

glucose metabolism as a potential target for pro-angiogenic therapies (such as in patients with inadequate blood supply to the heart or limbs) or anti-angiogenic therapies (for example, to tackle tumours). Metabolic enzymes make good drug targets, so this is an exciting possibility. The study also provides an additional explanation for why endothelial cells perform glycolysis rather than oxidative breakdown of glucose: rapid local generation of ATP can occur in glycolytic metabolons located in the lamellipodia and filopodia, which are too small to accommodate mitochondria and are often found at angiogenic fronts where oxygen is scant.

Like all seminal work, this study generates several questions. Does modulation of glycolytic flux in ways other than through PFK2 also affect angiogenic sprouting? Could non-enzymatic properties of PFK2 contribute to the observed phenomena? Such behaviour has been seen for pyruvate kinase, another key

enzyme in glycolysis that was recently found⁸ to be present in the cell nucleus and associated with transcription factors that drive gene expression. Does PFK2 modulate the activities of Rac, Akt and eNOS — key enzymes that regulate endothelial-cell motility — and, if so, how? How do Notch and VEGF signal to PFK2? Does glycolysis regulate migration of other cell types, such as smooth-muscle cells or macrophages, or even cancer cells? And is the pro-angiogenic activity of PFK2 altered when glucose homeostasis is perturbed, such as in diabetes?

These questions aside, De Bock and colleagues' study deepens our understanding of why some cells choose to forego the lucrative use of mitochondria to break down their glucose, even when, as is the case for endothelial cells, the cells are not highly replicative. The authors' findings also introduce a new concept in endothelial biology: that metabolic decisions can regulate the endothelial phenotype,

as well as vice versa. It turns out that, much like children, endothelial cells that gorge on sugar become hyperactive. ■

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ECOLOGY

Abundant equals nested

How ecological network structures are influenced by species coexistence, community stability and perturbations is a topic of debate. It seems that one overlooked correlate of nested structures is species abundances. **SEE LETTER P.449**

COLIN FONTAINE

Understanding the mechanisms that shape biodiversity is one of the main goals of ecology. Network approaches, which integrate species and the interactions among them into a single framework, have proved enlightening, revealing distinct 'architectural' patterns that are strongly associated with particular ecological interactions. For mutualistic networks — those in which the interactions benefit both partners, such as between a plant and its pollinator, or a fish and a cleaner fish — the pervasive pattern seems to be a nested one, whereby specialist species (which have few partners) interact with a subset of the many partners of more generalist species. The origin and implications of nestedness remain strongly debated. On page 449 of this issue, Suweis *et al.*¹ bring an innovative and intriguing contribution to this topic by demonstrating strong relationships among species abundances, nested architecture and community stability.

Nestedness is a pattern characterized by several features (Fig. 1), including a skewed distribution of the number of interacting partners per species, with

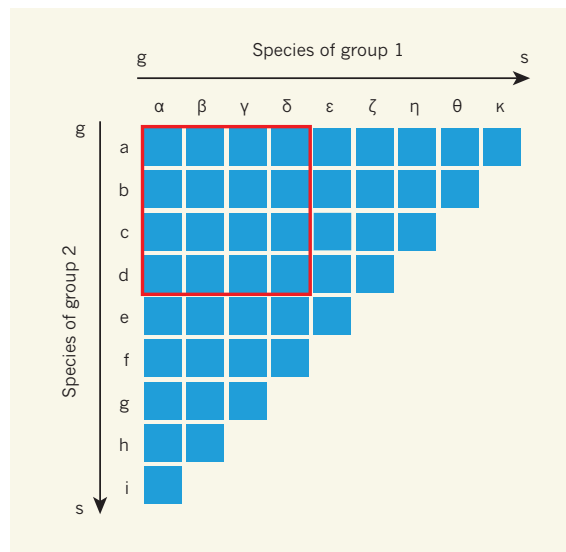


Figure 1 | A nested network. The interactions between two groups of mutualist species often assume a nested structure, in which specialist species (s), which have few partners, interact with a subset of the many partners of more generalist species (g). Here, the intersection of a row and column is blue if the species interact. Nested networks have certain characteristics, such as a continuum from highly generalist to specialist species, a core of highly connected species (red box) and a tendency for specialist species to interact with generalists (for example, the specialist i interacts with the generalist a). Suweis *et al.*¹ show that the abundances of species in a mutualistic network are positively related to the nestedness of the network.

many specialist species and few extremely generalist species. Nestedness also implies asymmetric specialization, such that specialist species tend to interact with generalist ones. Finally, the generalist species in the nested network form a single, highly connected core, making the networks very cohesive.

Three main hypotheses have been proposed to explain the biology behind this seemingly highly organized structure. One is that nestedness is 'neutral', meaning that all interactions between individuals are equally likely. Species abundances in many communities are well described by a log-normal distribution, with many rare species and a few common ones. Under this hypothesis, differences in species abundance result in differences in interactions at the species level: abundant species are expected to interact more frequently and with more species than rare species, and rare species tend to interact with abundant species rather than with other rare species. However, the empirical correlation between species abundances and species generalism is not easy to interpret². Do species become generalists because they are more abundant, or are they more abundant because they are generalists and therefore can access more resources?

The second hypothesis suggests that nestedness affects ecological dynamics, particularly species coexistence and community stability. A simple argument supporting this hypothesis is that it is much safer for specialist species to interact with generalist species than with other specialists, because generalist species are expected to have less-fluctuating population dynamics and so to be more reliable partners. Such constraints

on community persistence or stability could therefore be a driving force shaping interaction networks. However, no consensus on this topic has been reached among several investigations^{3–6} in recent years of the links between network nestedness and community dynamics in mutualistic species.

According to the third hypothesis, nested architecture may be shaped by the (co-)evolutionary dynamics of species interacting within a community. There are many examples of interspecies interactions affecting the fitness of individuals, and of the evolution of species traits controlling the identity of potential interaction partners. Closely related species in mutualistic interaction networks tend to have similar interacting partners, which emphasizes the idea that evolutionary history has an impact on the structure of mutualistic networks⁷. But, so far, no precise evolutionary process has been directly related to a nested structure.

Suweis *et al.* have drawn these three hypotheses together by demonstrating a two-step relationship between species abundances in a community and the nestedness of the interaction network that depicts that community. Using analytical and simulation approaches, the authors first show that, under stationary conditions that have a constant number and strength of mutualistic interactions, ‘interaction swaps’ (an exchange of interactions between two species couples) that lead to an increase in the abundance of the species also increase the total abundance of the community. Second, the researchers demonstrate that total community abundance is positively related to the nestedness of the network. This connection opens up fascinating perspectives.

To demonstrate the implications of their findings, the authors show that, under the condition that exchanges result in increased species abundance, iterative swapping ultimately converts random networks, with randomly distributed interactions among species, into nested networks. The interpretation of this is that any process that maximizes species abundance through changes in interspecies interactions will lead to a nested network. The question thus becomes, what biological process could select for higher population size? Selection at the population level involves group-selection processes such as hard selection^{8,9}. More work is needed to unravel the microevolutionary processes that affect network architecture, but this line of research seems promising.

Suweis and colleagues further demonstrate that the population size of the rarest species in the community is positively related to community resilience — the speed at which community dynamics return to equilibrium after a small perturbation. These results fuel the current debate about the relationship between network architecture and community stability^{3–6,10,11} by introducing the distribution of

species abundance as a key element. Again, however, the processes through which the abundance of the rarest species relates to community resilience remain to be identified. They may involve the rarest species directly, or may emerge from other mechanisms affecting both the rarest species and community resilience.

Last but not least, the relationship found by Suweis *et al.* between network nestedness and total community abundance goes both ways. Abundance is correlated with biomass, which is one of the main variables used in studies of biodiversity and ecosystem functioning, so the two-way relationship provides a bridge between the authors’ results and the rich literature on these topics. We already know that the structure of food webs, for example, can affect the relationship between biodiversity and ecosystem function¹². But little is known about the impact of mutualistic networks on the functioning of ecological communities. Like all exciting pieces of research, Suweis and colleagues’ work raises more questions than it answers. ■

EVOLUTIONARY BIOLOGY

A gut feeling for isolation

The far-reaching effects of the relationship between an animal and its resident gut microorganisms are becoming ever clearer. New findings suggest it can even create barriers that keep species separate.

GREGORY D. D. HURST & CHRIS D. JIGGINS

The process of speciation, whereby one lineage splits into two independent gene pools, has at its heart the evolution of barriers to gene flow that maintain differences when populations are in contact. Gene flow can be reduced in many ways, including failure to mate, sperm–egg incompatibility, and sterility or inviability of hybrids. Writing in *Science*, Brucker and Bordenstein¹ describe a novel source of reproductive isolation: the influence of resident gut microorganisms on hybrid survival.

The concept of microbial involvement in reproductive isolation is not new². In the 1990s, it was recognized³ that the very low survival rates of hybrid offspring from two closely related wasp species was influenced by the presence and strain of *Wolbachia* bacteria in the parents. More recently, it was demonstrated that environmentally induced changes in the composition of the gut microbiota could affect mate preference in *Drosophila* fruitflies⁴. Brucker and Bordenstein’s work likewise examined the role of gut microbiota

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in reproductive isolation, but focused on the death of hybrid larvae rather than mate preference, and studied a situation in which the pool of environmental microbes was constant.

Their study organisms were parasitic wasps of the genus *Nasonia*, which lay their eggs in the pupae of flesh and filth flies (Fig. 1). The fly host represents both a source of nutrition and an environmental pool of microbes, and the authors had previously established⁵ that different *Nasonia* species acquire distinct communities of resident gut microorganisms (their ‘gut microbiomes’) from this common microbial pool. This differentiation of microbiomes was linked to the hosts’ phylogeny: the microbiomes of individuals from the closely related species *Nasonia giraulti* and *Nasonia longicornis* were more similar than that of a more distantly related species, *Nasonia vitripennis*. Brucker and Bordenstein hypothesized that this differentiation creates a setting in which dysfunctional interactions could arise between hybrids and their gut microbiota.

To test this idea, the authors examined the male offspring formed by crosses between *N. vitripennis* and *N. giraulti*, most of which