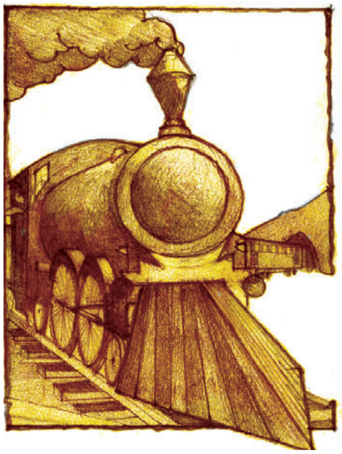
Keeping track of the literature isn't easy, so Outside JEB is a monthly feature that reports the most exciting developments in experimental biology. Short articles that have been selected and written by a team of active research scientists highlight the papers that JEB readers can't afford to miss.

Outside JEB

FLUID LOCOMOTION



LOCOMOTION USING A FLUID RATCHET

Small animals have a difficult life in the ocean, buffeted on all sides by waves and turbulence and pursued by predators much larger than themselves. It might seem that such environmental forces would completely overwhelm any locomotory efforts these tiny beasties could make.

Recent mathematical modeling work in the *Physics of Fluids* by Saverio E. Spagnolie and Michael J. Shelley indicates that small animals may not be quite so helpless – provided they can change their shape. In a simulation of a jellyfish-like creature, the researchers found that appropriately timed shape changes allowed the 'animal' to harness some fluid energy from its environment and to propel itself up or down in the water column, or to keep itself from sinking.

The mathematicians imagined a creature with a symmetrical body suspended in a flow that oscillates up and down, similar to the flow underneath a wave. They allowed the creature to change its shape to become more or less flattened – ranging from a sphere to a pancake. By solving the equations of fluid motion around the animal, they were able to see what might happen when it synchronized its shape changes at various times in the oscillating flow.

The results showed a behavior the researchers called a 'fluid ratchet'. If the beastie flattened into a pancake while the fluid moved up, it could ride that wave upwards. Then, if it squished into a ball as the fluid moved down, it could avoid being pushed back down too far. Surprisingly enough, after several pancake–ball cycles, the animal's wake came to resemble that of a jellyfish, even though the simulated creature wasn't able to jet fluid out the way a jellyfish can.

Further work showed that the ratchet works better for denser animals. The body's density helps to smooth out the ratchet, resulting in higher average speeds and lower fluctuations; but there is a caveat. Higher density is a problem if the creature is trying to use the ratchet to avoid sinking. Initially, the body's density helps to smooth the velocity, but after a while the gravitational force overcomes the ratchet and the animal sinks.

In the course of their simulations, Spagnolie and Shelley found another curious effect. Shape changes can also cause a velocity burst, which could be useful for escaping predators. If the creature is already moving, squishing the pancake into the sphere and on to something torpedo shaped reduces the drag force substantially, and results in a burst of speed – up to about 50% faster than the initial speed.

Although they show a number of interesting effects, the simulations do not address one key question: stability. The beastie was confined so that it could only move up and down. The researchers acknowledge that they do not know whether the fluid ratchet would be possible for a real animal that can move in any direction. Would the vortex shedding cause the animal to tumble, rather than moving steadily up or down? How would turbulence affect the movement? These are questions for future studies, but it might be that small, squishy animals can navigate their environments better than we once thought.

10.1242/jeb.021543

Spagnolie, S. E. and Shelley, M. J. (2009). Shape-changing bodies in fluid: Hovering, ratcheting, and bursting. *Phys. Fluids* **21**, 013103, doi:10.1063/1.3054143.

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THERMAL STRESS

GLOBAL WARMING COULD CANCEL ‘JOURNEY OF A THOUSAND MILES’

Pacific salmon – among the ‘elite’ athletes of the sea – hatch in rivers, spend their adult years in the ocean, and then make one last incredible journey up-river to reproduce in their natal streams. This final trek, or spawning run, returns 10 million salmon to North American west coast rivers annually where, for up to 1000 km, they encounter turbulent currents, narrow deep gorges (particularly the Fraser River’s appropriately named Hell’s Gate) and fluctuating temperatures. However, humans may have created a new hurdle that salmon may not be able to overcome. Tony Farrell and his colleagues in Canada suggest that increasing river temperatures profoundly affect the salmon’s athletic capacity, and are largely responsible for salmon vanishing from their migration routes.

Farrell’s team wondered why some salmon populations seemed to be more affected by temperature than others, and so they compared ‘aerobic scope’ between several populations. Aerobic scope is the range of swimming speeds that a fish can sustain before resorting to quick bursts of anaerobic exercise (not requiring oxygen) or suffering complete cardiovascular failure. As expected, athletic fish would possess a greater aerobic scope than couch potatoes. Furthermore, there is a swimming intensity within this range where the fish’s body captures and delivers oxygen to the animal’s working muscles most efficiently. Because oxygen capture and delivery is a temperature-sensitive process, it makes sense to understand how temperature influences aerobic scope.

The team collected salmon at various points along the Fraser River migration routes and determined their aerobic scope by testing how long the fish could swim at various temperatures and speeds before becoming exhausted. They found that some populations swam most efficiently in warm waters while others swam best at cooler temperatures. The team also noticed that when a wide range of temperatures are available, the salmon opted to swim predominantly at temperatures where they are physiologically most efficient and have the greatest aerobic scope.

To understand how efficiently salmon were exercising in the wild, the next step was to determine temperatures along the spawning routes. Farrell’s group equipped some of the migrating fish with tracking devices to monitor their locations and nearby water conditions, and then compared the present day temperatures to historic temperatures. The team discovered that current river temperatures are higher than have been recorded in 50 years! Rising river temperatures mean that some populations are forced to swim at temperatures near the boundaries of their aerobic scope, resulting in enormous energy expenditure. Essentially, migrating salmon are exercising at physiologically inefficient and potentially life-threatening temperatures.

As if the fish don’t have enough difficulties in hot water, temperature also signals when the fish should begin migrating. Unfortunately, increasing temperatures have confused fish into hurrying or delaying their journey, usually resulting in death before they reach their spawning grounds. However, the researchers in Canada did report one optimistic discovery. Some populations were observed ‘out-smarting’ thermal barriers, waiting in deep cooler tributaries or lakes until the river temperatures became safe for them to enter. Ultimately, this waiting strategy increases migration success and guarantees a next generation, but is only a short-term fix to the global problem. Farrell’s group concludes that temperature is the key to successful salmon migration, and suspects that global climate change may lead to the disappearance of the entire species if the thermal barriers that we have created prevent their epic journey home.

10.1242/jeb.023804

Farrell, A. P., Hinch, S. G., Cooke, S. J., Patterson, D. A., Crossin, G. T., Lapointe, M. and Mathes, M. T. (2008). Pacific salmon in hot water: applying aerobic scope models and biotelemetry to predict the success of spawning migrations. *Physiol. Biochem. Zool.* **81**, 697-709.

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DIVING PHYSIOLOGY

RISING TO THE CHALLENGE OF DIVING SEALS

Since the initial studies by Irving and Scholander in the 1940s, the focus of research on diving in marine animals has been on the classical ‘dive response’. This reflex serves to conserve oxygen by lowering heart rate and decreasing peripheral blood flow to preserve stored O_2 for the brain, heart, and lungs, the tissues considered most vulnerable to oxygen deprivation (hypoxia). Low blood flow also cools tissues and thus decreases energy demand, which coupled with typically high blood and tissue oxygen stores was thought to explain how diving marine mammals and birds can remain submerged for (in some cases) over an hour. But Lars Folkow and his colleagues at the University of Tromsø, Norway, still wondered how seals not only survive extended dives but also remain alert when blood oxygen levels drop so low that they would cause unconsciousness and neural damage in non-divers. They hypothesized that, like neonate mammals and anoxia-tolerant turtles, the brains of diving marine mammals are intrinsically resistant to low oxygen levels. Falkow knew they would have to measure brain electrical activity to find out how the tissue copes with low oxygen levels, but how could they set about doing electrophysiology studies on diving seals?

The team gained access to hooded seal brains while on a research cruise to the Greenland Sea and were able to investigate how the tissue responded to low oxygen levels, like those the seal brain experiences during a dive. Slicing the brains into thin sections and maintaining them under oxygenated warm artificial cerebrospinal fluid, the team then exposed the brain samples to severe hypoxia by bubbling 95% nitrogen through the fluid for 1 h. This rapidly reduced the O_2 tension to less than 2% at the surface of the cortical slices, and to undetectable levels midway through the slice. They also tried similar studies (on land!) on adult and neonatal mice. Adult mice die rapidly when exposed to severe hypoxia, and thus served as controls for 'typical' brain responses. Neonate mammals, by contrast, are relatively resistant to low oxygen, and these thus served as controls demonstrating hypoxia tolerance.

The investigators found that while the neuronal resting membrane potential was similar in all three animals, hypoxia caused a slight depolarization (about 13 mV in seals) and a depolarization of 21 to 26 mV in neonate mice during a 5 to 10 min hypoxic exposure. Thus the seals and newborn mice brains were relatively unaffected by the oxygen depletion, although the seals were better protected than the baby mice. By contrast, adult mouse neurons completely depolarized (65 mV) over 10 min hypoxia, and ceased to discharge at all within 5 min, showing that hypoxia is indeed fatal for the adult mouse brain tissue. In hooded seals and neonate mice, though, at least some neurons were still firing after 60 min hypoxia.

The investigators conclude that the neurons of the hooded seal, at least, are indeed highly hypoxia- tolerant. This tolerance is presumably due to the existence of similar energy-conserving pathways to those that have been well studied in the anoxia-tolerant turtle, such as reductions in ion flux, though the group points out that, unlike hibernating turtles, diving seals must remain alert and thus cannot completely suppress brain activity. The authors suggest that the seals perhaps employ selective hypometabolism, shutting down some sections of the brain while others remain alert. Simultaneous work and sleep, what a great idea!

10.1242/jeb.021584

Folkow, L. P., Ramirez, J. M., Ludvigsen, S., Ramirez, N. and Blix, A. S. (2008). Remarkable neuronal hypoxia tolerance in the deep-diving adult hooded seal (*Cystophora cristata*). *Neurosci. Lett.* **446**, 147-150.

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RECOVERING FROM HYPOXIA IS HARDER IN OLD FLIES

Biological research now benefits from a multitude of high throughput and large-scale data gathering technologies, which together have created the current 'omics' era. These tools and approaches are often used in isolation, but fields of research such as systems biology emerged to integrate all of this information. A recent study published in *Molecular Systems Biology* presents an impressive combination of these approaches, including genomics, metabolomics, metabolic flux modeling and whole-animal experiments; a rather daunting task! Laurence Coquin, Jacob Feala and their coworkers from the Burnham Institute and the Department of Bioengineering at the University of California San Diego used this approach to study aging in the fruit fly, focusing primarily on the effect of aging on the insect's ability to recover from hypoxic stress, a common problem in animals.

The study began by exposing two groups of flies, 3 day and 40 day old, to very low oxygen for several hours. The flies were knocked out by the severe hypoxia. The team looked at the insect's heart rate during recovery and the time it took the insects to recover and start moving again. Before, during and after the hypoxic exposure, the team measured the levels of ATP, glycogen, glucose and trehalose in the thoraxes of these flies. They also used a metabolomics approach, where they simultaneously measured the levels of 26 metabolites by proton NMR. Next, the team used available microarray data, which provides snapshots of gene expression patterns, and combined this information with a biochemical pathway database to produce a metabolic reconstruction of the thorax. Together these approaches allowed the team to pinpoint the metabolic differences between the young and old flies.

Scrutinising the metabolic results, Coquin and colleagues found that there were no differences between the young and old fruitflies during hypoxia. However, there were differences between the two age groups during their recoveries.

The young flies recovered much more quickly following a hypoxic stress. Young flies exposed to severe hypoxia for several hours recovered after approximately 30 min, while the old flies only start moving 4 h after hypoxia. Heart rate measurements during the recovery period also showed that young flies' hearts restarted beating during the first minute after oxygen was restored, while it took several minutes for the old flies' hearts to resume beating.

At the cellular level, the ATP concentration in the young flies' thoraxes was severalfold higher than in the old flies after recovery. The elderly flies' lower thorax ATP levels were also accompanied by lower levels of glycogen and trehalose, which are the main sources of fuel used to produce ATP. Monitoring the levels of anaerobic end-products generated as the flies switched to anaerobic metabolism during hypoxia, the team found that the two groups of flies accumulated anaerobic end-products to the same extent, but the old flies continued to accumulate one of the anaerobic end-products, acetate, during recovery. It was also clear from metabolic flux modelling that the old flies did not oxidise pyruvate, the main substrate used by mitochondria to produce ATP aerobically, as quickly as young flies. The pyruvate substrate was redirected towards the production of acetate, which is a much less efficient and anaerobic way to produce ATP.

The team showed that aging does not affect all aspects of cellular metabolism equally, with elderly flies taking longer to recover than youngsters. Metabolic flux models show that mitochondrial metabolism is impaired in elderly flies, making them rely more on anaerobic metabolism during recovery. The era of omics is an exciting time for integrative physiology, and we can now put these tools together and link changes in gene expression with their functional consequences on metabolic pathways.

10.1242/jeb.021626

Coquin, L., Feala, J. D., McCulloch A. D. and Paternostro, G. (2008). Metabolomics and flux-balance analysis of age-related decline of hypoxia tolerance in *Drosophila* muscle tissue. *Mol. Syst. Biol.* 4:233, doi: 10.1038/msb.2008.71.

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