the approaches that Hopkins and colleagues took to quantify the strength of reinforcing natural selection in the case of speciation in the *Phlox* system [20].

Hopkins and colleagues took painstaking measurements of the distribution of *P. drumondii*, *P. cuspidata*, and their hybrids across a large swath of their natural distribution and measured the fitness of each of the three genotypes across their geographical range. In total, the authors measured the flower color and hue of over 10,000 *P. drummondii* individuals from 32 populations across 5 transects. In all transects they found sharp changes in phenotypic frequency in *P. drummondii* flower color. The boundary can be explained by strong selection on flower color in populations of *P. drummondii* sympatric with *P. cuspidata*, but it does not provide precise estimates of the magnitude of selection. The authors next took their fine assessment of the geographic distribution of phenotypes and their fitness, and applied classical population genetics techniques to determine the most likely explanation for the distribution of the observed genotypes. For each genotype (two pure species and the hybrids), the model calculates the relative fitness in sympatry, the relative fitness in allopatry, the levels of dispersal between allopatric and sympatric populations, and the locations of the boundaries between the allopatric and sympatric zones in each of the five transects. With this population genetics model, they precisely estimated the strength of selection. Not only do their results confirm that selection against hybridization is exceptionally strong in *Phlox*, but the model also supports previous observations that weaker, but significant, selection favors alternative alleles at both flower color loci in sympatric and allopatric *P. drummondii* populations. This could explain why the dark red flower phenotype does not spread to the whole geographic range of *P. drummondii*.

Why is this study important? First, it demonstrates the utility of studying natural variation in traits involved in reproductive isolation across the whole geographic range of a species. Second, it revitalizes a classic population genetics approach (cline theory) to understand the strength of natural selection in nature. Finally, these results provide a cutting edge quantitative analysis of reinforcement in a taxon that has been crucial for our modern understanding of the speciation process, that mystery of mysteries.

References
1. Darwin, C. (1859). On the Origin of Species by Means of Natural Selection (London: Murray).
2. Coyne, J.A., and Orr, H.A. (2004). Speciation (Sunderland, MA: Sinauer Associates).
3. Rieseberg, L.H., Wood, T.E., and Baack, E.J. (2006). The nature of plant species. Nature *440*, 524–527.
4. Servedio, M.R., and Noor, M.A. (2003). The role of reinforcement in speciation: theory and data. Annu. Rev. Ecol. Evol. *34*, 339–364.
5. Hopkins, R., Guerrero, R.F., Rausher, M.D., and Kirkpatrick, M. (2014). Strong reinforcing selection in a Texas wildflower. Curr. Biol. *24*, 1995–1999.
6. Templeton, A.R. (1981). Mechanisms of speciation - a population genetic approach. Annu. Rev. Ecol. Evol. *12*, 23–48.
7. Sanderson, N. (1989). Can gene flow prevent reinforcement? Evolution *43*, 1223–1235.
8. Levin, D.A., and Kerster, H.W. (1967). Natural selection for reproductive isolation in *Phlox*. Evolution *43*, 679–687.
9. Hopkins, R., and Rausher, M.D. (2011). Identification of two genes causing reinforcement in the Texas wildflower *Phlox drummondii*. Nature *469*, 411–415.
10. Levin, D.A. (1985). Reproductive character displacement in *Phlox*. Evolution *39*, 1275–1281.
11. Koopman, K.F. (1950). Natural selection for reproductive isolation between *Drosophila pseudoobscura* and *Drosophila persimilis*. Evolution *4*, 135–148.
12. Higgie, M.A., Chenoweth, S.F., and Blows, M.W. (2000). Natural selection and the reinforcement of mate recognition. Science *290*, 519–521.
13. Matute, D.R. (2010). reinforcement can overcome gene flow during speciation in *Drosophila*. Curr. Biol. *20*, 2229–2233.
14. Dod, B., Smadja, C., Karn, R.C., and Boursot, P. (2005). Testing for selection on the Androgen-Binding-Protein in the Danish house mouse hybrid zone. Special issue: the genus Mus as a model for evolutionary biology. Biol. J. Linnean Soc. *84*, 447–459.
15. Palumbi, S.R. (2008). Speciation and the evolution of gamete recognition genes: pattern and process. Heredity *102*, 66–76.
16. Ortiz-Barrientos, D., Counterman, B.A., and Noor, M.A. (2004). The genetics of speciation by reinforcement. PLoS Biol. *2*, e416.
17. Hopkins, R., Levin, D.A., and Rausher, M.D. (2011). Molecular signatures of selection on reproductive character displacement of flower color in *Phlox drummondii*. Evolution *66*, 469–485.
18. Haldane, J.B.S. (1948). The theory of a cline. J. Genet. *48*, 277–284.
19. Slatkin, M. (1973). Gene flow and selection in a cline. Genetics *75*, 733–756.
20. Hopkins, R., and Rausher, M.D. (2014). The cost of reinforcement: selection on flower color in allopatric populations of *Phlox drummondii*. Am. Nat. *183*, 693–710.

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Neural Coding: Sparse but On Time

To code information efficiently, sensory systems use sparse representations. In a sparse code, a specific stimulus activates only few spikes in a small number of neurons. A new study shows that the temporal pattern across sparsely activated neurons encodes information, suggesting that the sparse code extends into the time domain.

Peter Kloppenburg[1] and Martin Paul Nawrot[2]

In a natural environment, the sensory information for all modalities is rich and highly dynamic in time. To make sense of this permanent flow of information, brains — as well as manmade artificial systems — need strategies to encode and process the information efficiently. In a sensory nervous system, information about the outside world is represented in different types of neural code. At the sensory periphery this is a dense population code, meaning that the information is represented in a large proportion of highly active (sensory) neurons. As the information is transferred to higher level processing stages, the neural code often changes from dense to sparse. In sparse coding [1] the information is represented by only a small fraction of all neurons (population sparseness) and each activated neuron generates only few action potentials (temporal sparseness) for a highly specific stimulus configuration (lifetime sparseness). The sparse code has been
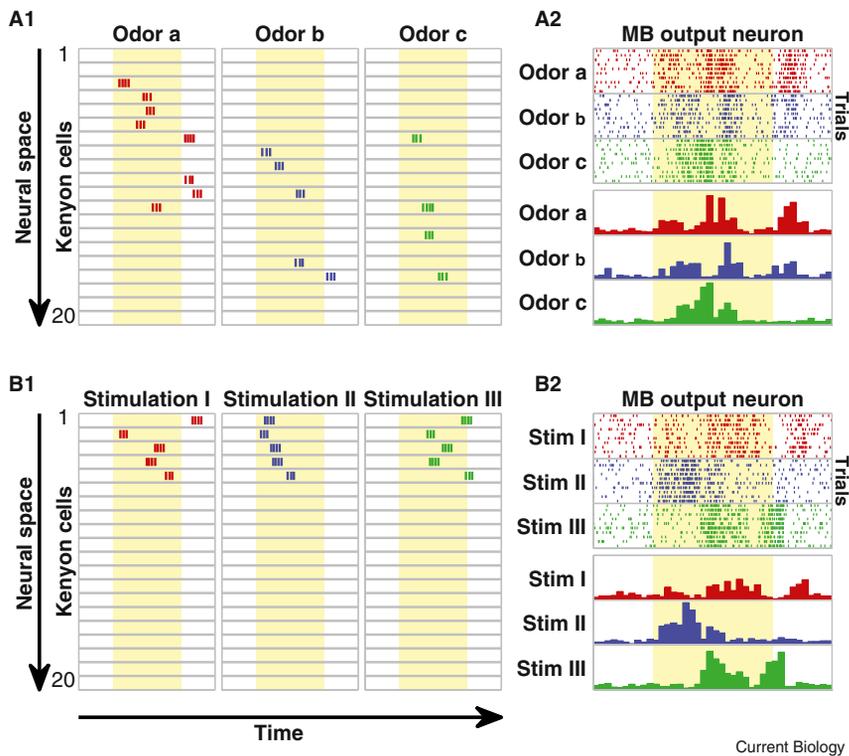
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Figure 1. Sparse coding in the Kenyon cell population and dense coding in a mushroom body (MB) output neuron.

(A1) Simulation: odor responses of Kenyon cells are population sparse (only few cells are activated) and temporally sparse (only few response spikes per Kenyon cell). Each cell responds to one or at most two odors and different odors evoke spatial response patterns with little overlap (lifetime sparseness). For display purposes only few silent Kenyon cells are shown. (A2) Odor responses in one mushroom body output neuron receiving converging input from the total Kenyon cell population in (A1). The spike trains during 10 repeated stimulation trials show a clearly odor-specific temporal activation pattern. Histogram estimates of the time-varying firing rate in 50 ms bins quantify the temporal differences in the firing rate. These time histograms underlie the classification approach in Gupta and Stopfer [13]. (B1) Simulation of three different Kenyon cell stimulation sequences. The same subset of Kenyon cells is stimulated in all 3 cases, although in a different temporal order. (B2) The spike response patterns and firing rate histograms (50 ms bin width) in the single mushroom body output neuron are distinct (on a time scale of ~100 ms) for the three different temporal stimulation patterns in (B1). This shows that a change of the temporal pattern in a fixed Kenyon cell population alone can lead to distinct activation patterns in the mushroom body output neurons.

shown to be implemented in both invertebrate and vertebrate sensory systems of different modalities, for example in the mammalian visual [2], auditory [3], somatosensory [4], and olfactory [5] cortices.

A particularly well-suited system to study sparse coding in the central brain are the insect mushroom bodies, multimodal sensory processing centers which are crucial for olfactory learning [6,7]. Mushroom bodies consist predominantly of a large number of Kenyon cells, which use an extremely sparse code for odor representation (for example, [8–12]). These neurons have a very low (close to zero) spontaneous activity and

specific odors are represented by very few action potentials in specific and small subsets of Kenyon cells (Figure 1A1).

In a study reported in this issue of *Current Biology*, Gupta and Stopfer [13] used this system to investigate the relevance of the time dimension for sparse odor coding. Their work reveals that the temporal structure of sparse neuron activation encodes odor information. The authors first confirmed that in Kenyon cells odors are represented by sparse responses with odor specific timing. Next, they recorded from mushroom body output neurons, which receive direct and converging input from

Kenyon cells. In accordance with earlier work [14], they found that these neurons represent information in a dense population code, in which individual neurons show odor specific temporal profiles of their firing rate.

In an elegant set of experiments, Gupta and Stopfer [13] used highly localized stimulation to induce controlled spatio-temporal activity patterns in Kenyon cells. In their central experiment (Figure 6 in [13]), they used four independent bipolar electrodes, which allowed them to independently stimulate four subsets of Kenyon cells. Activating these subsets in different temporal sequences caused clearly different temporal firing rate profiles in the mushroom body output neurons. This suggests that the temporal pattern of Kenyon cell activity shapes the dynamic read-out, since the very same overall Kenyon cell population was activated in all cases. This conclusion is supported by the simulation illustrated in Figure 1, where the temporal pattern of Kenyon cell activation in a fixed population of Kenyon cells modulates the activity in the read-out neurons.

In the broader context of latency coding the new paper [13] confirms that odor-specific latency patterns across neurons exist from the periphery throughout all processing stages [15] and across coding schemes. The results indicate that response latencies are not simply a nuisance to the system, but that the system makes use of these latency patterns. Note that the latencies explored in this context vary in the order of tens to hundreds of milliseconds. This aspect should not be confused with the different notion of temporal coding where temporally precise spike patterns in the millisecond range are thought to carry highly specific information [16]. In the future a crucial step will be to investigate the spatio-temporal code in the mushroom bodies under more natural stimulus conditions where the olfactory scene changes dynamically in respect to composition and concentration of odorants.

Taken together, the new experiments have revealed that the spatio-temporal sequence of Kenyon cell activation determines the spike rate profiles of the mushroom body output neurons. This suggests that

the sparse code extends into the time domain, in this case with a relevant time resolution of tens to hundreds of milliseconds. Extending into the time domain naturally increases the coding capacity at this stage of processing.

The Gupta and Stopfer paper [13] is also important because it sheds light on the read-out of sparse representations. While we have a reasonable understanding of sparse representations in the insect mushroom bodies and the vertebrate cortex, the read-out is still poorly understood. The authors clearly show that the representation changes from dense in the sensory system to sparse in the Kenyon cells and again to dense at the level of the output neurons. Changing coding schemes might be a common principle, because recent work in the mammalian cortex has shown that sparse representation in cortical input layers is transformed to a dense representation in output layers (for review see [4,17]). Notably, both cortex and insect mushroom bodys are involved in associative learning and theoretical studies have shown that sparse representations improve learning of associative representations (for example, [18,19]).

While the precise role of the mushroom body output neurons is currently not clear, it is unlikely that they constitute a 'simple' continuation of the olfactory pathway providing just another olfactory code. The mushroom bodies are centers for multimodal processing and associative memory, and reward-based mechanisms of plasticity have been shown in the synapses between Kenyon cells and output neurons [20]. Thus, the output neurons might be involved in recoding sensory representations to an experience-dependent value code that represents the behavioral relevance of sensory input. This notion would be in line with previous work, which found little odor identity coding, but strong odor-reward association encoding after memory consolidation at the mushroom body output [14]. A rapid representation of the behaviorally relevant stimuli might be a prerequisite for behavioral decision making based on experience-dependent memory.

While this new study [13] shows the importance of the time domain for sparse coding in biological systems, this concept might also be inspiring for computer science. In the field of machine learning high-dimensional sparse projections of inputs are used to improve stimulus classification with reinforcement learning. Since this analogy between sparse coding in biological systems and in machine learning has been repeatedly outlined (for example, [18]), it might be of interest to better explore temporal coding schemes for machine learning algorithms, for example, in order to increase the capacity of artificial object recognition systems.

References
1. Barlow, H.B. (1969). Trigger features, adaptation and economy of impulses. In Information Processing in the Nervous System (pp. 209–230). Springer Berlin Heidelberg.
2. Vinje, W.E., and Gallant, J.L. (2000). Sparse coding and decorrelation in primary visual cortex during natural vision. Science 287, 1273–1276.
3. Hromádka, T., DeWeese, M.R., and Zador, A.M. (2008). Sparse representation of sounds in the unanesthetized auditory cortex. PLoS Biol. 6, e16.
4. Wolfe, J., Houweling, A.R., and Brecht, M. (2010). Sparse and powerful cortical spikes. Curr. Opin. Neurobiol. 20, 306–312.
5. Isaacson, J.S. (2010). Odor representations in mammalian cortical circuits. Curr. Opin. Neurobiol. 20, 328–331.
6. Heisenberg, M. (2003). Mushroom body memoir: from maps to models. Nat. Rev. Neurosci. 4, 266–275.
7. Menzel, R. (2012). The honeybee as a model for understanding the basis of cognition. Nat. Rev. Neurosci. 13, 758–768.
8. Perez-Orive, J., Mazor, O., Turner, G.C., Cassenaer, S., Wilson, R.I., and Laurent, G. (2002). Oscillations and sparsening of odor representations in the mushroom body. Science 297, 359–365.
9. Ito, I., Ong, R.C.Y., Raman, B., and Stopfer, M. (2008). Sparse odor representation and olfactory learning. Nat. Neurosci. 11, 1177–1184.
10. Demmer, H., and Kloppenburg, P. (2009). Intrinsic membrane properties and inhibitory synaptic input of Kenyon cells as mechanisms for sparse coding? J. Neurophys. 102, 1538–1550.
11. Honegger, K.S., Campbell, R.A., and Turner, G.C. (2011). Cellular-resolution population imaging reveals robust sparse coding in the Drosophila mushroom body. J. Neurosci. 31, 11772–11785.
12. Farkhooi, F., Froese, A., Muller, E., Menzel, R., and Nawrot, M.P. (2013). Cellular adaptation facilitates sparse and reliable coding in sensory pathways. PLoS Comp. Biol. 9, e1003251.
13. Gupta, N., and Stopfer, M. (2014). A temporal channel for information in sparse sensory coding. Curr. Biol. 24, 2247–2256.
14. Strube-Bloss, M.F., Nawrot, M.P., and Menzel, R. (2011). Mushroom body output neurons encode odor–reward associations. J. Neurosci. 31, 3129–3140.
15. Gupta, N., and Stopfer, M. (2012). Functional analysis of a higher olfactory center, the lateral horn. J. Neurosci. 32, 8138–8148.
16. Gütig, R. (2014). To spike, or when to spike? Curr. Opin. Neurobiol. 25, 134–139.
17. Harris, K.D., and Mrsic-Flogel, T.D. (2013). Cortical connectivity and sensory coding. Nature 503, 51–58.
18. Huerta, R., and Nowotny, T. (2009). Fast and robust learning by reinforcement signals: explorations in the insect brain. Neural Comput. 21, 2123–2151.
19. Palm, G. (2013). Neural associative memories and sparse coding. Neural Networks 37, 165–171.
20. Cassenaer, S., and Laurent, G. (2012). Conditional modulation of spike-timing-dependent plasticity for olfactory learning. Nature 482, 47–52.

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Natural Selection: It's a Many-Small World After All

Understanding adaptive phenotypic change and its genetic underpinnings is a major challenge in biology. Threespine stickleback fish, experimentally exposed to divergent semi-natural environments, reveal that adaptive diversification can happen readily, affects many traits and involves numerous genetic loci across the genome.

Marius Roesti* and Walter Salzburger

Populations exposed to contrasting environments typically become different in phenotype and may ultimately split into distinct, reproductively isolated species [1].

The genetic basis of phenotypic change during this process remains poorly understood. Major drawbacks are that most research focuses on a few traits in lab-reared specimens, targets phenotypes with a simple genetic architecture or uses indirect