RNA might simultaneously promote loss of normal function and gain of toxic function, posing a quadruple threat.

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- DeJesus-Hernandez, M. et al. Neuron 72, 245–256 (2011).
- 2. Renton, A. E. et al. Neuron 72, 257-268 (2011).
- 3. Haeusler, A. R. et al. Nature 507, 195-200 (2014).

- Bochman, M. L., Paeschke, K. & Zakian, V. A. Nature Rev. Genet. 13, 770–780 (2012).
- 5. Fratta, P. et al. Sci. Rep. 2, 1016 (2012).
- Reddy, K., Zamiri, B., Stanley, S. Y. R., Macgregor, R. B. Jr & Pearson, C. E. J. Biol. Chem. 288, 9860–9866 (2013)
- Aguilera, A. & García-Muse, T. Mol. Cell 46, 115–124 (2012).
- Gijselinck, I. et al. Lancet Neurol. 11, 54–65 (2012).
 Xi, R. et al. Am. J. Hum. Genet. 92, 981–989 (2013).
- 9. XI, R. et al. Am. J. Hum. Genet. **92**, 981–989 (2013). 10.Sareen, D. et al. Sci. Transl. Med. **5**, 208ra149 (2013).
- 11. Donnelly, C. J. et al. Neuron **80**, 415–428 (2013).
- 12. Echeverria, G. V. & Cooper, T. A. *Brain Res.* **1462**, 100–111 (2012)

13.Mori, K. et al. Acta Neuropathol. (Berl.) **125**, 413–423 (2013).

14.Lee, Y.-B. et al. Cell Rep. **5**, 1178–1186 (2013). 15.Xu, Z. et al. Proc. Natl Acad. Sci. USA **110**, 7778–7783

- 16. Abdelmohsen, K. & Gorospe, M. RNA Biol. 9, 799–808 (2012).
- 17.Lagier-Tourenne, C. et al. Proc. Natl Acad. Sci. USA 110, E4530–E4539 (2013).
- 18.Therrien, M., Rouleau, G. A., Dion, P. A. & Parker, A. *PLoS ONE* **8**, e83450 (2013).
- 19.Ciura, S. et al. Ann. Neurol. 74, 180-187 (2013).

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NEUROSCIENCE

Ordered randomness in fly love songs

A systematic and painstaking analysis reveals that much of the complexity and variability of the courtship song of male fruit flies can be accounted for by simple rules that relate sensory experience to motor output. SEE LETTER P.233

BENCE P. ÖLVECZKY

ticket to fun times and reproductive success, whether you are a member of the Beatles or one of the many animals that woo their mates by singing. Although some troubadours serve up monotonous repetitions of stereotyped songs, most animals, including birds, mammals and insects, like to jazz things

up by varying their song patterns. But how the brain generates such variability, and improvisation more generally, remains largely a mystery. On page 233, Coen *et al.*¹ shed light on this issue by showing that much of the variability in the love songs of fruit flies can be predicted from the singers' movements.

Neuroscientists' fascination with the sex life of the fruit fly Drosophila melanogaster began more than 35 years ago with the discovery of fruitless, a gene essential for the male courtship ritual². This unique handle on a complex social behaviour, in an organism amenable to genetic modification, paved the way for an exceedingly detailed anatomical mapping of the underlying neural circuitry^{3,4}. Deciphering the details of what these circuits do and determining what they can teach us about brain function more broadly are major challenges that would be greatly helped by having a comprehensive description of the computations that the circuits perform and the behaviours they implement.

One thing that we know these circuits do is transform their male owners into mini Casanovas. On encountering a receptive virgin female, a male fly will gently tap her rear end, serenade her with a 'song' by vibrating one of his wings, and lick her genitalia⁵. Although these behaviours are part of any self-respecting fly's lovemaking repertoire, the duration and ordering of the different courtship elements can be highly unpredictable.

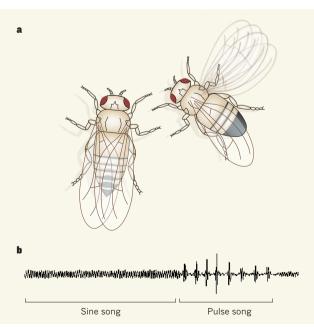


Figure 1 | **The male fruit fly's serenade. a**, Male fruit flies attract females by vibrating one of their wings. **b**, The fly has two distinct song types — the humming sine song and the purring pulse song — and switches between them to generate variable song sequences. Coen $et\ al.$ found that these switches can be predicted by the fly's movements. (Data depicted in **b** taken from Fig. 6 of ref. 11.)

What gives rise to such seemingly random behaviour? Is the variability due to stochastic fluctuations in the underlying neural networks (neural noise)^{6,7}, or the result of a dynamic sensory experience?

To address these questions, Coen and colleagues focused on the male fly's song, itself a variable sequence of distinct elements ^{1,8}. Just as the Beatles made a career of mixing 'love', 'you', 'me', 'she' and 'baby' in different ways, so male fruit flies switch between 'sine' and 'pulse' songs to impress their audience (Fig. 1). By eavesdropping on more than 100,000 love songs while carefully monitoring the whereabouts of the courting couple, the authors suggest that a logic and order exist in the apparent musical randomness.

Coen *et al.* performed a statistical analysis of their high-resolution behavioural data, and found that transitions between sine and pulse songs can be predicted from the courted female's movements. The authors further discovered that the male's visual experience of the female shapes his song through neural circuits

that control locomotion. In fact, the best predictor of song structure is not the female's movements, but the singer's own. Even blind flies, who are induced to sing by the scent of virgin females, show a bias in their song transitions that can be predicted from their movements. The picture that emerges from all of this is one in which the male fly executes a tightly integrated song-and-dance number, inspired by (if he can see her) his partner's movements.

As impressive as that may be, the extent to which the female cares about the details of her lover's intricate performance remains unclear. Does she use information embedded in his song pattern to determine his desirability? Does his ability to couple changes in his song to body movements — his or hers — correlate with other qualities that she would want in a mate? In other words, is song patterning an example of a carefully tuned signalling system, or does it reflect a coupling between leg and wing movements that evolved for unrelated reasons?



50 Years Ago

Recent investigations have shown that the fluoride content of Greek teeth from the cities of Athens and Salonika was considerably high. This may explain, at least in part, the low prevalence of dental caries observed in Greece ... With the exception of sea salt, however, the fluoride content of other foods commonly produced and consumed in Greece is not known ... The analyses showed that the fluoride content of olive oil from the Island of Crete was 0.36 p.p.m. and that from the area of Kalamai 0.63 p.p.m... it appears that the inclusion of olive oil in the daily Greek diet does not make any significant contribution to the amount of ingested fluoride. Thus, at present, sea salt remains an important source of dietary fluoride in Greece for protection against dental caries. This may well be the case in other countries, such as Taiwan, Ceylon and Lebanon, where because of local food customs the amount of sea salt consumed has been estimated to be considerable: about 16-20 g per person per day. From Nature 14 March 1964

100 Years Ago

Think of the Niagaras of speech pouring silently through the New York telephone exchanges where they are sorted out, given a new direction, and delivered audibly perhaps a thousand miles away. New York has 450,000 instruments — twice the number of those in London. Los Angeles has a telephone to every four inhabitants ... Our whole social structure has been reorganised. We have been brought together in a single parlour for conversation and to conduct affairs, because the American Telephone and Telegraph company spends annually for research ... a sum greater than the total income of many universities.

From Nature 12 March 1914

Initial experiments to address these questions have failed to provide clear answers. Coen et al. show that song transitions are similar whether or not the singer is ultimately successful in mating. Yet pheromone-insensitive males, who sing for normal durations but have altered song patterning⁸, tend to be slower and less successful in convincing females to mate^{1,8}. Whether these flies are handicapped in the courting game because of a defect in how they vary their songs, or because of unrelated effects, remains to be seen. But whether song patterning matters to females or not, we now know that its variability, and probably the variability of many other 'fixed' behaviours, is not simply the consequence of noise in nervous-system function 6,7 . Rather, a sizeable fraction of that variability is likely to reflect computations performed by reliable and predictable brains on an ever-changing sensory environment.

Importantly, this insight was made possible by simultaneously observing, at high temporal resolution, the sensory environment and behavioural output of a genetically tractable organism during a complex social interaction. Such detailed analysis applied to natural behaviours has the power, as Coen et al. aptly demonstrate, to distil seemingly complex and unpredictable behavioural patterns into simple rules and sensorimotor transformations^{9,10}. With such an

approach, rather than being the fog that prevents us from understanding nervous-system function, behavioural variability and complexity can be the searchlight that helps us to identify the computational problems that brains evolved to solve. ■

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- 1. Coen, P. et al. Nature 507, 233-237 (2014).
- 2. Hall, J. C. Behav. Genet. 8, 125-141 (1978).
- Stockinger, P., Kvitsiani, D., Rotkopf, S., Tirián, L. & Dickson, B. J. *Cell* **121**, 795–807 (2005).
- Yu, J. Y., Kanai, M. I., Demir, E., Jefferis, G. S. X. E. & Dickson, B. J. Curr. Biol. 20, 1602-1614 (2010).
- Spieth, H. T. Annu. Rev. Entomol. 19, 385-405 (1974).
- Faisal, A. A., Selen, L. P. J. & Wolpert, D. M. Nature Rev. Neurosci. 9, 292-303 (2008)
- 7. Destexhe, A. & Rudolph-Lilith, M. Neuronal Noise (Springer, 2012).
- Trott, A. R., Donelson, N. C., Griffith, L. C. & Ejima, A. PLoS ONE 7, e46025 (2012).
- 9. Katz, Y., Tunstrøm, K., Ioannou, C. C., Huepe, C. & Couzin, I. D. Proc. Natl Acad. Sci. USA 108,
- 18720–18725 (2011). 10.Censi, A., Straw, A. D., Sayaman, R. W., Murray, R. M. & Dickinson, M. H. PLoS Comput. Biol. 9, e1002891 (2013).
- 11. Rideout, E. J., Dornan, A. J., Neville, M. C., Eadie, S. & Goodwin, S. F. Nature Neurosci. 13, 458-466

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EVOLUTIONARY BIOLOGY

Speciation undone

Hybridization can cause two species to fuse into a single population. New observations suggest that two species of Darwin's finches are hybridizing on a Galapagos island, and that a third one has disappeared through interbreeding.

PETER R. GRANT & B. ROSEMARY GRANT

The process of speciation, in which one species splits into two, is vulnerable to collapse in its early stages through interbreeding and the exchange of genes, a process referred to as introgression. As explained by the evolutionary biologist Theodosius Dobzhansky¹, "Introgressive hybridization may, then, be a passing stage in the process of species formation. On the other hand, the adaptive value of hybrids may be as high as that of their parent; introgressive hybridization may lead to obliteration of the differences between the incipient species and their fusion into a single variable one, thus undoing the result of the previous divergent development." Writing in American Naturalist, Kleindorfer et al.2 offer a possible example of this process, in a study suggesting that one population of Darwin's finches has become extinct through interbreeding with another.

Until Kleindorfer and colleagues' report, three species of tree finch were known to occur together in the highlands of Floreana Island in the Galapagos (Fig. 1). They differ in body size and in the size and shape of the beak, but, unlike many birds elsewhere, not in plumage. The medium tree finch (Camarhynchus pauper) is present only on Floreana, whereas the small tree finch (Camarhynchus parvulus) and large tree finch (Camarhynchus psittacula) also occur together on several other islands. The pattern of distribution and size differences led evolutionary biologist David Lack to suggest³ that speciation had occurred on Floreana through the invasion of large tree finches from Isabela Island, followed by evolutionary reduction in average size. The resulting medium tree finches did not interbreed with the large tree finches that arrived later, apparently from Santa Cruz Island.

Kleindorfer and colleagues now report that this pattern no longer exists: the large tree finch