TITLE: Fahrenheit 101

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Having recently become very interested in the way organisms balance heat production against 'useful work', I have stumbled into an old-chestnut question in biology. That is, why do birds and mammals maintain their body temperature close to 40°C – at least during periods of normal circadian activity – regardless of their size or their local environment? This question comes into even sharper focus when realizing that the vast majority of organisms on our planet do not do anything like this, and still thrive at temperatures anywhere between below the freezing and above the boiling point of water. Warm-blooded animals as a whole represent only a fraction of a percent of the total biomass on Earth. Most animals live at or very close to environmental temperature. Moreover, birds and mammals inhabit similar environments to all those other organisms, ranging from the cool depths of the oceans to the dramatic temperature fluctuations of the world's deserts. The male emperor penguin (*Aptenodytes forsteri*) overwinters on the landward side of the Antarctic sea ice, remaining almost motionless for months, whilst incubating his egg at air temperatures some 70-80°C cooler than that of his own body, without even factoring in the additional chill of frequent gale-force winds. And then goes off foraging in the comparatively warm waters at the ice edge and beyond, maintaining all the time his body temperature at the same 38-39°C. The only significant deviation from the 40°C rule is the special case of hibernation and torpor, although the extent and frequency of the associated body temperature decrease(s) vary greatly between species.

Whenever I have posed this question to colleagues or students or just about anyone, I invariably get a similar answer: that this must be the optimal temperature for life. For the stability of proteins; for the functionality of enzymes; for just the right amount of membrane fluidity to facilitate cell-cell signaling, endocytosis, exocytosis and charge separation; for the highest fidelity of nucleic acid and protein synthesis. Even if these assertions are true – and I am not aware of compelling evidence that they are – this flies in the face of the fact that the vast bulk of non-homeothermic organisms are not to be found in the very few environments on the planet that come close to the range of avian and mammalian body temperatures. Instead, life seems concentrated in the cool soil and oceans, and in great forests found in equatorial, temperate and even sub-polar climes alike. The most biologically productive zone of the world's oceans isn't even in the tropics, but at the Antarctic convergence, which is teeming with animal, plant and bacterial life. Moreover, if 40°C were so favourable, wouldn't homeothermy geared to maintaining that temperature have evolved countless times, in different organisms? Or, for that matter, wouldn't the proteins and membranes of birds and mammals have evolved so as to function better at temperatures closer to the global average of around 10-15°C, instead of wasting all that energy to stay warm? After all, if the Antarctic sea urchin (*Sterechinus neumayerii*) has adapted over a few tens of millions of years to live and develop perfectly well at -1.5°C [1], just more slowly than its close relatives in temperate or tropical waters, what's stopping us from having turned down the heat by the same amount?

I anticipate that you are now expecting me to reveal a brilliant idea to explain everything. But all I have to offer are new meanderings and wrong turnings. The first is the idea that, like the traditional explanation for our cellular and blood salinity being close to that of the ancient ocean, maybe that ancient ocean was stable at 40°C for most of evolutionary time. Except that it wasn't. It was closer to 80°C throughout at least the first half of our planet's history, when the major cellular forms evolved [2], and after that cooled down to below the magic 40°C and remained there ever since, albeit with large fluctuations. During the period when warm-blooded creatures are believed to have arisen, the oceans never rose to 40°C and, in any case, this evolutionary step is generally assumed to have occurred on land, not in water.

Do our own observations that mitochondria are 10-12°C warmer than the cells in which they reside [3] have any bearing on the question? Is this again some kind of happy medium, whereby the maximum efficiency of oxidative phosphorylation dictates a certain heat output which naturally maintains the cell's temperature at around 40°C? But if this were the case, other eukaryotes that didn't maintain any kind of internal thermoregulation at the whole-organism level would also tend to be at 40°C, with their mitochondria at 50°C. But mitochondria in *Drosophila* cells are again about 10°C warmer than their surroundings, but at much cooler ambient temperatures [4]. And prolonged exposure to 40°C represents a lethal heat-shock for wild-type *Drosophila* [5]. Poikilotherms simply lose excess heat to the environment, whereas homeotherms must use specific mechanisms both to generate, as well as retain, additional heat when needed, and radiate excess heat to the outside, so as to maintain a constant internal temperature.

Is there some other defining feature of mammalian and avian biology that might default body temperature to the observed constant? After much reflection, I can't think of one. But perhaps it is possible to construe an argument in the opposite direction, that having evolved mechanisms to maintain a constant body temperature, birds and mammals have, as argued elsewhere [6], been able to colonize extremely diverse habitats, remain active at night and perhaps resist mass extinction events driven by climate change a bit better than other taxa. But this didn't help the dinosaurs. And it doesn't explain why 40°C is any better than 80 or 20°C, or why it is so evolutionarily stable, in birds of paradise as in penguins, or kangaroos as in polar bears.

Perhaps one can cobble some argument together by combining the adaptive range and mitochondrial arguments; plus the fact that it is probably easier to envisage single mutations that can shift the balance between metabolic heat production and useful work, to maintain 40°C, as opposed to the many mutations required to re-optimize biological processes for a different temperature. But I'm not very convinced: evolution normally mirrors environmental change, rather than resisting it.

If an intelligent insect were writing this column, they would no doubt herald the virtues of the arthropod lifestyle in being able to go with the climactic flow and not waste so much energy keeping warm or cool like all those primitive furry and feathered creatures, yearning for their balmy but non-existent Eden. Maybe some reader out there will come up with a cute idea that will prove experimentally testable and eventually seem self-evident, yet has escaped me and all others who have pondered this question. But I'm now going out to frolic in the snow. Over to you.

[1] Foo SA et al (2016) https://doi.org/10.1007/s00227-016-2903-1
[2] Knauth LP (2004) https://doi.org/10.1016/j.palaeo.2004.10.014
[3] Chrétien D et al (2018) https://doi.org/10.1371/journal.pbio.2003992
[4] Terzioglu M V& Jacobs HT (unpublished observations)
[5] Stefanou G & Alahiotis SN (1982) https://doi.org/10.1002/dvg.1020030404
[6] Grigg GC et al (2004) https://doi.org/10.1086/425188