reorientation contributes to restricting growth at the tip of the sepal and could thus terminate growth, some unclear aspects remain. The stress pattern-driven alignment of microtubules is only prominent at the very tip of the sepal. Elsewhere, the microtubule patterns seem more heterogeneous. Such noisy patterns may reflect local differences in growth rates, and thus in mechanical stress. It is likely that other players are also involved. In particular, very little is known about long-range biochemical gradients that may play a role parallel to the mechanical feedback. This aspect would be worth further investigation.

This work illustrates the pervasiveness of mechanical feedback in morphogenesis. At the cell scale, mechanical cues maintain the shape of plant cells [12], control cell division, polarity and fate in animals [17,18] and are used by a whole organ to trigger large morphogenetic changes, differentiation and growth arrest [6,7]. Mechanical feedbacks as a proprioceptive shape-sensing mechanism would provide a parsimonious mechanism for one of the so far fundamental ‘mysteries in developmental biology’ [19]. Clearly, this paper provides a step forward in the analysis and understanding of mechanics-driven growth regulation.

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Quantity Cognition: Numbers, Numerosity, Zero and Mathematics

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Physical quantities differ from abstract numbers and mathematics, but recent results are revealing the neural representation of both: a new study demonstrates how an absence of quantity is transformed into a representation of zero as a number.

Mathematics has guided the development of science and technology since the time of Plato and Archimedes. Because mathematics is a uniquely human practice, cognitive neuroscientists have long sought the basis of numerical and mathematical cognition in the human brain [1]. A vital advance came with the discovery of neurons in macaque monkeys that respond to specific visual object numbers, or numerosities [2]. This

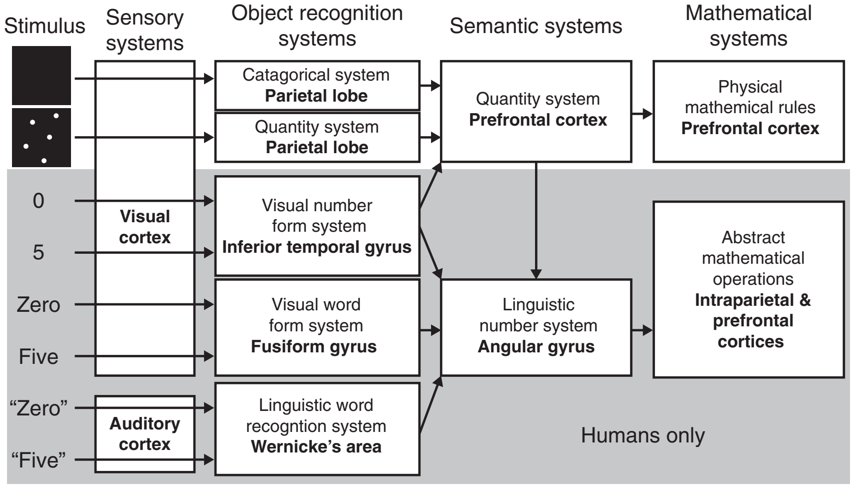

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Figure 1. Proposed organization of numerical cognition in primates and humans.

Top: empty sets are represented as a separate category from other object numbers (numerosities) in the parietal lobe. In the prefrontal cortex, zero becomes part of the numerosity continuum [7]. This prefrontal quantity system also responds to simple physical quantitative concepts like proportions [13] and comparisons [11]. Bottom: humans also represent quantities using abstract linguistic concepts, number symbols and words. These are each processed by separate linguistic systems, and then integrated (with physical quantity) into a linguistic numerical system that supports abstract mathematical reasoning.

numerosity processing system has since been investigated thoroughly in macaques and humans [2–6]. However, the relationship between the brain's representation of simple physical quantities like numerosity and more abstract mathematics remains unclear, largely because animals provide poor models of human mathematics. For example, the number zero is vital to mathematics, yet the concept of zero as a number (rather than simply an absence) developed remarkably late in human history, being first thoroughly described by the seventh century Indian mathematician Brahmagupta. In this issue of *Current Biology*, Ramirez-Cardenas *et al.* [7] demonstrate zero objects is represented as a separate category from other numerosities in the macaque parietal cortex, but is transformed into part of the numerosity continuum in the prefrontal cortex.

Mathematical cognition has been investigated thoroughly by behavioral and developmental approaches. Basic concepts of object number and simple arithmetic are found in pre-linguistic five-month-old infant humans, and thus are likely innate aspects of human psychology [8]. The advent of neuroimaging demonstrated increased neural activity during calculation tasks in the human parietal lobe, centered in the intraparietal sulcus [9,10]. This was followed by the demonstration of numerosity-selective responses in macaque prefrontal cortex: neurons responding maximally when the animal views a specific object number, with response amplitudes decreasing with distance from this preferred numerosity [2]. Subsequent reports described intraparietal neurons that respond slightly sooner than the prefrontal cortical neurons, suggesting they pass numerosity information to the prefrontal cortex [5]. This work, led by Andreas Nieder, has developed into an extensive literature on the neurophysiology of primate quantity processing [7,11–13].

However, these experiments examined positive integer object numbers only. More complex numerical concepts like zero, negative numbers, fractions and written (symbolic) numerals were not investigated. Indeed, it is unclear whether these concepts would be meaningful to any animal lacking an elementary school education. Perhaps the easiest of these concepts to approach is zero. Even without education, an animal might understand that if Jordan has two apples, then gives Jessie two apples, Jordan then has no apples. But is the concept of 'no apples' a particular number (zero) or just an absence of apples?

Ramirez-Cardenas *et al.* [7] trained macaques to match displays by their numerosity, and included zero in that group of numerosities. This implicitly associates the empty set with positive integer sets: they show the animals that zero can be a number. They then recorded from both intraparietal and prefrontal areas while the animals performed this task. While some intraparietal neurons responded maximally to zero, their response to positive numerosities decreased little (if at all) from one to four. In other words, these neurons did not represent zero objects as part of the continuum of object numbers, despite responding specifically to zero objects. This was quite different in the prefrontal cortex: here, neurons that responded maximally to zero objects decreased their response with increasing distance from zero. The neurons represented zero as closer to one than two, as part of the numerosity continuum, and as a number rather than an absence.

This distance effect was also evident in the animals' behavior: they were more likely to match an empty display with a display containing one object than two. So prefrontal neurons' activity correlated more with behavioral responses than intraparietal neurons' activity did. This suggests a hierarchy of processing. Intraparietal neurons describe physical quantities, where zero is an absence of quantity. Prefrontal neurons inform and predict behavior, where zero is a number that is relevant for accurate task performance (Figure 1). This result mirrors the concept of zero as both an absence and a number.

Numerosity-selective responses show that we can examine the brains' representation of numerical cognition exceptionally precisely. But numerosity is quite distinct from the abstract concept of number that we use in mathematics. Numerosity is a physical quantity of a stimulus, like size or length. Indeed, selective responses to numerosity, size, and length have all been found in the same parietal areas [12,14], forming a generalized quantity processing system [15]. An abstract number system should give similar responses to written symbolic numerals and number words, which represent all these quantities in human language. However, animals lack such symbolic and linguistic concepts.

Advanced neuroimaging methods now allow us to measure numerosity-selective responses in humans [3,4,6], though in less detail than animal recordings. Parietal neurons are organized into topographic numerosity maps, where numerosity preferences change gradually across the cortical surface, grouping neurons with similar responses into populations that can be recorded at the relatively coarse resolution of functional magnetic resonance imaging [4,14]. These human numerosity-selective neural populations do not respond similarly to symbolic numerals [3,4,16]. Instead, a distinct 'visual number form area' responds to symbolic numerals, in the posterior temporal lobe near the visual word form area that is implicated in word reading [17,18] (Figure 1). There seem to be relatively weak relationships between these symbolic and physical quantity systems [3,16], together with a third, linguistic number representation centered on the parietal lobe's left angular gyrus [9,19]. So, for the brain, the numeral 5 may have the same abstract relationship to seeing five objects as any written word has to our physical experience of the world. This would allow considerable cognitive flexibility, as the same numeral can represent five objects, five meters, or five minutes. We can then use the same abstract mathematical operations for any physical quantity. So abstract numerical and mathematical cognition relies on the abstraction inherent in language.

Non-linguistic animals therefore lack abstract mathematical operations; however, some simple mathematical concepts have clear roles in guiding behavior and may provide selective advantages for any animal. Macaques can judge proportions and ratios of sizes. Indeed, Nieder's group [13] has described prefrontal neurons selective for particular line length ratios regardless of absolute lengths. Such ratios may represent a primitive form of division operation. Macaques can also evaluate 'greater than' and 'less than' comparisons of numerosity. Nieder's group [11] has also described prefrontal neurons that respond to each of these comparisons regardless of the numerosities involved. These prefrontal neuron classes therefore encode simple mathematical rules regarding physical quantities, likely precursors of human abstract mathematical cognition. Finally, long-term training to associate numerosities with their symbolic numbers produces similar responses to both in prefrontal (but not parietal) numerosity-selective neurons [20]. Such associations may represent precursors to human symbolic cognition.

Of course, the range and complexity of human mathematical operations far exceeds that found in other primates. When considered with our unique use of symbolic/linguistic number representations, and the massive expansion of parietal and frontal lobes in the human brain, it seems unlikely that advanced mathematical cognition can be understood using animal models alone. Functional imaging studies have consistently identified neural activity in intraparietal and prefrontal regions during calculation tasks [9,10] (Figure 1), but they have not identified the underlying neural mechanisms. A combination of advanced computational neuroimaging methods that build on Neider's animal neurophysiological approaches may soon determine the neural and computational mechanisms underlying specific abstract mathematical functions in humans.

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