

Figure 2. Proposed neural networks underlying the motion after-effect for voluntary movements.

The motion after-effect for voluntary movements may arise from the dynamic interplay of neural networks for visual motion analysis and motor control. Area MT and the extrastriate body area (EBA) analyse visual motion of objects and bodies. Both regions are reciprocally connected to areas in the posterior parietal cortex (PPC), which compute spatial transformations from retinotopic frames of reference to effector-centered frames of reference. PPC sends and receives information from frontal networks for motor control, which involve the premotor cortex (PMC).

Although this view is tempting, complex sensorimotor behavior is rarely generated by individual brain centers, but is more often the orchestrated product of large neural networks. Furthermore, the authors make the strong assumption that the sense of ownership is 'coded' in PMC, which is, however, controversial [15].

We suggest an alternative view (Figure 2). The hand-centered motion after-effect for visible movements points at the interdependency between visual motion circuits for objects (targeting MT) and bodies (involving the extrastriate body area, EBA) [19], and frontal networks for motor control. PPC is likely to be the key communication node between these networks [1], possibly tuning MT activity in a frame of reference anchored to the body [20]. Future studies may shed light on the neural mechanisms that allow voluntary actions to structure the visual space.

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Development: The Maternal–Zygotic Transition Revisited

The handover from maternal to zygotic control has to be carefully orchestrated. In most animal embryos, maternal products drive early embryogenesis, and the genome of the zygote is only switched on later. However, in the nematode *Ascaris* the zygotic genome is never silent, and the maternal products are rapidly eliminated.

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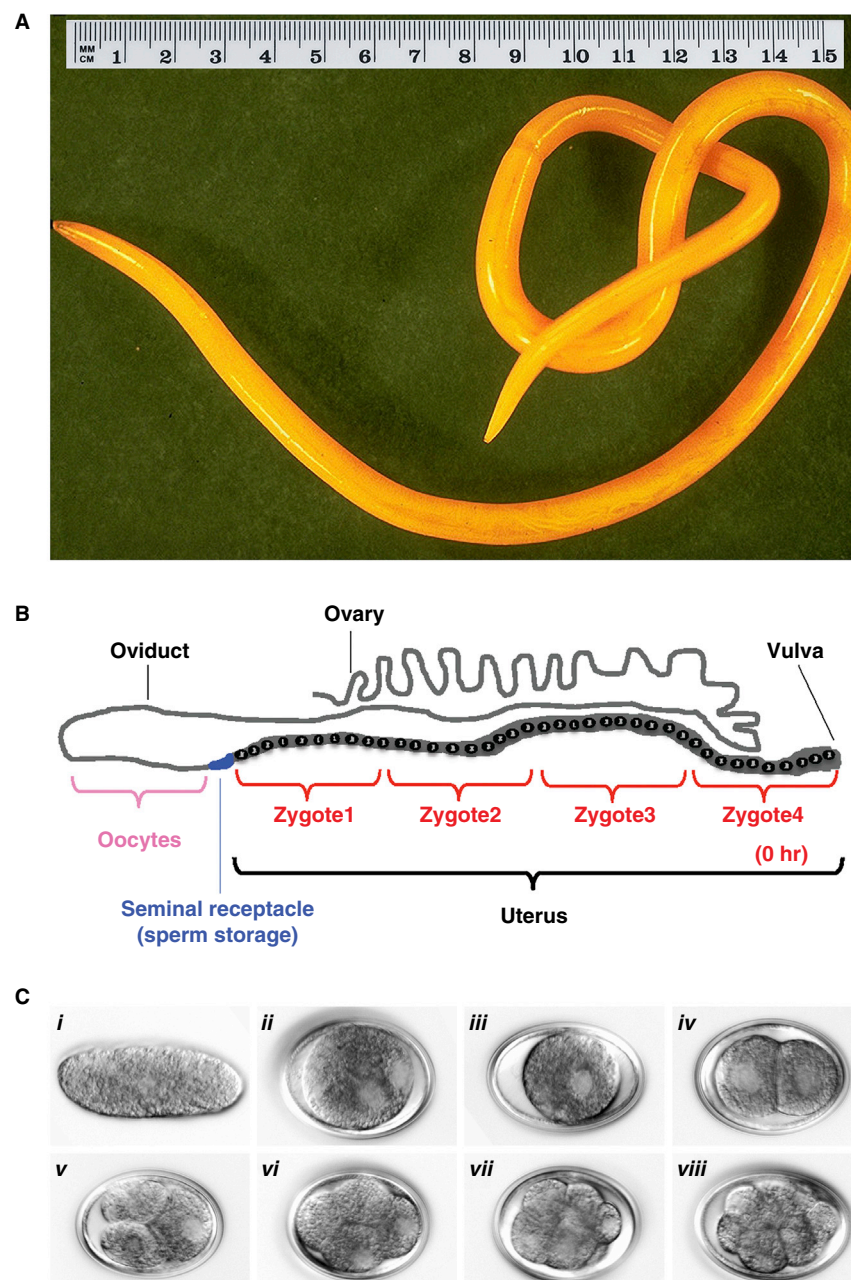
In 1883, Édouard van Beneden published “*Recherches sur la*

maturation de l'oeuf, la fécondation et la division cellulaire” [1]. This beautifully illustrated monograph describes in exquisite detail the

structure of the oocyte, the meeting between oocyte and sperm, and the intricate dance of male and female pronuclei as they fuse and divide. The story is familiar to all biologists, and the details reminiscent of the highest quality of analyses possible today, but all achieved without fluorescent probes, confocal microscopy or timelapse video. How did van Beneden achieve such detail, and accuracy? He was an extraordinary scientist, and a brilliant microscopist, but a key reason for his being able to describe the dynamics of fertilisation and early cleavage in an animal embryo was his choice of study organism.

van Beneden was studying '*Ascaris megalocephala*' (now known as *Parascaris equorum*), a common gut-parasitic nematode of horses. Ascaridids are still revealing experimental subjects, and in this issue of *Current Biology* Wang *et al.* [2] apply one of the modern embryologists' high-resolution tools, next-generation transcriptomics, to the related species *Ascaris suum* to explore the genomics of early development. Ascaridid nematodes were ideal for these studies because of their extreme fecundity (the 10 cm long females produce tens of thousands of eggs per day), because oogenesis and zygote formation is laid out linearly in a 40 cm long gonad, and because development is remarkably protracted (Figure 1). In addition, fertilised zygotes arrest before pronuclear fusion (in natural infections, these eggs are voided with the faeces). These can be synchronously activated by mimicking the acid conditions in a new host's stomach when they are reingested. Post-activation, early cell division cycles are slow, taking ~13 hr (as compared to ~30 min in the distantly related nematode *Caenorhabditis elegans*).

Parascaris and other ascaridids of pigs and humans were popular 19th and early 20th century research organisms: their relatively simple nervous systems were mapped in fine detail [3], and the early embryonic lineage described (identical to that of *C. elegans* [4]). Ascaridid research is still important, as approximately a billion humans are infected with *A. lumbricoides*, and a majority of the world's farmed pigs are infected with *A. suum*. Most effort is thus expended on efforts to eliminate these species through drug and vaccine



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Figure 1. Oogenesis and early embryogenesis in *Ascaris suum*.

(A) Image of an adult female *A. suum*. (B) Diagram of *A. suum* female reproductive system. The length of the system is ~240 cm. Pronuclei in the zygotes (1–4) remain unfused as the zygote undergoes maturation inside the uterus. (C) Nomarski images of *A. suum* oocyte and early embryos. The embryo is ~100 x 45 μm in size. i, oocyte; ii, zygote prior to pronuclear fusion; iii, zygote with pronuclei fused (~24 hr of development); iv, 2-cell (~48 hr of development); v, 3-cell (~55 hr of development); vi, 4-cell (~62 hr of development); vii, 6-cell (~72 hr of development); and viii, 8-cell (~80 hr of development). Timing is for development at 30°C. (Figure courtesy of J. Wang.)

development. However, *A. suum* can still offer important insight into general mechanisms, including, for example, genome stability (*A. suum* undergoes chromatin diminution in somatic cells

[5]), miRNA biology, and the mechanisms of splicing of mRNAs [6]. In their latest study, Wang *et al.* investigate the roles of maternal and zygotic transcripts in embryogenesis.

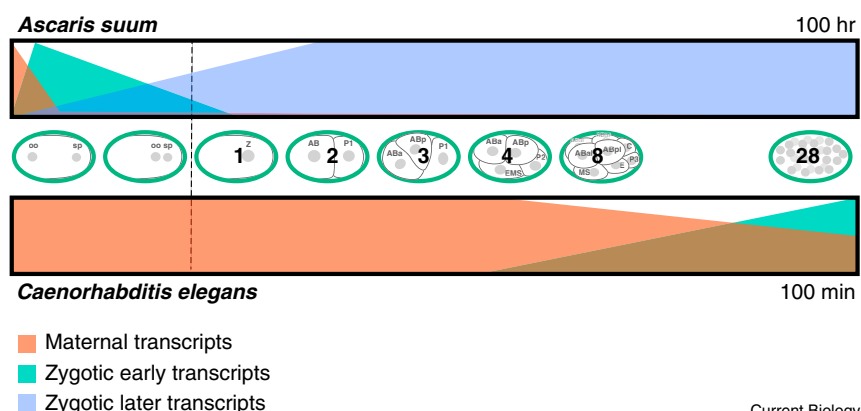


Figure 2. Contrasting dynamics of maternal and zygotic contributions to development in two nematodes.

The control of development in *Caenorhabditis elegans* is largely controlled by maternally supplied mRNAs through to the 28-cell, gastrulation stage (lower panel). In *Ascaris suum*, maternal mRNAs are degraded rapidly on fertilisation, and before the formation of the zygotic nuclei (dashed vertical line). Transcripts from the pronuclei and zygotic nuclei thus must be in control of *A. suum* development (upper panel). *A. suum* development is protracted (100 hr) compared to *C. elegans* (100 min), but their cell lineages (indicated by the stylised embryos in the middle panel) are near identical.

In most animals, the egg contains not only nutrient stores but also proteins and RNAs involved in orchestrating the first stages of development. In frogs, fertilised zygotes from which the nucleus had been removed were still able to carry out the first steps of normal development [7], showing that maternal machinery stored in the egg could act independently of the zygotic genome. The point at which the enucleated embryos failed is termed the maternal-zygotic transition (MZT), and similar phenomena have been observed (using genetic or chemical tricks rather than microsurgery) in *Drosophila melanogaster* fruit flies, *C. elegans*, mice, zebrafish and other animals [8,9].

The MZT is often linked with another major developmental event, that of activation of transcription from the zygotic genome. Transcription from gametic genomes is tightly regulated, for reasons associated with avoidance of activation of selfish DNA elements, reprogramming of the genome and, in sperm, dense packaging of the nucleus. Switching on of the zygote genome is thus a carefully orchestrated event, and has been characterised as a two-stage process. Initially, a few genes are switched on, and these then regulate both the expression of additional waves of zygotic genes and also the targeted destruction of maternal mRNAs [10]. For example, in zebrafish, this switching on of zygotic

genes has recently been shown to be regulated by maternally supplied stem cell pluripotency transcription factors, Nanog, Pou5f1 and SoxB1, emphasising the deep integration of this switch into vertebrate development [11].

The reasons why the mother should so provision her egg and the developing embryo are multiple. The delivery of mRNAs and proteins that can carry out early developmental regulation may buffer the embryo against any environmental perturbation. Genome replication conflicts with transcription, and thus maintaining transcriptional silence may be part of the facilitation of the rapid replication of the genome observed in many embryos. The remodeling of zygotic chromatin to permit totipotency may also be incompatible with transcription. Maternal provisioning in a much larger oocyte may have roles in suppressing potential paternal interference in or manipulation of development. Reliance on maternally provided components may also protect the early embryo (and unsequestered germ-line) from the action of genomic parasites.

These findings are common across animals: the zygotic genome is transcriptionally silent for some period after fertilisation, is switched on in a two-stage process, and maternal provisioning is sufficient to direct early

development up to a point. However, the relative timing and extent of these two processes differs [9]. In sea urchins, for example, zygotic expression is evident from before pronuclear fusion, but the MZT is not observed until after the formation of the free-swimming pluteus larva. In *Drosophila* and *Xenopus*, zygotic expression is first observed in the ~256 cell embryo and zygotic genome activation is established in the ~4,000–6,000 cell embryo, but the MZT is not observed until much later in development. In *C. elegans*, with its highly lineage-driven development [4], the MZT is at gastrulation (~28 cell stage), and is bracketed by early zygotic gene activation (a few genes at the 4-cell stage) and the major activation of the zygote genome (at ~100 cells) [12].

Wang *et al.* [2] generated RNA-seq data from staged *A. suum* zygotes and embryos. They identified nearly 1,200 genes with elevated expression in unfertilised oocytes: these correspond to the expected maternal RNAs. However, the mRNAs for these genes were rapidly degraded following fertilisation. Surprisingly, they identified *de novo* transcription of 1,600 zygotic genes in the fertilised zygote before pronuclear fusion. That this was functional was affirmed by mapping of markers of active RNA polymerase II activity to both male and female pronuclei, and demonstration that new transcripts were associated with polysomes (indicating that they were being translated). Similarly, gene expression from the zygotic genome was identified in embryos from the single-cell stage, and active RNA polymerase II was identified in early somatic and germ-line nuclei. Thus there is no quiescent phase in *A. suum* zygotes, and the zygotic genome is an active, driving partner in development (Figure 2). The contrast with *C. elegans* is particularly striking when genes that are maternally provisioned in the model nematode are considered. About 80% of the *A. suum* orthologues of these maternal genes are exclusively or largely expressed from the zygotic genome.

These new data on *A. suum* are important, not only because describing organismal diversity is exciting, but also because they emphasize that development is not a fixed, invariant process, even in groups that have an apparently invariant developmental

system. The extraordinarily early and extensive gene expression in *A. suum* embryos shows that repression of zygotic gene expression is not a law, but a phenotype that requires explanation. The extended development of *A. suum* embryos may be permissive of transcription because of reduced conflict with genome replication or remodeling. It is notable that genome methylation is absent or much reduced in chromadorean nematodes (*C. elegans* and *A. suum*; methylation is present in enoplean nematodes such as *Trichinella spiralis* [13]), and thus chromatin remodeling to produce a totipotent state may not be as difficult in these species. Extensive, early zygotic gene expression might be observed in other taxa with extended embryonic division timings. Expression observed in pronuclei may be part of the production of arrested eggs. Is pronuclear gene expression also observed in other dormant eggs? Has *A. suum* evolved a distinct method of protection against genomic parasites? Is there a mechanistic link with chromatin diminution?

The second object lesson from these data is that development evolves, and that the mechanisms and patterns of development are adapted to the life history strategies of the animals they produce. It is particularly striking that *C. elegans* and *A. suum*, which have near-identical early cell cycles and cell determination patterns (albeit with very different timings), differ so profoundly in how development is

delivered in the embryo. In *C. elegans*, the maternal contribution is extensive and essential. In *A. suum* it is not yet known which components of the maternally provided transcriptome are essential, but it is clear that many mRNAs that are essential and maternal in *C. elegans* are zygotic in *A. suum*. The production of the same (or highly similar) outcomes through different mechanisms has been termed developmental system drift: the output remains the same while the underpinning circuitry changes [14]. The extensive expression from zygotic genes from fertilisation in *A. suum* allows us to revisit the questions of why zygotic gene expression is silenced in many species. Which of the arguments best explain the observed patterns of maternal provisioning and zygotic silence across species? While the model species have revealed some of the answers, only by using a diverse sample of contrasting, but accessible, species can the truth, or falsity, of inferred laws be determined.

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Organelle Size: A Cilium Length Signal Regulates IFT Cargo Loading

Cilia grow by assembling structural precursors delivered to their tips by intraflagellar transport. New work on ciliary length control indicates that, during ciliary growth, cilia send a length signal to the cytoplasm that regulates cargo loading onto the constitutively trafficking intraflagellar transport machinery.

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Almost every cell in vertebrates possesses a primary cilium that plays key sensory roles in development and homeostasis [1]. Although we are beginning to learn the cellular mechanisms for assembling this

organelle, whose structural core is the set of nine outer microtubule doublets that constitute the axoneme, our understanding of the mechanisms that regulate ciliary length has lagged behind [2]. During ciliary assembly, cells use intraflagellar transport (IFT) to deliver ciliary components from the

cytoplasm to the ciliary tip [3,4]. The highly conserved IFT machinery has two microtubule motors — an anterograde kinesin-2 and a retrograde cytoplasmic dynein — and a set of associated cargo carriers called IFT particles (themselves composed of IFT-A and IFT-B complexes). The current model for growing a cilium is straightforward: the IFT complexes bind to a ciliary precursor cargo (e.g., a structural component of the axoneme) near the base of the organelle, bind to the anterograde motor, and are carried to the tip of the growing axoneme, where they release their cargo, which assembles on to the end of a growing microtubule doublet of the