and halteres and how they are connected to the thorax. This must have been deeply disappointing to the aspiring neuroscientist.

The fly's chassis, clutch and gearbox

Students often fall in love with the domain of their research, such as neurobiology for example, or the methods they employ. Blowing a glass electrode to record the electrical activity of single neurons – now, how sexy is that?

It requires a great deal of maturity to remain focussed on a question even if answering it needs a change of method or even crossover to another domain. Such maturity usually comes late, often not at all.

But Tanvi Deora is different. Sane says, "Overnight, Tanvi went from being an aspiring neurobiologist to a practising biomechanist. In collaboration with a junior research fellow, Amit Kumar Singh, she performed a series of meticulous experiments that uncovered the mechanical connectivity in the thorax".



An example of the setup used in Sane's lab to record the patterns and timing of movement of wings and halteres. The inset on the right shows what the cameras sees. Here, the test subject animal is the common house fly (Musca domestica). Photo: Abin Ghosh

The biomechanical experiments showed that purely mechanical linkages passively coordinated both wing-haltere and wing-wing coordination on the fly's thorax. Adding to the 'gearbox' idea already postulated, they now proposed a clutch mechanism to engage or disengage the wings, one at a time.

The analogy to automobile transmission systems cannot be missed. But the small size of the flies makes such a mechanism most impressive, leading them to claim that "their study provides important design principles for engineers in their efforts to develop micro-robotic insects".

In a follow-up study, they reduced wing length to simulate wear and tear, deformed various parts of the thorax or added weights to the halteres to test the robustness of the fly's flight system.

Here is another backstory of interest. After completing these follow-up experiments and submitting a paper for publication, Tanvi flew off to Washington University to do a postdoc – who can blame her?

But meanwhile, the reviewers of the manuscript demanded digitisation and analysis of many more videos. This is how science works in real life. Tanvi was stuck in the US, and Sane could not find an intern because of the prevailing COVID-19 pandemic. So, what does he do?

He turns to his son. Siddharth had just finished his high school exam and seemed bored sitting at home. He asks: "Would you work on a project with me?". "I was just waiting for you to ask!" came the reply. And so Siddharth Sane mastered the programming language Python, learnt how to digitise videos, contributed significantly to this work and became a co-author at a young age.

For the senior Sane, science knows no boundaries between home and lab: his spouse Namrata Gundiah, who is at the Department of Mechanical Engineering at the neighbouring Indian Institute of Science, joined him and his students to review the literature on the mechanics of the thorax in flies.

But as I said of Dethier, Sane's ever-lasting contribution may well be the next generation he has inspired. It warmed my heart when he told me, "Every student – graduate, intern, JRF, high school – that enters my lab mandatorily starts with Dethier's *To Know a Fly*."

Like the chain letter that Kathryn Schulz describes in *The New Yorker*, with such humour and elegance, Sane has kept Dethier's legacy alive. It is now up to his students to inspire yet another generation, and I dare say that they will not find *To Know A Fly* wanting.

Raghavendra Gadagkar is a Department of Science and Technology (DST) Year of Science Chair Professor at the Centre for Ecological Sciences at the Indian Institute of Science, Bengaluru.

Gadagkar, R., 2022. More Fun Than Fun: The Fly in The Room. The Wire Science. URL https://science.thewire.in/the-sciences/to-know-a-fly-vincent-dethier/