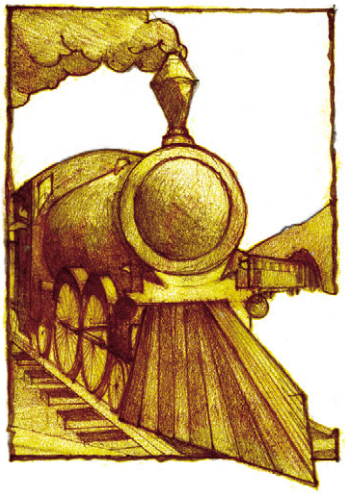
Keeping track of the literature isn't easy, so Outside JEB is a monthly feature that reports the most exciting developments in experimental biology. Short articles that have been selected and written by a team of active research scientists highlight the papers that JEB readers can't afford to miss.

Outside JEB

OCTOPUS ARM MOVEMENTS



AGILE ANIMALS

An octopus can be a canny customer – by shortening, bending, elongating and twisting its highly dexterous arms it can catch prey, build a shelter and even open jars. The dazzling array of delicate tasks that they can perform is well documented, but how exactly do they do it? Yoram Yekutieli and colleagues at the Hebrew University and Wiezmann Institute of Science in Israel built a series of octopus arm models to help answer how an octopus moves its arms and controls arm movement. The team wanted to find out if the control of the movements in an octopus' arm is as complicated as their dexterity suggests.

Octopuses have a dynamic skeleton called a muscular hydrostat, where all the muscles in the limb generate forces in different directions and provide skeletal support. Because the volume of the limb is always maintained, force can be transferred from one set of muscles to another. The range of movements is much greater than a limb made of bone and muscle, which is physically restricted in the range of movements it can make.

In the first of two papers, the team built a computer model to describe octopus arm reaching movements. The computer arm was divided up into 20 segments with a constant volume, connected to each other by virtual muscles. The model took into account the forces acting on the arm both internally and externally, including muscle force, gravity and drag. When a live octopus reaches for an object, a bend is created in its arm, usually near the base, which then travels up the arm towards the tip. This is likely to be caused by a wave of muscle activation that propels the bend to the end of the arm. Rather than contracting different sets of muscles out of phase with each other to produce a bend, the team's model suggests that all the muscles in an arm section are activated simultaneously to move the bend along the arm.

In the second paper, the team refined the model to investigate the neural signal that causes arm movements and how these movements are coordinated. When the team tested the model with a simple neural signal that caused all of the muscles along the arm to contract, the model arm produced a movement very similar to that of a real octopus arm. They found that by controlling the signal amplitude (i.e. its height) and velocity along the arm, they could make their model re-enact the movements of a real arm. Above a minimum threshold level at which muscles would contract, the team discovered that further increases in the signal amplitude increased the force in the muscles but did not change the kinematics of the model arm's movement. These increased muscle forces mean that the arm is more stable in the face of external forces that could knock it off course.

The model indicates that the control of octopus arm movement is very simple and robust and doesn't require complex coordination between different sets of muscles; a simple signal that causes all the muscles to contract can reproduce natural octopus arm movements. Understanding how an octopus produces different movements might aid the design of control systems for flexible robotic arms that need to perform a wide range of octopus-like movements.

10.1242/jeb.01887

Yekutieli, Y., Sagiv-Zohar, R., Aharonov, R., Engel, Y., Hochner, B. and Flash, T. (2005). Dynamic model of the octopus arm. I. Biomechanics of the octopus reaching movement. *J. Neurophysiol.* **94**, 1443-1458.
Yekutieli, Y., Sagiv-Zohar, R., Hochner, B. and Flash, T. (2005). Dynamic model of the octopus arm. II. Control of reaching movements. *J. Neurophysiol.* **94**, 1459-1468.

Laura Blackburn
University of Cambridge
lmlb2@cam.ac.uk

GLIDING PERFORMANCE

FLYING LIZARDS FALL FAST

A 'flying' lizard doesn't actually fly, it glides, which means that the power involved in remaining aloft comes from the animal's potential energy (how high it is, and how much it weighs). Sure, a little work is generally done by limb muscles to initiate a glide or control the shape and position of the aerodynamically active patagial membranes, or 'wings', but essentially, gravity is the ingredient fueling a flying lizard's aerial activities. In Malaysia, Borneo and Sumatra, species of the flying lizard genus *Draco* can range in body mass over an order of magnitude, and some of the greatest instances of size disparity are seen among sympatric species whose microhabitats overlap. In a recently published paper, J. A. McGuire and R. Dudley test whether size impacts gliding performance in *Draco* lizards and explore how this might relate to the ecology of these fascinating animals.

To conduct gliding performance trials, McGuire and Dudley persuaded lizards from 11 different *Draco* species to glide 9 m between two poles, 4–6 m in height. They allowed the lizards to climb to the top of the takeoff pole and then used a long bamboo rod to encourage the animals to glide to the landing pole. McGuire and Dudley recorded the animals' glides on video at 60 fields s^{-1}, digitized the videos and produced two-dimensional plots of each glide trajectory. They determined three measures of performance for each trial: (1) maximum velocity, (2) total height lost over the distance between poles and (3) total glide angle, which is the angle between the point of takeoff and point of landing (or projected intersection with the landing pole), relative to the horizontal. To explore possible correlations between the animals' body size and performance variables, the pair sacrificed the animals and took morphological measures.

McGuire and Dudley's morphological analyses revealed that larger animals have higher wing loading (more weight is supported by a given area of patagial membrane), which suggests that larger lizards should be less effective gliders than small ones. Indeed, the pair found a positive correlation between wing loading and total height lost during an animal's best glide; larger lizards lose more height, and thus have larger glide angles, than their smaller congeners. Finally, they noticed that performance variation decreases with increased wing loading. For example, large lizards consistently lose nearly 5.5 m in height over a 9 m horizontal glide distance, whereas small lizards lose anywhere from 2.6 to 5.5 m. Such results suggest that smaller lizards have the capacity to glide well – i.e. lose little height – yet have the flexibility to not have to do so. By contrast, large lizards always glide relatively poorly but are probably trying to maximize performance, nevertheless, because they have little margin for error.

What do the authors think this all means for flying lizards? Given their greater height losses during a glide, bigger animals are not as likely to utilize the lower parts of trees, implying a lower capacity for niche exploitation. In fact, 6 m would seem to be the minimum height from which a large lizard could successfully glide to a tree 9 m away, a typical distance in the forests these lizards inhabit. Clearly, bigger is not always better.

10.1242/jeb.01888

McGuire, J. A. and Dudley, R. (2005). The cost of living large: comparative gliding performance in flying lizards (Agamidae: *Draco*). *Am. Nat.* **166**, 93-106.

Gary B. Gillis
Mount Holyoke College
ggillis@mtholyoke.edu

PARKINSON'S DISEASE

MOVING WITHOUT DOPAMINE

Parkinson's disease (PD), a condition characterized by muscle stiffness and uncontrollable shaking, is caused by the progressive degeneration of midbrain neurons that control motor function. These neurons produce the neurotransmitter dopamine (DA), which has long been associated with motor function. As the neurons deteriorate, dopamine levels plummet, eventually leading to the symptoms of this debilitating disease. To understand the pathological processes leading to PD, researchers have developed rodent models that either recapitulate the loss of DA or recapitulate the neurodegenerative process. But many of these models only achieve incomplete DA depletion, often precluding an accurate recapitulation of the neurological manifestations of PD. Now, Tatyana Sotnikova and colleagues have successfully induced a reliable but transient recapitulation of PD symptoms in mice.

Normally, neurons have a large intracellular storage pool of DA. After its release, DA is rapidly recycled back into neurons' dopaminergic terminals by the dopamine transporter (DAT). To create their new PD model, the team knocked out the dopamine transporter in a group of mice, creating DAT-KO mice that have virtually no intracellular DA stores. Unlike normal mice, which have plenty of dopamine in storage, DAT-KO mice depend upon the DA produced by ongoing synthesis. So, by blocking DA synthesis in these mice, the team could now eliminate all DA in these animals. When they administered the DA synthesis inhibitor αMT to the DAT-KO mice, the animals immediately showed reliable symptoms of PD; they became immobile and displayed extreme rigidity, body tremors and droopy eyelids.

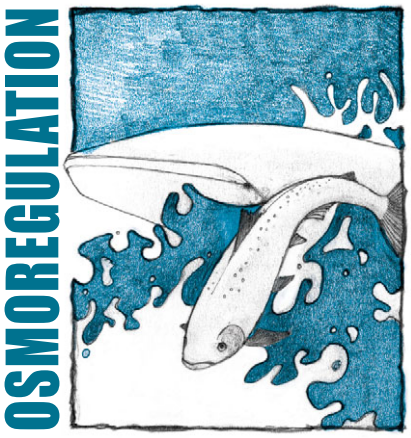
Now that the team had successfully created a mouse model of PD, they set out to identify drugs that could relieve the symptoms of PD. They first tested the effects of administering L-DOPA, a DA precursor that is commonly given to PD patients, to DAT-KO mice. They discovered that L-DOPA is just as effective in mice as it is in humans in the early stages of PD; the drug successfully restored locomotion in DAT-KO mice. Testing several amphetamine derivatives, the authors discovered that MDMA (better known as ecstasy) also restored movement control sufficiently to allow the mice to move forwards. Since amphetamines are thought to act through the dopamine system to affect movement, this was a surprising result, because the team was unable to detect measurable DA levels in the midbrain neurons of these mice. They conclude that ecstasy must be acting through an unknown DA-independent mechanism. When the team paired a lower dose of ecstasy with a minimally effective L-DOPA dose, a synergistic effect occurred: it caused the same effect as a higher dose of either ecstasy or L-DOPA alone. Thus, the DA-independent locomotor effect of ecstasy can be markedly enhanced with additional DA stimulation.

It is currently unclear how this synergistic effect occurs, but amphetamines can clearly affect neuronal systems involved in motor control through mechanisms independent of dopamine. Amphetamines interact with proteins called trace amine receptors, and the authors suggest this interaction as a possible mechanism. Since very little is known about the physiological role of these receptors, more research is needed to delineate the DA-independent mechanism of amphetamines in locomotion. But in the search for new treatments for Parkinson's disease, this study certainly offers a glimmer of hope.

10.1242/jeb.01890

Sotnikova, T. D., Beaulieu, J.-M., Barak, L. S., Wetsel, W. C., Caron, M. G. and Gainetdinov, R. R. (2005). Dopamine-independent locomotor actions of amphetamines in a novel acute mouse model of Parkinson disease. *PLoS Biol.* **3**, e271.

Susan Sangha
Otto-von-Guericke Universitaet Magdeburg
susan.sangha@medizin.uni-magdeburg.de



FISH OSMOREGULATE WITH OUABAIN

Ouabain, a potent inhibitor of the enzyme Na^+/K^+-ATPase, is known to be a steroid hormone in mammals that is involved in blood pressure and volume regulation. Recently, a group from the University of Hawaii examined whether ouabain also acts as a hormone in fish and reported that ouabain is present in the plasma and various tissues of the euryhaline Mozambique tilapia, *Oreochromis mossambicus*. When the researchers transferred tilapia between fresh and salty water, they discovered that changes in plasma concentrations of ouabain in tilapia were well correlated with changes in plasma osmolality and cortisol, an important hormone during salinity change. Now, this same research group has followed up with an equally intriguing analysis of the functional role of ouabain in fish osmoregulation.

The present study set out to establish whether ouabain interacts with growth hormone and prolactin (known osmoregulatory hormones in fish) in the same manner as cortisol. During seawater acclimation, cortisol stimulates Na^+/K^+-ATPase activity and the proliferation of chloride cells that are responsible for the active extrusion of Cl^-. In addition, cortisol stimulates the release of growth hormone, which is also involved in seawater adaptation, and inhibits the release of prolactin, an important hormone in freshwater osmoregulation, from the pituitary gland. Prolactin release is dependent on calcium entering pituitary gland cells and the synthesis of cAMP, both of which are prevented by cortisol.

To assess the role of ouabain in fish osmoregulation, Kajimura, Grau and the group examined the release of osmoregulatory hormones by tilapia pituitary glands. They isolated whole pituitary glands from tilapia and placed them individually in a 96-well plate containing 200 μl of incubation media. With this *in vitro* preparation, they measured prolactin and growth hormone release from tilapia pituitary glands in response to different doses of ouabain. To see if ouabain, like cortisol, inhibits prolactin release by preventing calcium uptake and cAMP synthesis, they measured prolactin release in response to calcium (using the calcium ionophore A23187) and to cAMP (using the analogue dbcAMP and the phosphodiesterase inhibitor IBMX) in the presence or absence of ouabain. The group found that at physiological concentrations, ouabain exerted a dose-dependent inhibitory effect on prolactin, whereas supra-physiological doses of ouabain stimulated prolactin release. By contrast, ouabain stimulated growth hormone release at lower concentrations but had an inhibitory effect at higher levels. Both A23187 and dbcAMP + IBMX had stimulatory effects on prolactin release, and these effects were inhibited by ouabain when it was also placed in the incubation media. This suggests that, like cortisol, ouabain regulates the mechanism of prolactin release. Furthermore, using microspectrofluorometry and a calcium-sensitive dye, the team was able to quantify 'real-time' changes in calcium levels within pituitary cells. Their data indicated that at physiological concentrations, ouabain rapidly reduces intracellular calcium concentrations, just as cortisol does.

The group has shown convincingly that, similar to the actions of cortisol during salinity change, ouabain plays an important role in fish osmoregulation by inhibiting the release of prolactin *via* the Ca^{2+} and cAMP signal transduction pathways. The team believes that ouabain in the hypothalamus of the brain may be involved in the regulation of pituitary prolactin release and hope to prove this hypothesis in the future by using a ouabain-specific antibody and immunocytochemistry. Until then, we will wait for more news about this exciting new fish hormone!

10.1242/jeb.01889

Kajimura, S., Seale, A. P., Hirano, R., Cooke, I. M. and Grau, E. G. (2005). Physiological concentrations of ouabain rapidly inhibit prolactin release from the tilapia pituitary. *Gen. Comp. Endocrinol.* **143**, 240-250.

M. Danielle McDonald
RSMAS, University of Miami
dmcdonald@rsmas.miami.edu