catalytic (kinase) domain abuts a 'regulatory interface' (formed from the carboxy-terminal domains of the α- and β-subunits), with its substrate-binding site facing away from the rest of the complex (Fig. 1a). The activation loop, which houses T172, is well resolved in the structure, and interacts with the regulatory interface; this would restrict the access of phosphatases to phosphorylated T172 (Fig. 1b).

Xiao and colleagues' structure also provides an elegant explanation for how AMP binding to site 3 prevents T172 dephosphorylation. In the α-subunit, a long linker peptide that connects the catalytic and carboxy-terminal domains includes a structure termed the α-hook; residues at the tip of the hook interact with AMP in site 3 (Fig. 1a). The authors propose that a favourable interaction between the α-hook and AMP (or ADP) in site 3 stabilizes the binding of the catalytic domain to the regulatory interface, thus blocking phosphatase access to T172. They also suggest that, when ATP is bound, this interaction would be disrupted, causing the catalytic domain to dissociate from the regulatory interface and exposing T172 for dephosphorylation. Their biochemical analysis supports this model.

Naturally, puzzles remain. For instance, the structure provides no clues to how AMP binding to site 1 might allosterically activate the catalytic domain. It has been proposed[8] that this involves the auto-inhibitory domain (AID, residues 305–330), which follows the catalytic domain on the α-subunit. In the new structure no residues of the AID were resolved, suggesting that it was unfolded and mobile. Although it is possible that the AID folds up when AMP binds to site 1, they are quite remote from each other (Fig. 1b), making it difficult to see how the two events would be connected. What's more, a previously proposed idea[9] that AMP promotes phosphate attachment to — as well as inhibiting phosphate removal from — T172 was recently resurrected[10]. The new structure gives no indication of how this might happen.

Perhaps the most interesting finding of the paper[2] is that ADP prevents phosphate removal, which seems likely to be of physiological relevance. Normally, cellular concentrations of AMP are much lower than those of ADP, except in situations of severe energy deficit. During mild energy stress, displacement of ATP by ADP at site 3 would activate AMPK by preventing phosphate removal from T172; the allosteric effect of AMP binding at site 1, however, would amplify this response during more severe stress. This dual mechanism would allow AMPK to sense energy deficit progressively over a wide range of energy availability. ■

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BIOMECHANICS

# Swimming in the Sahara

**The sandfish, a type of desert lizard, can vanish into a sandy substrate in a blink of an eye. Approaches that draw on mathematics, physics and engineering provide complementary insights into how the animal achieves this feat.**

STEPHANIE B. CROFTS & ADAM P. SUMMERS

Biomechanists, with help from Isaac Newton and William Froude, have developed a good understanding of the forces involved in locomotion on solid ground[1]. Even if an animal should slip beneath the waves and undulate into the deep there are equations and techniques, courtesy of Claude-Louis Navier, George Stokes and computational fluid dynamics, that nicely explain and predict its motion[2].

However, when an animal moves through a granular material, predictability and theoretical underpinning have been as elusive as seeing a world in a grain of sand. In a paper in the *Journal of the Royal Society Interface*, Maladen and his colleagues[3] describe how they have used a refinement of their resistive force theory to show that a sand-swimming lizard moves forward about as fast as it can. Their model will allow biologists and engineers to explore locomotion in granular solids with unprecedented ease and speed.

Sandfish (*Scincus scincus*), also known as skinks, are not fish but lizards. They are drab, tan-coloured creatures with short, sprawling limbs. But they have one impressive ability —when startled, a sandfish can vanish completely into a North African or Middle Eastern dune in less than a second (Fig. 1). If you dig at the spot where it vanished you will find nothing but sand, the lizard having wriggled away under the surface.

In earlier work using X-ray videography, Maladen and colleagues[4] found that sandfish move not by paddling with their legs but by undulating their bodies from side-to-side to swim through the sand. The sandfish throws its body into an S-shape with an amplitude of about 20% of its length. This sinusoidal wave travels backwards along the body at about twice the speed with which the animal moves forward, amounting to a wave efficiency of about 0.5. In their new work, the researchers used this conclusion as a benchmark for further studies with simulations, mathematical models and a robotic lizard.

The behaviour of a granular material such as sand is tricky to understand because it can act as both a solid and a fluid. The many small particles can flow like water but, under the right conditions, sand can be as unyielding as the rock from which it came. This is where resistive force theory (RFT) comes in.

The theory was inspired by models of tiny aquatic organisms moving in water, where movement is constrained by the viscosity of the fluid. In granular materials, however, it turns out that frictional drag is more important than viscosity, and drag values for short segments of the submerged object are an important input of RFT. One innovation of this work[3] is the use of drag values derived from simulations rather than those laboriously gathered by pulling objects through media of differing density. Using the simulation-derived drag values and kinematics measured from videos, Maladen *et al.*[3] found that RFT predicted the wave efficiency reasonably well, although not perfectly.

D. HEUCLIN/NHPA

**Figure 1 | Going, going, almost gone.** *Scincus scincus* dives head first into the sand.

An alternative to RFT is a numerical modelling technique that takes into account the interactions of spherical grains with each other and with a deforming, submerged solid shaped like a sandfish. However, simulating sand-sized particles would take weeks of computer time. Fortunately, sandfish are happy to burrow in glass beads 3 millimetres in diameter. By observing the lizards moving through the beads, and then using the larger particle size in the simulations, Maladen *et al.* cut computing time to 'mere' days. The agreement between the simulation and the lizards' performance was better than that derived by RFT, but the procedure was much more time-consuming.

The advantage of both the RFT and numerical modelling techniques is that parameters can be varied to explore patterns and seek optima. Initially, the most striking result was the finding that wave efficiency continues to rise as the animal's body is thrown into higher-amplitude waves. But these sharp bends mean that the sandfish covers less forward distance with each undulation. When the forward speed was plotted against the ratio of amplitude to wavelength, the peak speeds occurred at ratios ranging from 0.19 to 0.27 for the various simulations. The authors found that the data collected from actual lizard performance lie at this same peak. Thus, it seems that when fleeing from a potential predator, kinematic efficiency takes a back seat to a speedy retreat.

Designing a biomimetic robot teaches you as much about biology as it does about engineering[5,6]. In this case, Maladen and colleagues[3] used a sand-swimming robot to determine whether the theory, and the practice as demonstrated by the lizard itself, could be translated into the realm of engineering. The robot consisted of six connected segments, powered by servos, packed in a latex sock and wrapped in a spandex swimsuit.

The researchers showed that the robot is able to swim in granular media at similar speeds to those observed in the other models and in live organisms, but at efficiencies 30% below the predicted maximum. By simulating the segmented robot in the numerical model, they determined that this discrepancy in performance was due to the robot's low number of intersegmental joints. It was not until the researchers used more than 15 segments, creating a robot capable of forming a smoother curve, that wave efficiency approached a maximum. Perhaps the reason that many sand swimmers are elongate, smooth-bodied and small-limbed, with many vertebrae, is to better fall into a curve without the sharp bends that sap energy. ■

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SPECTROSCOPY

# A closer look at polymer annealing

**Solvent vapour annealing processes are used to optimize the material properties of thin films of semiconducting polymers used in electronic devices. One such process has now been examined at the molecular level.**

YI FU & JOSEPH R. LAKOWICZ

Single-molecule spectroscopy and microscopy (SMS) techniques have had a tremendous impact in biophysics — in studies of the motion of individual protein molecules, for example. SMS techniques are also suitable for investigating the underlying heterogeneity in complex liquids and solids, such as that associated with different molecular conformations, and for directly observing dynamic changes in materials at the molecular level. Polymeric materials would therefore seem a natural fit for single-molecule studies, as they are, by definition, structurally heterogeneous. Yet SMS has so far not been widely used in polymer science, apart from in studies of certain fluorescent polymers[1–4].

Reporting in *Angewandte Chemie*, Vogelsang *et al.*[5] now describe the use of SMS techniques to reveal the conformational dynamics of single polymer chains during solvent vapour annealing (SVA) — an industrially important process in which the exposure of polymer films to solvent vapour enables the polymer molecules to reach conformational equilibrium, thus optimizing the films' useful properties. An understanding of SVA at the molecular level should lead to improvements in this widely used process.

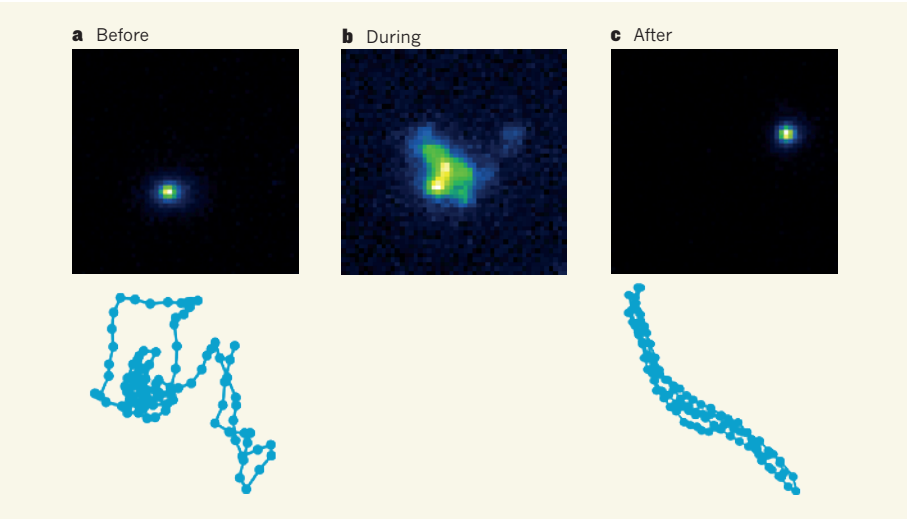


**Figure 1 | Monitoring single polymeric chains.** Vogelsang *et al.*[5] have used single-molecule spectroscopy and microscopy to study the conformational changes of individual MEH-PPV polymer molecules isolated in a thin film of PMMA (another polymer) before, during and after solvent vapour annealing. Each of the panels **a** to **c** shows accumulated images, taken over 60 seconds, of the same MEH-PPV chain embedded within an 8×8-micrometre region of PMMA film. **a**, Before annealing, single MEH-PPV chains are visible as static fluorescent spots, which correspond to collapsed, disordered polymeric conformations (such as the structure shown beneath the fluorescence data). **b**, During annealing, the spots are mobile and the background fluorescence increases. Here, the fluorescent spot is extended and blurred because of the motion of the single chain as it moves from left to right. **c**, After annealing, static spots are again visible, but these now correspond to extended, highly ordered polymer conformations, such as the one shown. (Figure adapted from ref. 5.)