depends on both the nature of the two quasiparticles and how their paths through space-time intertwine or 'braid' — a latitude that led to these quasiparticles being dubbed 'anyons' (see also 'Braiding anyons'[2] on page 804). Anyons in a fractional quantum Hall fluid with filling factor $1/m$ are predicted to have fractional statistical phase $\pi/m$.

And indeed, the fractional quantum Hall states observed so far do largely follow that prediction. But remember that $m$ is supposed to be an odd number; thus, the discovery some 20 years ago[7] of a no-resistance quantum Hall state with an even denominator, at a filling factor of 5/2, was initially puzzling. This state was soon realized to have very special properties[8,9]: the associated quasiparticles would also have fractional charge, but would obey non-abelian statistics.

The definition of non-abelian statistics is complex, but one facet is that the state of a system of many quasiparticles obeying non-abelian statistics cannot be completely determined by knowing the quasiparticles' spatial coordinates. Several linearly independent wavefunctions are possible: a system with four quasiparticles, for instance, can have two different states. In this situation, the final state of an exchange interaction is a linear combination of the two initial states, and the braiding process as particles interact and their trajectories intertwine is encoded in a two-by-two matrix. More generally, for a system with $2n$ quasiparticles, there are $2^{n-1}$ states. In general, because any pair of quasiparticles in the quantum fluid can become intertwined, these states do not commute with each other — in other words, the order in which the exchange interactions between quasiparticles occur will determine the system's final state. This order-dependence of the state is crucial to the proposed use of non-abelian quasiparticles as the basic 'qubits' of information in a topological quantum computer[2,10,11].

Dolev and colleagues' detection[1] of a quasiparticle of charge $e/4$ is a first step in that direction. The discovery was made in a shot-noise experiment similar to those in which the original quasiparticle states were found[5,6]. But the new measurement was much harder to make than those pioneering experiments: the 5/2 state is so delicate that to study it requires a sample quality such that the mean free path of electrons before they collide with impurities in the semiconductor structure is very long (about 0.5 millimetres). It also requires low temperatures so that thermal fluctuations do not obscure the state.

Naively, one would have expected that the quasiparticle in the 5/2 state, with its denominator of 2, would have a charge of $e/2$ (the multiplier of 5 in the numerator is not relevant to these considerations). But through a series of non-trivial consistency checks, Dolev *et al.* show that the charge at filling fraction 5/2 is consistent with $e/4$, but not with $e/2$ (at integer filling fraction, the measured charge is just $e$ and at a filling fraction 1/3 it is $e/3$). For that reason, this quasiparticle is also called a 'half-vortex' state.

Measuring the charge to be $e/4$ is a necessary, but not sufficient proof of a non-abelian state: there is a conceivable (but very unlikely) possible 'strongly paired' abelian state with the same filling fraction and charge. But an independent (and as-yet unpublished)[12] direct-current transport measurement at a point contact has not only measured the same value of the fractional charge, but also a tunnelling probability consistent with the predictions for a non-abelian state.

Further tests of the statistics of these intriguing quasiparticles at single point contacts will be the next step. They will be the key to the development of well-controlled, multi-contact quantum inteferometers that are needed to test the properties of these intriguing quasiparticles, and thus to construct the qubits of a topological computer. ■

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SYSTEMS BIOLOGY

# Genome rewired

Matthew R. Bennett and Jeff Hasty

**Within a genome, genes are connected to each other through a complex network of interactions. One way to assess how robust and evolvable such genomic networks are is to introduce new links between unrelated genes.**

Change in the genetic code is the driving force of classical evolution. Typically, it is thought that mutations in single nucleotides within the DNA sequence ensure such change, but other random alterations such as deletion, duplication and recombination of gene sequences can also occur. The robustness of organisms to such changes, which are necessary for evolution, is of fundamental interest, and so previous studies have investigated the sturdiness of gene-regulatory networks by either deleting[1] or overexpressing[2] individual genes. On page 840 of this issue, Isalan *et al.*[3] describe a different approach. They used high-throughput assay techniques to systemically rewire the architecture of the genetic network of the bacterium *Escherichia coli*. Their findings provide insight into not only the robustness but also the evolvability of this network.

The DNA sequence of a given gene generally consists of two parts: a regulatory promoter and an open reading frame (ORF). The promoter interacts with gene transcription factors to either increase or decrease the level of the gene's expression. Once transcription is initiated, the gene's ORF is transcribed into

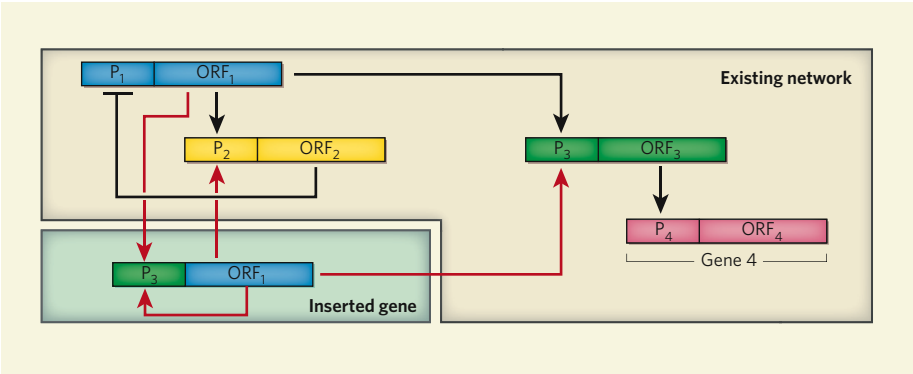


**Figure 1 | Intra-network communication.** A simplified example of Isalan and colleagues' experiment[3], in which they rewired the network of genes for *E. coli* transcription factors to create new network connections, is shown. Here, the existing network consists of four genes. The promoter of gene 3 ($P_3$) can be fused to the ORF of gene 1 ($ORF_1$) to create a new gene. On insertion of this 'hybrid' gene into the normal cell, the new gene creates new regulatory links (shown in red) that could alter the functionality of the network.

messenger RNA. Isalan *et al.* recombined the promoters and ORFs of unrelated genes, encoding many of the 300 transcription factors in the *E. coli* genome, to create about 600 new promoter–ORF connections, or genes. They then placed each of these genes, one at a time, into *E. coli* cells and measured their viability.

This type of genetic rewiring is akin to randomly placing wires between nodes within a computer's central processing unit, where the new wires would reroute signals from one section of the processor to another — perhaps unrelated — section. The introduction of new network connections will almost certainly preclude a central processing unit from operating properly, if at all. Surprisingly, Isalan and colleagues[3] find that the genetic network of *E. coli* is much more robust to rewiring than its electronic counterpart. Of the roughly 600 new connections the authors introduced into the network, almost all were well tolerated by the cells. Furthermore, the vast majority of connections showed no apparent deleterious effects, and some strains even grew better than the original.

These observations indicate that small-scale rewiring events probe the network landscape for fitness of the associated changes, without causing great detriment to the organism. From an evolutionary standpoint, therefore, they indicate that organisms can evolve by changing the architecture of their genetic network. This certainly makes sense, otherwise new network functionality could evolve only by large-scale rewiring events, which are probably extremely rare.

This conclusion also flies in the face of the popular misconception among opponents of the evolutionary theory, who believe that the genetic code is irreducibly complex. For instance, advocates of 'intelligent design' compare the genome to modern engineered machines such as integrated circuits and clocks, which will cease to function if their internal design is altered. Although sometimes it is instructive to point to similarities between the design principles behind modern technology and those behind genetics, the analogy can only go so far. Engineered devices are generally designed to work just above the point of failure, so that any tampering with their construction will result in catastrophe. In the event of failure, new clocks can be purchased or central processing units replaced. But nature does not have that option. To survive — and so evolve — organisms must be able to tolerate random mutations, deletions and recombination events. And Isalan and colleagues' work provides an important step forward in quantifying just how robust the genetic code can be.

In addition to screening the new strains for fitness, the authors measured the activity levels of genes that were most directly affected by network rewiring. They predicted that, if a new gene introduces a feedback loop into the network, the protein levels of its 'parent' gene should be altered accordingly. For instance, the synthetic gene inserted into the simple gene-regulatory network depicted in Figure 1 introduces a positive feedback loop into the creation of the protein encoded by $ORF_1$. Therefore, levels of that protein should be higher in the mutant than in the normal strain. But this is not what Isalan *et al.* find. Instead, introduction of direct feedback loops (either positive or negative) led to no significant differences in the levels of the proteins concerned.

There could be two explanations for why new feedback loops have almost no effect on protein levels. For one, the dynamics of large-scale, transcriptionally regulated genetic networks are probably more complicated than thought. In other words, analysing large networks by decomposing them into simpler subnetworks, as Isalan *et al.* have done, may lead to faulty conclusions about how the subsystems work within the whole. Alternatively, it may be that transcriptional regulation is less important than expected. Perhaps post-transcriptional regulatory mechanisms[4,5] that affect mRNA translation regulate the network to a larger extent. But considerable effort has gone into the creation of synthetic gene networks[6,7] that are controlled at the transcriptional level, and many of these studies have had great success[8,9]. So the findings of Isalan *et al.*[3] should be seen both as a cautionary tale and as encouragement for research into the regulatory mechanisms of large-scale networks. ■

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ECOLOGY

# Destabilized fish stocks

Nils Chr. Stenseth and Tristan Rouyer

**Fishing of natural populations increases the variability of fish abundance. A unique data set from the southern California Current has allowed an evaluation of three hypotheses for why that should be so.**

Understanding variation in the abundances of plants and animals has long been a central topic in population ecology[1]. It is one of particular significance when it comes to exploited populations, such as those of many fish stocks, and is revisited by Anderson *et al.* on page 835 of this issue[2].

Extensive fluctuations of harvested fish stocks are clearly undesirable economically — too much uncertainty in expected income will adversely affect fishing communities. Such fluctuations are also harmful from a conservation perspective, as high variability may increase the (local) probability of extinctions. It has long been suggested[3] by fisheries ecologists that fishing might itself increase the temporal variability of exploited populations. But long-term data on unexploited populations are needed for comparative (control) purposes, and the lack of such data has made it difficult to separate the effects of fishing from the effects of variations in environmental conditions.

In 2006, such a long-term data set — the California Cooperative Oceanic Fisheries Investigations (CalCOFI) record of larval fish abundance — was subject to comparative analysis by Hsieh *et al.*[4], from which they concluded that, as their title put it, 'Fishing elevates variability in the abundance of exploited species'. But this study, pioneering as it was, did not look into the nature of the underlying mechanisms. Anderson *et al.*[2], a group that includes many of the same authors, now report an extended analysis of the 50-year CalCOFI data set under the title 'Why fishing magnifies fluctuations in fish abundance'. In doing so they provide valuable, empirically based insights into the fluctuations of exploited populations. Their analysis convincingly shows that the observed increased variation of harvested fish stocks is caused by the selective removal of the larger (and older) individuals, leading to a decreasing average size and age of the fish that destabilizes the population dynamics.

Anderson *et al.*[2] looked at three hypotheses. They found no support for the first one, that the observed variability of exploited fish stocks is a direct effect of variable fishing intensity. Then there is the selective removal of larger and so older individuals by fishing, known as the age-truncation effect. This 'juvenescence' of the population can affect the dynamics in two ways, leading to the second and third hypotheses.

The second hypothesis is that younger, smaller individuals may be more susceptible