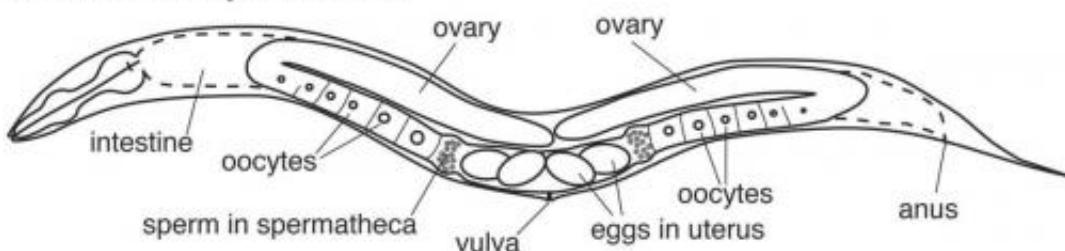


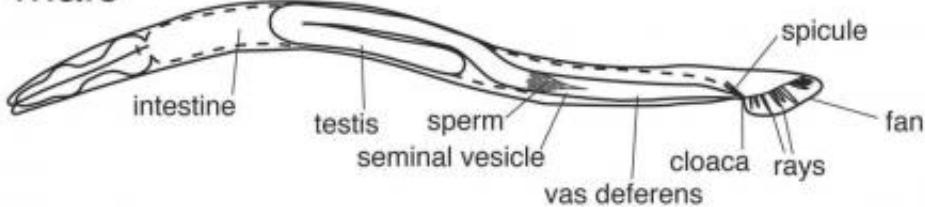
Temperature dependence and the thermal limits of embryogenesis

February 11 2015, by John Hewitt

XX hermaphrodite



XO male



XX and XO worm configurations. Credit: wormbook.org

(Phys.org)—Raising the temperature is one easy way to get chemical reactions to speed up. This temperature dependence can be accurately described by a simple exponential relation known as the Arrhenius equation. A commonly accepted generalization of this equation is that the reaction rate tends to double for every 10 degree Celsius temperature increase. Many biological phenomena, like rates of firefly flashes or the speeds of working ants, have also been shown to follow similar kinetics. A recent paper in *Cell Reports* now shows that not only does the timing

of cell division cycles in the early embryo follow the temperature prescription called for by Arrhenius, but that this developmental dependence is what ultimately constrains the thermal limits of the organism itself.

The worm [*c. elegans*](#) is an ideal organism to use to crack the secrets of multicellular life. Researchers are now on a first name basis with all the cells found in its developing embryo, and can track each them as they asynchronously cleave off and reform to establish various organs and planes of symmetry—much as you or I would watch an elaborately choreographed Superbowl halftime show. The authors focused their attentions on the timing of what is probably the most important division in the embryo, the first one. Specifically, they measured the interval between the time the pronuclei first meet and the onset of cytokinesis.

To give some idea of the kinds of numbers we are talking about here, the authors reported a nice exponential fit from 5°C to 25°C, where cell division time correspondingly fell from 50 minutes down to 5 minutes. Above these temperatures there began to be subtle signs that all was not well in wormland. At 25°C they would start to get sterile worms, presumably because germ cell specification was disrupted at this point. Above 28°C, the precision Arrhenius sensitivity began to break down with embryos unable to establish proper symmetry. By 30°C, there would be failure to reach the first division cycle all together.

The authors also looked at cell division in *C. briggsae*, a high-temperature-tolerant worm hailing from India. Although this lineage apparently split from *C. elegans* over 18 million years ago, it is almost identical in morphology and reproductive detail. The authors found there was a shift, rather than an expansion of the thermal sensitivity relation for *C. briggsae*. This result led them to speculate that such adaption may not require multiple independent mutations acting on specific tissue or cell types, but rather the thermal sensitivity of the whole organism is

shifted in response to evolutionary pressure by some other kind of mechanism.

It was found when [cell cycle](#) timing deviates from an exponential temperature relation, coordination of events that depend on the first cell division, and all subsequent development is impaired. The authors suggest that these observed temperature relations may be the key to evolving coordinated biological processes that are able to remain synchronized even as the genetic or environmental landscape changes. They do note, however, that not all high level developmental processes (like cell division) will be expected to occur with Arrhenius kinetics. The breakdown of the nuclear envelope prior to cleavage, for example, happens earlier than would be predicted. Other kinds of events, like unfolding of proteins in response to heat stress, will be expected to happen more-or-less above some hard threshold temperature.

Perhaps the best way to try and explain how different worms, and organisms, in general can control their thermal behavior (like the upper temperature limits of cell division) is through the unifying rate mechanisms of their mitochondria. We recently discussed the [involvement of mitochondria](#)—and the temperature they set through the heat and chemical energy they make available—in the specification of individual blastomeres of developing embryos. In suggesting that the maximum rate of mitochondrial activity may be a fundamental limit on the rate of [cell division](#), the authors note that the *C. briggsae* worms have a comparatively lower mitochondrial membrane potential and lower levels of reactive oxygen species—an observation that squares with its slower cell cycle and increased temperature resistance.

When cellular respiration is experimentally manipulated by using a technique known as RNA interference (RNAi), embryonic cell cycle turnover and progression through developmental milestones is slowed down. One reason this RNAi seems to work so well is that researchers

are finding that RNA is naturally used to perform all kinds of tricks in germ cells. We mentioned above that *C. elegans* germline specification was found to be highly temperature sensitive. As with most animals, these cells are typically set aside after just four cell divisions. The latest research now indicates that once they are made these germ cells continue to receive instructional inputs in the form of RNA not just from researchers via injection or ingestion and subsequent migration to germ cells, but from a home grown RNA source synthesized by distant somatic cells and delivered through the network of their own nervous system.

More specifically, it was found that neurons handing-off double stranded RNA to germ cells results in transgeneration gene silencing in corresponding matching sequences. Moreover, this directly heritable effect lasts at least 25 generations. In other words we now have another fine example where full-blown Lamarckian pandemonium runs wild, and the entire organism via its nervous system, is essentially understood as one massive antennal harvester of information capable of transducing environment to germ.

Extrapolating effects like temperature dependence, or mitochondrial and RNA-based control to other kinds of creatures, will take some care. Mammals, who tend to do embryogenesis a little differently, generally don't need to swim across entire oceans just to assure themselves of finding a place with a predictable temperature to stow their eggs. On the other hand, even if mammals routinely scuttle mobile RNAs from nerve to germ like the worm, there is no guarantee that inherited effects would escape the epigenetic informational reboot that may or may not blank significant life experience gained in each generation.

More information: Temperature Dependence of Cell Division Timing Accounts for a Shift in the Thermal Limits of *C. elegans* and *C. briggsae*, *Cell Reports*, www.cell.com/cell-reports/abstract...

[2211-1247\(15\)00007-8](#)

Abstract

Cold-blooded animals, which cannot directly control their body temperatures, have adapted to function within specific temperature ranges that vary between species. However, little is known about what sets the limits of the viable temperature range. Here we show that the speed of the first cell division in *C. elegans* N2 varies with temperature according to the Arrhenius equation. However, it does so only within certain limits. Outside these limits we observe alterations in the cell cycle. Interestingly, these temperature limits also correspond to the animal's fertile range. In *C. briggsae* AF16, isolated from a warmer climatic region, both the fertile range and the temperature range over which the speed of cell division follows the Arrhenius equation, are shifted toward higher temperatures. Our findings suggest that the viable range of an organism can be adapted in part to a different thermal range by adjusting the temperature tolerance of cell division.

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