Quick guide

Siphonophores

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What are siphonophores? Many biologists and beach-goers will be familiar with the Portuguese Man o' War, *Physalia physalis*, even if they may be unaware that it belongs to an extraordinary group of carnivorous colonial animals, the siphonophores. Siphonophores are members of the Cnidaria — which includes corals, sea anemones, jellyfish and hydroids. There are about 175 described siphonophore species to date.

What do they look like? Unlike *Physalia*, most siphonophores are active swimmers that spend their entire lives in the deep-sea. They are typically elongate and rope-like, with some reaching lengths of 40 meters or more, making them the longest animals in the world — even longer than a Blue Whale. Siphonophores are gelatinous and most of them disintegrate when sampled with nets. The difficulty of collecting intact siphonophores makes the study of most species very challenging. Despite their size and abundance, we therefore know very little about even basic aspects of siphonophore biology. We do know, however, that siphonophores are unique in many respects. In particular, they have taken coloniality to an unparalleled extreme, and in so doing obtained a unique form of individuality that has led some to call them 'superorganisms'.

How are siphonophores different from other colonial animals? Colonial animals consist of many multicellular individuals — called zooids — that are each homologous to solitary free-living organisms. Zooids within a colony are all derived from the same embryo and thus genetically identical. Colonial animals, such as a head of coral or a clump of bryozoans, add new zooids through asexual reproduction, such as budding or fission, that is not followed by physical separation. Thus, offspring zooids remain attached and physiologically integrated. Social insects are somewhat similar to colonial animals *sensu stricto*. Within a social insect 'colony', individuals share resources — though they aren't physically connected — and are closely related, but not genetically identical. Siphonophores are distinctive because they show the highest degree of division of labor between the individual zooids of any colonial organism. Being a siphonophore is as if you were to bud thousands of conjoined twins throughout your life, some with only legs to move everybody, others with only mouths to ingest food, others with enlarged hearts to circulate the shared blood, and others fully dedicated to the sexual production of new offspring colonies. There can be a dozen or more such functional classes of zooids in siphonophore colonies, and they are arranged in precise species-specific patterns. This pattern is usually reiterated along a linear stem, with the exact same sequence of specialized zooids occurring over and over.

What's so interesting about their colonial structure? The division of labor between siphonophore zooids parallels the evolution of functional specialization at other levels of biological organization — such as between cells in a multicellular organism or between casts in eusocial insects. There is wide interest in the evolutionary origins of the division of labor, and the developmental mechanisms that orchestrate the precise differentiation of specialized reiterated units within organisms. Siphonophores provide an opportunity to study these issues, but at an entirely different level of biological organization. This will make it possible to test the generality of conceptual frameworks, such as the potential for developmental mechanisms to mediate conflict between different levels of selection within an organism. This is directly relevant to cancer, germ line segregation, and the ability to distinguish self from non-self. It is even conceivable that siphonophores could get 'colony cancer' if some zooids had somatic mutations that allowed them to proliferate at the expense of other zooids and the colony as a whole.

What are we learning about the colony-level biology of siphonophores? It has been known for some time that siphonophore colonies are arranged in reiterating patterns, and that there are well-defined growth zones where the stem elongates and zooids are added. However, the significance of these reiterating patterns of zooids has remained unclear and so have

Figure 1. The deep-sea siphonophore *Marrus orthocanna.*

This specimen was collected off the coast of Maine at a depth of 580 m. The shown portion is about 20 cm long. A carbon monoxide filled float is at the top left of the colony, followed by four propulsive zooids for swimming and then a densely packed repeating sequence of feeding and other zooids. Image by Casey Dunn.

the mechanisms by which buds arise and differentiate. Recent work has shown that in most species each reiterated sequence — rather than each zooid — arises as a single bud within the growth zone and then gives rise to multiple zooids through subdivision. Siphonophores also have complex symmetry properties that deviate from the simple radial symmetry usually associated with cnidarians. The colonies can even be directionally asymmetric, with some structures consistently displaced to one side or the other just as our own heart is usually displaced towards the left sides of our body.

What is it like to work with siphonophores? Siphonophores are a joy to study. When reading about some aspect of their biology, one is just as likely to reach for a mid-19th century monograph or a paper that came out in the last year. So many questions are wide open — some requiring the same tools and approaches as the naturalists of the Age of Exploration, others necessitating modern high-throughput sequencing technologies. When collecting deep-sea specimens with submersibles, many of the acquired siphonophores are often undescribed species. Rarely do biologists have such an excellent opportunity to pull together such disparate tools in the pursuit of core conceptual questions. In addition, one siphonophore species has been cultivated through its full life cycle in the lab, while others can routinely be collected in the field. Expressed sequence tag (EST) libraries are currently under development that will enable analyses of colony development at the molecular level.

Where can I find out more?

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Essay

Binding reactions: epigenetic switches, signal transduction and cancer

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Simple binding interactions lie at the heart of disparate biological functions. Multiple negative and positive ‘add-ons’, often with small individual effects, make elementary systems that work, work better. Cancer illustrates various of these fundamental processes gone awry.

Molecular biology continues to explode with new facts and details along with the occasional surprise. There is, I believe, an unexpected bonus: a few basic principles underlie many complex processes — signal transduction, gene expression, the maintenance or destruction of gene products, the construction of epigenetic switches, and so on. In some human diseases — cancer, for example — these processes go awry, and a conceptualization of the underlying strategies helps us understand how that can happen. Here I emphasize nature’s reiterated use of the simplest of reactions: *binding*.

By binding, I mean the non-covalent interactions of macromolecules: proteins with other proteins, DNA, RNA, or membranes; of RNA with DNA, and so on. The typical interaction I refer to is reversible under physiological conditions, and its essential function is apposition, bringing one macromolecule in contact with another. In this essay I discuss a few examples of how binding reactions are deployed to different ends. Molecular details differ, but similar general strategies are found at work in these systems. The essentials are illustrated by the workings of an epigenetic switch in bacteria, my starting example.

An epigenetic switch: lessons from lambda

The bacteriophage lambda switch ensures that when one set of genes (those for lysogenic growth) are on, another set (the genes for lytic growth) are off, and *vice versa*. Once the repressor gene (*cI*) is switched on (Figure 1, left) and the lysogenic state established, that pattern of the gene expression is self-perpetuated for many bacterial divisions. The switch can be flipped by an environmental signal — such as UV light — but none of the operations of the switch entails a change in DNA sequence. Rather, the switch comprises a set of binding reactions involving two DNA-binding regulatory proteins (repressor and cro), the enzyme RNA polymerase and DNA. Here are some further salient points describing, or inferred from, the switch. These matters, as well as certain others discussed later in this article and not explicitly referenced, have been discussed previously [1,2].

- *Epigenetics.* The self-perpetuating (and hence epigenetic) character of the switch is not an inherent property of any of its components, but rather is a property of the system conferred by the pattern of binding reactions. There are two ways to make epigenetic switches, and lambda’s switch includes both: a double-negative loop, in which the product of one gene (repressor) turns off expression of the other gene (*cro*) and vice versa; and a positive feedback loop, in which repressor (despite its name) activates transcription of its own gene. The original name my colleagues and I gave to this switch — we called it a ‘genetic’ switch — is misleading because, as just mentioned, there is no change in DNA sequence involved [3]. Epigenetic switches comprising lambda-like components are found in many developmental pathways in eukaryotes.
- *Cooperativity.* The switch requires that proteins bind specifically to sites on DNA. For example, a lysogen repressor must bind to its designated sites in DNA and, more precisely, it must bind predominantly to two of three such sites as shown in Figure 1, on the left. This specificity