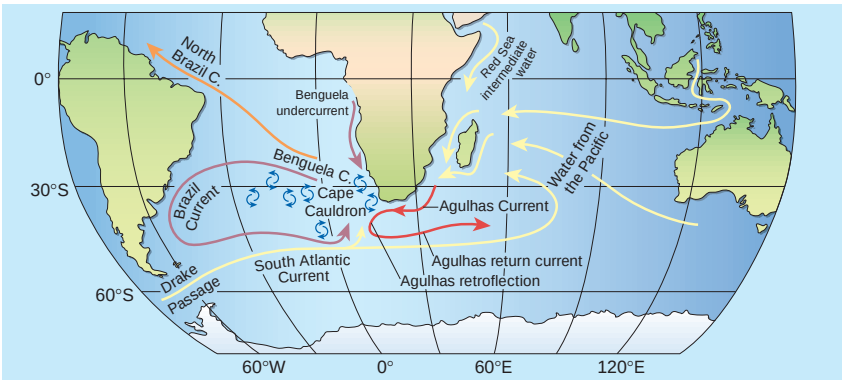

Figure 1 **The Agulhas system and associated flow patterns. The Agulhas Current draws water from the Pacific Ocean through the Indonesian throughflow and Drake Passage, and from the Tasman Sea. It abruptly turns back towards the Indian Ocean near 20° E. Here, at the Agulhas retroflection, 'leakage' of water occurs within an array of cyclonic (clockwise) and anticyclonic (anticlockwise) eddies that are injected into the vigorous stirring and mixing environment of the Cape Basin (the 'Cape Cauldron'). The South Atlantic Current adds water to the cauldron, as does the subsurface flow of the Benguela undercurrent along the west coast of Africa, and salty Red Sea water along the east coast. A blend of these waters spreads into the Brazil and North Brazil currents. The latter is part of the large-scale 'overturning circulation' induced by the formation of North Atlantic Deep Water.**

powerful eddies, 100–400 km in diameter. All of these eddies are generated within or along the periphery of the retroflection, some of them originating from the Indian Ocean, others from the South Atlantic Current (Fig. 1). These eddies are not just large anticyclonic rings, cast off from the retroflection at an average rate of six per year. Rather, they are a hodgepodge of types, which interact with each other and with the main retroflection, in a general milieu of vigorous stirring and mixing. Indian Ocean water is trapped within the eddy cores, and is often lost in the process, blending into the regional background (this is usually 'thermocline water' — that is, water from above about 800-m depth — but can take in the upper kilometre or two).

Studies of specific, newly formed Agulhas rings have exposed their turbulent birth and early evolution as they drift into the cauldron, with numerical simulations adding further detail to our picture of the complex Cape Basin circulation. These simulations can resolve quite fine-grained behaviour, and they reveal the coexistence, in dipoles, of anticyclonic eddies intensified at the surface with cyclonic partners intensified at the sea floor. The cyclonic eddies are caged in by the topography of the Cape Basin. But the anticyclonic eddies can break out of the basin and enter the South Atlantic, although with substantial energy loss.

Other authors in the special issue[2] describe how the witch's brew of the Cape Cauldron feeds blended water, via the Benguela Current, into the subtropical gyre of the South Atlantic. Some of this water remains within the gyre, eventually finding its way back to the Indian Ocean in what can be thought of as a super-subtropical gyre spanning the South Atlantic and Indian Oceans. But some enters the Northern Hemisphere within the North Brazil Current, as part of the NADW overturning circulation. About three Agulhas rings shed from the retroflection survive the blender, and make stately progress over the mid-ocean ridge and into the western South Atlantic Ocean. There, three to four years later, they will impinge upon the Brazil Current. It is encouraging to note the close agreement of the RAFOS float speeds to results of the MODAS — Modular Ocean Data Assimilation System — model, which assimilates satellite altimetric measurement of sea-level variability.

There is still a great deal to learn about the Agulhas valve, and its variation under different climatic conditions. Ensuring that it is properly represented in global ocean and climate models remains a daunting challenge. But this collection of papers[2] shows how the brotherhood of observers armed with new tools, aided by satellite-based remote sensing, and modellers with their increasingly realistic simulations, can take us forward. ■

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Cell polarity

From embryo to axon

Melissa M. Rolls and Chris Q. Doe

Many cell types in our body, ranging from neurons to the epithelial cells that line the lungs and skin, must be polarized to function properly. The same mechanism may establish the polarity of many of these cells.

How are we to make sense of the complexity of our brains? Filled with billions of nerve cells, each making hundreds or thousands of precise connections to other neurons, this organ develops anew in each of us. Not only that, but if you were to take a closer look at the individual cells, you would see that they come in thousands of stunning shapes. But there is a theme that emerges from studying these shapes. In vertebrates, most neurons have a single long protrusion, the axon, that is specialized to transmit signals to other cells, as well as many shorter, branched protrusions called dendrites that are specialized to receive signals (Fig. 1). Perhaps understanding this fundamental polarity would be a good starting point for understanding the brain's complexity. Over the past few years, progress has been made in defining how axons and dendrites differ. But less is known about how they are initially established. Writing in *Cell*, Shi and colleagues[1] provide clues to the process; their results point to a mechanism for establishing cell polarity that functions from embryos to axons.

Until now, two classes of proteins have been implicated in establishing neuronal polarity. The first class is involved in remodelling actin filaments, one of the major components of the cellular 'skeleton'. Actin remodelling must take place during any change in cell shape, such as axon or dendrite protrusion, and is particularly important during the initial steps of axon formation[2]. The proteins in question include the Rho family of enzymes, and are thought to enable the rapid growth required by an extending axon[3]. The second class of proteins includes modulators of another type of cytoskeletal filament, microtubules. Proteins in this class are either unique to, or used differently by, neurons. Axons are enriched in several neuron-specific microtubule-binding proteins,

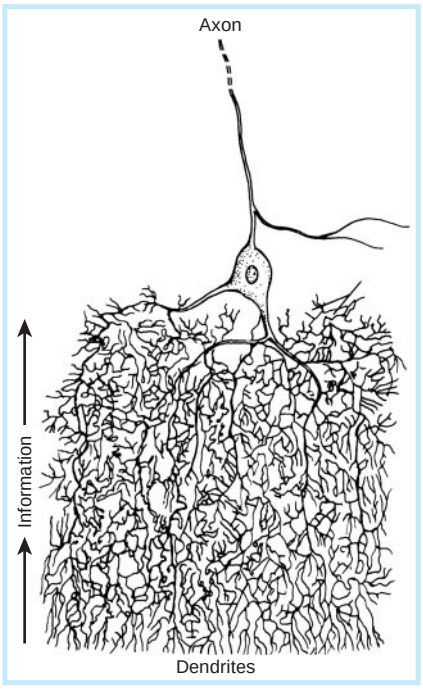

Figure 1 **Neurons are highly polarized. This Purkinje neuron, from the cerebellum region of the brain, has a single long axon and a highly branched dendrite. (Modified from ref. 8.)**

including tau and CRMP-2 (ref. 3). Dendrite microtubules are organized in part by the motor protein MKLP1 (ref. 4), which is not known to regulate polarity in other cells.

A general conclusion from these data could be that neurons use 'universal' actin-regulating proteins to initiate cell-shape changes, and use microtubule-regulating proteins to generate or maintain differences in axon and dendrite morphology. Is, then, the use of these actin-remodelling proteins the only shared feature in the establishment of polarity in neurons and other cell types?

One place to start looking for common regulators of cell polarity is the Par proteins, first identified in the tiny worm *Caenorhabditis elegans* for their ability to determine the polarity of the fertilized egg. Par-3 and Par-6 in particular seem to be part of an evolutionarily conserved protein complex that controls polarity in a range of cell types[5,6] (Fig. 2). In worms these two proteins localize to the anterior of the fertilized egg, and coordinate aspects of cell polarity that ultimately distinguish the head and the tail of the adult wiggling worm. In organisms from mammals to fruitflies, Par-3 and Par-6 are distributed asymmetrically in epithelial cells (which line the stomach, lungs and skin, for instance). Here, the Par proteins are distributed to the cellular apical side — which faces the outside world, in these examples the air or stomach contents — helping to distinguish it from the basal surface. In addition, Par-3 and Par-6 control the polarity of neural precursors in many organisms.

Shi *et al.*[1] have now looked at the role of Par-3 and Par-6 in determining the polarity of neurons from the hippocampal brain region in rats. When such neurons are cultured they initially extend several similar protrusions, called neurites. One neurite then grows rapidly and takes on the characteristics of an axon (notably long length and the presence of tau protein), and later the remaining neurites mature into dendrites[7]. Shi *et al.* show that Par-3 and Par-6 are at first present throughout the neuron, but during the initial phase of axon outgrowth they relocalize to the tip of the growing axon. Overexpression of either protein causes the cells to develop multiple projections with a length characteristic of axons. These results suggest the exciting possibility that neuronal polarity makes use of the same Par complex that regulates polarity in epithelia, neural precursors and early embryonic cells.

But what exactly do Par-3 and Par-6 do in neurons? Work on these proteins in other systems provides some clues. Par-6 can bind to enzymes of the Rho family, leading to an attractive model in which Par-6 recruits these enzymes to the end of the axon, where they remodel actin filaments and facilitate growth. In many cell types Par-3 and Par-6 localize together with another enzyme, atypical protein kinase C, and Shi *et al.* also provide pharmacological evidence that this enzyme has a role in axon outgrowth. They suggest that this might be due to an effect on microtubule dynamics.

Another interesting set of questions pertains to the very earliest events of axon outgrowth. What triggers the loss of Par-3 and Par-6 from immature neurites and their enrichment in the developing axon? Here studies of other systems provide few clues, because little is known about how Par-3 and Par-6 become localized in any cell type. It is also unknown how the timing of Par-3/Par-6 localization in cultured neurons, which lack normal environmental cues, relates to the situation *in vivo*.

Can we learn anything from the presence of Par-3 and Par-6 in developing axons about the flip side of neuronal polarity: the specification of dendrites? Perhaps these proteins are required for any type of polarized neurite growth, including that of dendrites. It is possible that during dendrite outgrowth, which occurs after the stage looked at by Shi *et al.*, Par-3 and Par-6 relocate to these structures. If, however, Par-3 and Par-6 uniquely define axons, perhaps there are other proteins that have an analogous function in specifying dendrites. Proteins that are localized opposite the Par-3/Par-6 domain in fertilized eggs, neural precursors or epithelia would be obvious candidates. The Staufen protein, for instance, is localized opposite Par-3 and Par-6 in dividing neural precursors and to dendrites in mammalian neurons. This is an appealing idea. But so far we know of no protein that is found opposite Par-3 and Par-6 in all cell types (Fig. 2).

For now, the key finding is that neurons may exploit a core complex of proteins that is used to generate polarity in many different cell types and many different organisms. Neurons certainly use unique proteins to generate their highly polarized morphology — one that underlies our ability to read News and Views articles and to design elegant experiments — but there is no doubt that many future experiments will build on this newly discovered link between axons, epithelia and embryos. ■

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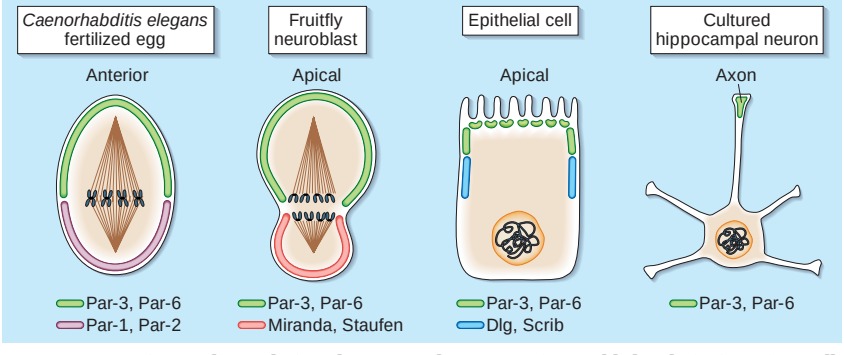

Figure 2 **Par proteins produce polarity. The Par-3 and Par-6 proteins establish polarity in various cell types, including the fertilized eggs of the worm *Caenorhabditis elegans*, fruitfly neural precursors (neuroblasts), epithelial cells from fruitflies and mammals, and — as shown by Shi *et al.*[1] — cultured hippocampal neurons. Par-3 and Par-6 show a polarized localization in these cell types and restrict other (cell-type-specific) proteins to different regions of the cell.**

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