the top of the atmosphere of a planet or star.

The notion that the ratio δ_E/δ_T might determine the character and properties of rotating, stratified flows is not especially new. It was applied[4] in the 1980s to such problems as models of the circulation in the ocean thermocline, which is currently the subject of a controversy concerning Sandström's theorem on the nature and energetics of the thermohaline ocean circulation[5,6]. In that problem, the (highly turbulent) Ekman and thermal boundary layers play a clear role in the oceanic meridional circulation, so their importance in governing convective heat flow is not surprising.

In the convective problem considered by King *et al.*, however, it is less clear precisely what role the Ekman boundary layers play in the detailed transport of mass and heat. So the authors' results are all the more surprising and impressive. In the problems they have considered, however, heat enters or leaves the convecting region strictly by thermal conduction through the bounding walls, which is not exactly how heat is introduced or extracted in real planets or stars. So it remains to be seen to what extent their results can be applied to more general mechanisms for driving convection. ■

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SYNTHETIC BIOLOGY

The yin and yang of nature

Jeff Gore and Alexander van Oudenaarden

Oscillations in gene expression regulate various cellular processes and so must be robust and tunable. Interactions between both negative and positive feedback loops seem to ensure these features.

Periodic oscillations are the basis of timekeeping. For many millennia, the main timekeeper was the water clock, in which time is recorded by the regular dripping of water into or out of a basin. In the seventeenth century, the water clock was replaced by the pendulum clock, following Galileo's famous discovery that the period of a pendulum's swing is independent of the size of the swing. This clock offered a substantial improvement because pendulum oscillations are robust and the period can be altered by changing the length of the pendulum arm. As three papers[1–3] now indicate, similar improvements are occurring in our ability to generate increasingly robust and tunable oscillations in biological systems. On page 309 of this issue, Tigges *et al.*[1] demonstrate this feat in mammalian cells, and not long ago Stricker *et al.*[2] reported it in bacteria. These two advances are nicely complemented by Tsai and colleagues' recent detailed theoretical study[3], which elucidates the essential 'design principles' underlying oscillatory networks in nature.

The simplest way to generate oscillations is by negative feedback with a delay. We are probably all familiar with this phenomenon from our attempts to maintain the proper water temperature in the shower. Because of the delay inherent in the system, we often overshoot, leading to a sometimes comical oscillation between scalding and freezing temperatures. An early example of a synthetic biological oscillator was a network called the repressilator[4], in which three genes sequentially repressed one another. The three repressive interactions led to net negative feedback, with a delay due to the multiple biochemical processes involved in gene expression. The repressilator did indeed oscillate, but the oscillations were not robust. Only half of the cells had observable oscillations, and those oscillations that did occur were variable. Moreover, the repressilator is not tunable; changing the rate constants of the various reactions generally abolishes the oscillation rather than changing its frequency[3].

Nonetheless, both robustness and tunability are important features of an oscillatory system, whether it be a gene circuit or a clock. For example, despite slight variations in the individual components of a clock, the oscillation period must remain a precise number of seconds. Similarly, if the physical environment changes, it may be necessary to retune the system to compensate: moving a pendulum clock from the ground floor to the top floor of a tall building requires retuning the clock, to correct for the small change in the acceleration due to gravity.

In the recent set of papers[1–3], a common theme is that supplementing the core negative feedback circuit with a positive feedback loop can make the oscillations both robust and tunable. Stricker *et al.*[2] demonstrated this experimentally by implementing a simple transcriptional circuit in the bacterium *Escherichia coli*. Their oscillator was composed of two genes driven by the same hybrid promoter sequence: the gene encoding the LacI protein generated the core negative feedback loop to suppress transcription, whereas that encoding the AraC protein generated the positive feedback loop. The resulting oscillation period could be tuned between 13 and 100 minutes depending on the concentration of the molecules used to induce transcription and on the temperature of the system. This oscillator design was based on a previously published theoretical study[5], although the authors[2] found it necessary to explicitly model intermediate steps such as multimerization, translation and protein folding.

Tigges *et al.*[1] construct a tunable oscillator in mammalian cells — using sense/antisense logic — by supplementing a central time-delayed negative feedback loop with a positive feedback loop. Here, negative feedback was provided by post-transcriptional repression of the gene encoding tTA by antisense RNA, whereas positive feedback was present because tTA enhanced its own transcription. The authors could tune the oscillation period by varying the number of copies of the genes encoding components of the oscillator. Whether varying the concentration of transcription inducers, while keeping the copy number of genes constant, would allow tuning of the oscillation period remains an intriguing question.

In their theoretical study, Tsai *et al.*[3] computationally analysed many different network topologies that might lead to oscillations, and also concluded that a positive feedback loop is likely to be necessary for tunable oscillations. The authors pointed out that bioengineers are simply learning tricks discovered by evolution long ago. Many biological networks that drive oscillations of variable period (such as the cell cycle) have a positive feedback loop, in addition to the central negative feedback loop that is mainly responsible for generating the oscillation. Indeed, Tsai and colleagues found that such a positive feedback loop is present in many oscillatory networks that do not require tunability (such as the circadian rhythm that tracks the day–night cycle). A possible function of the extra feedback loop in these networks of fixed frequency could be to make the oscillations robust — that is, more resistant to changes in kinetic parameters — thus perhaps increasing the 'evolvability' of the oscillation.

Advances in generating biological oscillations are similar to those made in the seventeenth century that led to our widespread adoption of the pendulum clock. What advances lie in store for our ability to construct synthetic biological oscillations? In the latest experiments[1–3], the phase of the oscillations was partly passed on to daughter cells, although individual cells gradually lost their synchronization. For any coordinated action, it is desirable for the population to oscillate in phase, thus requiring some mode of cell-to-cell communication to synchronize oscillations. More generally, a way to entrain or pause the oscillations is often necessary. For example, circadian oscillations must be entrained by daylight, and the cell-cycle oscillation must be paused under low-nutrient conditions. Further advances combining theoretical modelling with experimental synthetic biology will both increase our understanding of natural networks and allow us to use the cell as a platform for future developments in biological engineering. ■

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CONDENSED-MATTER PHYSICS

Going with the flow

Jonathan Keeling and Natalia G. Berloff

Observations of superfluid behaviour — flow without friction — of unusual character in a condensed-matter system pave the way to investigations of superfluidity in systems that are out of thermal equilibrium.

When in 1937 liquid helium was first observed to flow with negligible viscosity through a narrow gap, it was clear that, at low temperatures, helium was different from ordinary fluids. This prompted Pyotr Kapitza to name the phenomenon superfluidity[1] by analogy with superconductivity. Since then, experiments on liquid helium and cold atoms have revealed other aspects of superfluidity (Table 1), including quantized vortices, undisturbed flow past an obstacle (for example, a structural defect), and (metastable) persistent flow in a doughnut-shaped geometry.

Experiments by Amo *et al.*[2], reported on page 291 of this issue, reveal a new variety of dissipationless flow in semiconductor microcavity polaritons — entities comprising both matter and light. The properties of the polariton fluid demonstrated by Amo *et al.* have their origin in the way polariton–polariton interactions modify the propagation of these quasiparticles, preventing scattering from structural defects in the microcavity. The question of how the finite lifetime of polaritons distinguishes these systems from previous examples of superfluidity provokes questions about the relationships between different aspects of superfluidity[3].

The system studied by Amo *et al.* is a semiconductor microcavity, consisting of a pair of mirrors (built from layers of semiconductors with alternating refractive indices) and a semiconductor quantum well, placed between these mirrors. The quantum well confines excitons (electronic excitations in the semiconductor) and the mirrors confine light. Because excitons can recombine and emit light, and light can create new excitons, repeated interconversion leads to new quasiparticles: microcavity polaritons[4,5]. These quasiparticles inherit properties from both of their constituents: from light comes their very small effective mass (about 0.0001 that of the electron); from the exciton come the polariton–polariton interactions.

Polaritons also have properties that neither of their constituents has alone. Crucially for

Table 1 | Superfluidity checklist

	Quantized vortices	Landau critical velocity	Metastable persistent flow	Two-fluid hydrodynamics	Local thermal equilibrium	Solitary waves
Superfluid ^{4}He/cold atom Bose–Einstein condensate	✓	✓	✓	✓	✓	✓
Non-interacting Bose–Einstein condensate	✓	X	X	X	✓	X
Classical irrotational fluid	X	✓	X	✓	✓	✓
Incoherently pumped polariton condensates	✓	X	?	?	X	?
Parametrically pumped polariton condensates	?	✓	?	?	X	✓

Aspects of superfluid-like behaviour that have been demonstrated (ticks), shown not to exist (crosses), or remain to be verified (question marks) in different condensed-matter systems. Amo *et al.*[2] add a new system (red) to the table.

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50 & 100 YEARS AGO

50 YEARS AGO

In 1949 it was found that water applied to the tongue of the frog elicited an electrical response from the glossopharyngeal nerve. This response was produced by specific fibres. It was first thought that these 'water' fibres might serve a particular purpose in water regulation in amphibians living in fresh water. These findings also revived the old problem of whether warm-blooded animals and man possess similar specific taste fibres mediating what we might call a water taste. The late Prof. David Katz of Stockholm, who believed this to be the case, often asked in his examinations: What is the taste of water? The correct answer was 'wet' ... It seems to us most likely that water does not elicit any positive taste sensation. The action must be of negative character in that water abolishes or decreases the resting activity of taste fibres ... The specific effect of water on taste in man can thus be looked upon as being of the same nature as that of blackness upon vision.

ALSO:

The world low air temperature record of −102.1 °F at the South Pole ... was exceeded in the polar night of 1958 at the Russian International Geophysical Year Antarctic stations Sovetskaya and Vostok. The Sovetskaya station recorded −86.7 °C (−124.1 °F) between 1900 and 2000 L.M.T. on August 9.
From *Nature* 17 January 1959.

100 YEARS AGO

At the recent conference on the conservation of resources which met at the White House at the invitation of the President of the United States, notes of warning were sounded concerning the coming exhaustion of coal, wood, ores, and soils. Whether or not we accept as exact the estimates furnished by experts on that impressive occasion, there is no doubt that we are approaching the end of our available resources, and that the near future will have momentous problems to face.
From *Nature* 14 January 1909.