Segmentation, body symmetry and the organization of the central nervous system in echinoderms

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The organization of the echinoderm central nervous system (CNS) is striking because it varies widely from that of vertebrates and other bilaterians; however, the basis for this is unknown. In the present paper, I identify echinoderms as compound and I show that this is the basis for their radial symmetry and the organization of their CNS. The asteroids, as I show, comprise of bilaterally symmetrical zooids arranged radially. Furthermore, I show that variation in the CNS organization between echinoderms and planarian flatworms can be accounted for by segmentation and the arrangement of these segments, and that varying extents of segmentation is the mechanism by which the gene *Sonic hedgehog* (*Shh*) bifurcates and duplicates patterning.

Keywords: nervous system organization, bilateral symmetry, radial symmetry, compound animals, echinoderm body plan, cnidarian body plan

Body symmetry and the organization of the CNS varies widely among the various groups of bilaterians. The asteroids are radially symmetrical while planarian flatworms have a pair of longitudinal nerve cords. However, the basis for this variation is unknown. Here I show that it can be accounted for by segmentation and the arrangement of these segments, and that varying extents of segmentation is the mechanism by which *Shh* bifurcates and duplicates patterning.

Results and discussion

Previous research has shown that when a section of tissue at the posterior edge of the chick wing bud, known as the zone of polarizing activity (ZPA), is transplanted in the anterior edge of the wing bud, it results in a mirror-image duplication of the digits, such that the duplicated anteroposterior patterning is of reverse polarity in organization relative to the proximodistal axis[1]. ZPA signalling has been isolated to the Shh morphogen[2]. There is an equivalent *hedgehog* gene in *Drosophila* that, as with *Shh*, was shown to be involved in the duplication and polarity of patterning[3]. Shubin and Alberch[4] suggested that vertebrate limbs originated by a pattern forming process involving bifurcation, segmentation and condensation. The fin bones of flying fish (Exocoetidae) display a morphology consistent with this idea (Fig. 1a). Likewise, the wings of spongeflies (Sisyridae) display the same pattern (Fig. 1b). A hedgehog protein signals the patterning of the wing skeleton of insects as it does in the limb bones of vertebrates[5,6]. A previous study proposed that the limbs do not develop by a branching mechanism[7], yet here it can be seen, in the fins of flying fish, a consistent pattern of bifurcation from proximal to distal skeletal elements. In addition to its role in the patterning of the limb bones[2,8], *Shh* is also involved in the branching of the lung[9]. And it plays a part in the development of the median hinge point (MHP) of the neural plate[8]. During neurulation, the neuroepithelial cells at the MHP become predominantly short, wedge-shaped and line a furrow, while those in the adjacent areas of the neural plate remain mainly long and spindle-shaped[10–12]. Prior studies have shown that the MHP does not drive bending of the neural plate, which can still occur in the absence of the MHP, but is instead involved in the development of the normal cross-sectional form of the neural tube in which it consists of thin floor and roof plates, a narrow lumen and thick lateral walls[11,12] (Fig. 2). Furthermore, the MHP segments the neural plate. For example, in addition to the furrow[11,12], *Pax-2*, *Pax-3* and

Pax-6 expression occurs within each of the two lateral walls of the neural tube but not across the floor plate[8]. When there is no MHP, expression of these genes is continuous across the ventral neural tube[8], which is thick like the lateral walls[12]. Additionally, past experiments have replicated pattern duplication via segmentation. For example, Spemann[13,14] showed that when he constricted the eggs of the newt *Triturus vulgaris* with a ligature along the cleavage furrow at the two-cell stage, it later resulted, in some cases, in the development of newts with anterior duplication. The extent of the duplication corresponded with the degree of constriction, and when the eggs were divided completely, it sometimes resulted in twins[13,14]. Such constriction is segmentation of varying degrees. Segmentation is, as such, the underlying role of the MHP, and segmentation is the mechanism by which *Shh* is involved in pattern duplication. *Shh* is involved in segmentation, and segmentation leads to development resulting in pattern duplication. Furthermore, bifurcation is partial segmentation in which only part of the structure is duplicated into a homologous pair, as evident by the aforementioned experiments involving newts. It is a means by which to increase complexity, such as in the lungs and limbs, and it is a different form of segmentation from that which results in metameres. Segmentation is particularly apparent when the segments are diverged, and the aforementioned experiments demonstrate that segmentation is sufficient to lead to pattern duplication.

A cross section of the vertebrate spinal cord reveals two virtually identical central nerves divided by the posterior median sulcus, the anterior median fissure and linked by commissures. Each of the two central nerves extend from the respective brain hemisphere. By contrast, planarian flatworms have a ladder-like CNS, with two longitudinal nerve cords that are interconnected by transverse commissures (Fig. 3). The two longitudinal nerve cords of planarians also extend from the respective brain hemisphere, and the same applies with respect to insects, snails and earthworms. The echinoderms appear unusual in their adult form: most of the asteroids produce bilaterally symmetrical larvae, but the adults are radially symmetrical[15]. Each of a sea stars rays are structurally complex yet virtually identical, which suggests that they are homologous and, therefore, the result of duplication. The blue sea stars (*Linckia laevigata*) typically have five rays and can be radially divided into five virtually identical segments, which suggests that each of these segments is a zooid because they comprise entirely of them, such that when the duplicate segments are removed, that which is left is that which is duplicated in whole. Furthermore, each segment is almost self-contained with a set of organs needed to survive and reproduce that is echoed in each of the other segments, like each zooid in compound ascidians. This morphology can be referred to as *radially compound*. Basket stars are radially compound like sea stars, but each of their rays bifurcate multiple times. Like the ophiuroids, the crinoids and echinoids are also radially compound for the same reason as sea stars due to their relatively similar body plan, although sea urchins have the general outer shape of a spiny oblate spheroid. The nervous system of sea stars and the other aforementioned echinoderm groups is distinct: each zooid has a longitudinal nerve cord that forms one of the radial nerves in the complete animal. Hence, the compound morphology is the basis for the organization of the CNS and radial symmetry in these animals. The compound ascidians *Botryllus schlosseri*, for example, are radially symmetrical chordates in which the zooids radiate from a central cloacal siphon, and the nervous system of each zooid is, likewise, radial to the complete animal. The zooids of these radially symmetrical bilaterians, like those of the aforementioned echinoderms, are bilaterally symmetrical but radially arranged. The centre of radially compound animals is the anterior or posterior end of each zooid. Holothurians have an elongated body and, like planarian flatworms, their nerve cords run in parallel (Fig. 4). The nerve cords are not permanently parallel in the radially compound animals, instead they radiate about a central axis. Cnidarians are also radially symmetrical. Moon jellies (*Aurelia aurita*) comprise of virtually identical quarters in the medusa. And as with sea stars, this suggests that these repeating segments are homologous, which further suggests that they are zooids because these animals also comprise entirely of them, such that they too are radially compound. Furthermore, they have gonads in each of the four segments. Sea stars have gonads in each of their rays. All radially symmetrical body plans that comprise entirely of homologous segments about their central axis are radially compound.

The compound ascidians consist entirely of identically repeating segments, and it is the arrangement of these segments that give them their body symmetry. And the same applies with respect to the asteroids. Furthermore, the organization of their nervous system can be accounted for by segmentation and the arrangement of these segments. The nervous system of asteroids is radially segmented; however, in the brittle stars, each radial nerve bifurcates multiple times. Hence, each radial nerve is also segmented, but it is the result of varying extents of segmentation.

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Consent for publication

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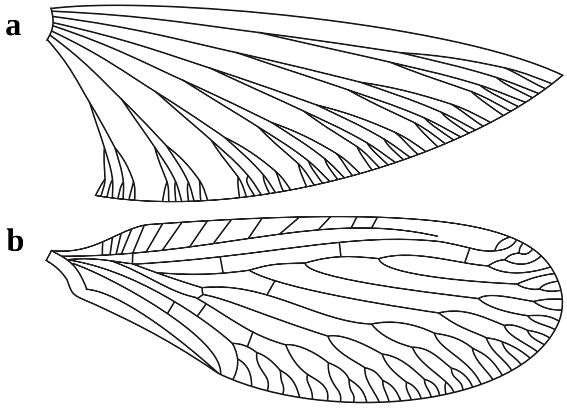

Fig. 1: Bifurcation in the skeletal pattern schematic. a, **b**, The branching pattern seen in the fin bones of flying fish (**a**) is analogously also found in the wings of sponge flies (**b**).

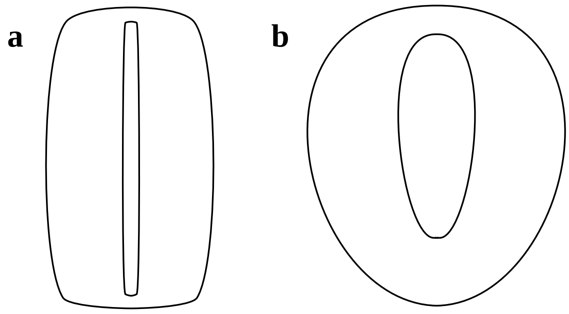

Fig. 2: Neurulation and the MHP schematic. a, The characteristic cross-sectional form of the neural tube consists of thin floor and roof plates, a narrow lumen and thick lateral walls[14]. Bending of the neural plate is concentrated at the MHP, which is located at the ventral midline of the neural tube where the cells line a furrow[12–14]. **b**, If there is no MHP, then the ventral neural tube remains thick like the lateral walls, and bending is distributed more evenly[14].

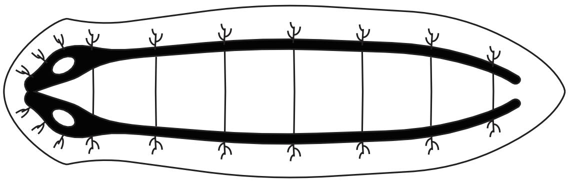

Fig. 3: Planarian nervous system schematic. These animals have two brain hemispheres and two longitudinal nerve cords that each extend from the respective hemisphere.

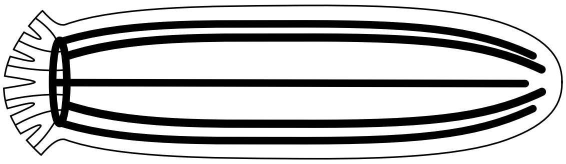

Fig. 4: Sea cucumber nervous system schematic. The longitudinal nerve cords of these animals are parallel with one another like those of planarians. In the sea stars, the radial nerves are not parallel, instead they radiate about a central axis.