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.

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[1]Biocenter, Institute for Zoology, Cologne Excellence Cluster on Cellular Stress Responses in Aging Associated Diseases (CECAD), University of Cologne, 50674 Cologne, Germany. [2]Theoretical Neuroscience, Institute of Biology, Freie Universität Berlin, 14195 Berlin, Germany.
E-mail: peter.kloppenburg@uni-koeln.de, martin.nawrot@fu-berlin.de

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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

Figure 1. Co-occurring benthic and limnetic stickleback, and their natural and reconstructed habitats.

(A) Four benthic-limnetic species pairs have been officially listed by the Committee on the Status of Endangered Wildlife in Canada (COSEWIC) so far, of which Hadley Lake stickleback went extinct in the 1990s and the species pair in Enos Lake has collapsed into a hybrid swarm. Both these events are associated with invasive species. A fifth species pair was discovered in Little Quarry Lake in 2007. (B) The shallow-water benthic habitat of Paxton Lake, the contrasting deep open-water limnetic habitat (pictures courtesy of Jenny Boughman [benthic], Gina Conte [limnetic]), and a representative adult male stickleback from each habitat type (pictures courtesy of Gerrit Velema; note that the benthic specimen originates from close-by Priest Lake). (C) Bird's eye view of the experimental pond facility at the University of British Columbia (Vancouver, Canada). Each pond measures 25 by 15 meters, holds 750,000 liters of water, and mimics a natural lake with both a benthic and limnetic zone (picture courtesy of Thor Veen).

inference from population genomic surveys that lack functional trait information. To better understand the genetics underlying ecological divergence, we should therefore investigate the complete set of traits that bring whole individuals closer to their performance optimum in a particular natural environment [2,3]. This task has proven extremely difficult, and uncovering the genetic basis of adaptation remains a challenge. In a recent study, Arnegard and co-workers [4] take on this challenge by using genetic mapping to study niche divergence in threespine stickleback under semi-natural conditions.

Stickleback fish are an important model system for speciation research, especially in a few postglacial lakes in British Columbia, Canada, where both inshore (benthic) and offshore (limnetic) stickleback species (sometimes referred to as 'ecomorphs') have evolved repeatedly in less than 12,000 years (Figure 1A) [5]. These co-occurring species are reproductively isolated through different morphological, behavioral and physiological adaptations to their contrasting habitats (Figure 1B). Hybrids with intermediate phenotypes are occasionally found, but their performance is relatively low in both habitats as compared to the pure species [6,7]. These aspects make benthic and limnetic stickleback one of the most explicit examples of natural selection's predominant role in the origin of new species.

In their experiment, Arnegard *et al.* [4] released F1 hybrids from artificial crosses between benthic and limnetic stickleback collected from Paxton Lake (Figure 1A,B) into a large experimental pond (Figure 1C). This pond, which includes both shallow-water benthic and deep-water limnetic zones, approximates the distinct habitats the two species occupy in the wild. The authors allowed the F1s to mate freely and, after six months, sampled more than 600 second-generation F2 hybrids throughout the pond. Among these F2s, stable isotope profiles and stomach content analyses indicated extensive variation in niche exploitation along the benthic–limnetic axis. Importantly, hybrids at both ends of the benthic–limnetic diet spectrum (those close to pure species phenotypes) grew larger, suggesting that they performed better than other hybrids (those deviating from pure species phenotypes). Variation in niche use was further associated with functional and morphological divergence in their feeding apparatus and body shape.

To decipher the genetic architecture of this divergence, Arnegard *et al.* [4] used quantitative trait locus (QTL) mapping, an approach that provides a strong test for causality by linking phenotypic to genetic variation within an experimental cross population. The authors found that many loci across the stickleback's genome, each with a small to moderate effect at the phenotype level, underlie benthic–limnetic divergence. Moreover, several QTLs contributed additively and more or less evenly to whole-organism niche performance. That is, the addition of a favorable allele at any of these QTLs brought an individual's overall phenotype a similarly small step closer to its fitness optimum. In contrast to the well-adapted benthic and limnetic hybrids, F2 individuals with an intermediate diet signature were smaller, had a mixed combination of

benthic and limnetic alleles and were intermediate in phenotype. Finally, F2 individuals showing the strongest growth deficits exhibited conflicting combinations of the ecologically relevant traits, making them particularly maladapted for either of the two trophic habitats. Arnegard *et al.* [4] thus provide an elegant and rare demonstration for how variation in the genotype translates, through the phenotype, to fitness differences among individuals.

The study also confirms a general finding emerging from high-resolution genome scans between ecologically divergent populations [8–12]: adaptation is a complex process involving many genetic loci. A first reason is that adaptation is likely to require shifts at many phenotypic traits, including behavior, morphology, physiology and life history. A second reason is that even single ecologically relevant traits are commonly controlled by many genetic loci, each with a small phenotypic effect [2]. Although some traits certainly do have an underlying simple (nearly Mendelian) genetic basis [13,14], high-resolution sequencing technology has revealed that some of these 'single locus with large phenotypic effect' examples are in reality much more genetically complex than initially thought [15,16]. These insights raise an important question: to what extent are the few straightforward cases of genotype-to-phenotype relationships for single traits representative of adaptation's complexity as a whole?

When studying something as complex as adaptation, it is essential to choose an appropriate methodology and to recognize its possible limitations [17]. For example, the crux with traditional QTL mapping is the focus on a few traits and only a single cross — that is, all F2 individuals derive from the same two grandparents. The genetic variation in such a cross does not capture the allelic richness available to selection in a natural population and is likely to limit the available phenotypic variation. Furthermore, most QTL studies cannot easily connect their results to the natural context (but see, e.g., [18,19]). Arnegard *et al.* [4] reduced these limitations by using semi-natural ponds and first-generation F1 hybrids from four independent crosses. In this way, instead of having a maximum of four allelic variants per locus, as is the case in a single F2 QTL cross (two alleles from each grandparent), up to 16 possible variants were exposed to selection in their study. In addition, all individuals were free to choose their mating partners, habitat, and diet. This puts the study by Arnegard and colleagues [4] far beyond traditional QTL mapping. Most notably, the authors are able to link their phenotypic and genetic findings to adaptive population divergence, and hence, fitness consequences within distinct semi-natural habitats.

Nevertheless, some limitations associated with QTL mapping remain. The relatively low marker density used to genotype the individuals (less than 500 markers) and the constraints given by only a single generation of genetic admixture (from first to second generation hybrids) inevitably result in a relatively limited resolution when inferring genomic regions associated with phenotypic traits [2,17]. These limitations make it impossible to determine whether mapped genomic regions contain multiple close-by loci, each with a very small and possibly non-additive contribution to trait variation, or a single locus with a relatively larger phenotypic effect. Improvements could include sampling a QTL cross population after more generations, increasing marker resolution and adding association mapping in natural, highly variable populations. Even so, these approaches remain constrained to finding loci with relatively large phenotypic effects [20]. Also, because F2 hybrids were exposed to ecologically different habitats throughout their lives, some portion of their trait variation might reflect phenotypic plasticity, which could confound QTL inference. A solution here would be to re-map the focal traits in an F2-cross raised under the same standardized conditions. Finally, we need to establish to what extent our current methodological toolkit is biased towards detecting additive over more complex non-additive genetics [2].

Interestingly, the experiment also yielded an unpredicted outcome: the smallest F2 individuals, which showed mismatches in functional traits, were feeding on springtails, a food resource fortuitously abundant within the experimental pond but largely absent in the natural habitat. We can only speculate as to how this new resource could have influenced evolution in the pond if the experiment had been run for more generations. Despite the availability of this alternative food type, the springtail-feeders might not persist through future generations. It is also possible, although rather unlikely, that this group becomes well-adapted to the new springtail-foraging niche, resulting in a brand new ecomorph next to the limnetic and benthic stickleback. Finally, these small intermediate phenotypes could facilitate gene flow between the benthics and limnetics, allowing some combinations of benthic and limnetic alleles to be relatively fit. This in turn might hinder further adaptive divergence between the pure ecomorphs and counteract any possible experimental speciation. The occurrence of the springtail-feeders shows how difficult it is to precisely reconstruct the ecological conditions shaping divergence in the wild. Furthermore, it highlights that learning about the predictability of evolution requires comparable and replicated studies, within and across organisms.

Overall, the study by Arnegard *et al.* [4] demonstrates that, despite involving many traits and loci, important fitness variation can emerge immediately when the right allelic variants are available to selection. Another interesting finding is that the genetic architecture underlying reduced environment-*dependent* hybrid viability and thus reproductive isolation might be largely additive. This contrasts with the idea of environment-independent reproductive isolation (i.e., due to intrinsic genetic incompatibilities) that is mainly caused by deleterious non-additive gene interactions. These exciting novel insights point to the future promise of taking experimental (genetic) approaches out into nature.

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Zoological Institute, University of Basel, Vesalgasse 1, 4051 Basel, Switzerland.
*E-mail: marius.roesti@unibas.ch

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Pericentrin: Critical for Spindle Orientation

Mutations in the pericentrin (PCNT) gene cause Majewski osteodysplastic primordial dwarfism type II (MOPDII). Recent work reveals that a discrete set of centrosome proteins require PCNT for their robust localization to mitotic spindle poles. Critically, this complex is crucial for mitotic spindle orientation and involved in the pathogenesis of MOPDII.

Yi Luo[1] and Laurence Pelletier[1,2,*]

The centrosome is the major microtubule-organizing center of animal cells. It is composed of a centriole pair, which recruits more than 100 proteins, collectively referred to as pericentriolar material (PCM). It participates in the regulation of cell motility, adhesion, intracellular transport and mitotic spindle assembly. During mitosis, centrosomes undergo a dramatic increase in size and nucleation capacity, a process called centrosome maturation. Centrosome maturation potentiates robust mitotic spindle assembly and is a prerequisite for the accurate segregation of chromosomes to progeny cells. Indeed, centrosome and spindle abnormalities are frequently observed in human tumors and are associated with genomic instability.

PCNT is a large, elongated coiled-coil molecule that plays a crucial role in centrosome biogenesis and mitotic spindle assembly [1,2]. PCNT acts as a scaffold for the recruitment and anchoring of a plethora of PCM proteins including CDK5RAP2, NEDD1 and γ-tubulin ring complexes. Mutations in PCNT are associated with several human disorders including the primordial dwarfism MOPDII [3]. A study published in this issue of *Current Biology* by Chen *et al.* [4] reports a novel role for PCNT in the control of spindle orientation through the recruitment of a specific subset of centrosome components.

Previous genetic linkage analysis revealed that biallelic loss-of-function mutations in PCNT caused MOPDII in all 25 patients [3]. However, the precise molecular mechanisms underlying MOPDII pathology had remained unclear. To address this issue, Chen and colleagues generated PCNT$^{-/-}$ mice and mouse embryonic fibroblasts (MEFs). PCNT$^{-/-}$ mice exhibited known features of MOPDII including small body size, microcephaly, craniofacial developmental anomalies, structural kidney defects and vascular development anomalies. Detailed analyses of PCNT$^{-/-}$ MEFs and patient-derived epithelial cells revealed a dramatic reduction in the amount of astral microtubules and consequently defects in spindle positioning. Moreover, careful examination of PCNT$^{-/-}$ mice revealed that brain, heart and kidney tissues displayed defects consistent with abnormal asymmetric division and diminished cell proliferation. This phenotype is analogous to microcephaly, where asymmetric divisions produce differentiating cells instead of stem cells, which yields a sharp reduction in the total number of neurons [5].

To provide molecular insights into the spindle positioning defects in PCNT$^{-/-}$ cells, Chen *et al.* surveyed the levels of known centriole and centrosome proteins at spindle poles. Three proteins (CDK5RAP2, Ninein and Centriolin) were most drastically reduced in absence of PCNT. Mutations in Ninein and CDK5RAP2 have been associated with microcephaly, suggesting that these proteins contribute to the MOPDII syndrome though their interplay with PCNT [6,7]. Consistently, the *Drosophila* homologue of CDK5RAP2, Centrosomin (Cnn), is required to maintain mitotic PCM in the vicinity of centriole and to promote astral microtubule formation [8]. Ninein is also required for the maintenance of spindle pole integrity through spatial control of Astrin distribution [9]. In their study, Chen and colleagues show that