cancer indicates a similar scenario, whereby MET amplification and mutation in the T790 residue of EGFR coexist in patients and in cell lines that have never been exposed to EGFR-inhibitor drugs (J. Bean and W. Pao, personal communication). Together with another study[6] showing that some drug-resistant forms of the cancer-associated kinase BCR–ABL have enhanced oncogenicity, there is growing evidence that these drug-resistant proteins also have a role in tumour progression.

The most important implication of the work of Stommel *et al.*[3], which is yet to be clinically tested, is that a much larger spectrum of cancers, not just those with driver kinase mutations, might be sensitive to cocktails of kinase inhibitors if such mixtures are delivered in the right combination. But how will we recognize these multiple-kinase-dependent cancers? Borrowing from the approach used by Engelman *et al.*[2] and Stommel and colleagues[3] to uncover the RTK-switch phenomenon, one possibility is to look at the cellular profile of RTK activation in tumour biopsies, thereby distinguishing between single-kinase-dependent and multiple-kinase-dependent cancers.

Technologies for conducting extensive profiling of proteins that carry signs of kinase activity in tumour cells, such as mass spectrometry and antibody-based approaches, are readily accessible. So 'signatures' of RTK activation in tumour biopsies could complement information gained through analysis of gene mutation status — information that is currently used to define tumours with mutations in genes encoding kinases.

Preclinical strategies to estimate the fraction of multiple-kinase-dependent cancers might also be feasible using large panels of tumour-cell lines. Such high-throughput, cell-based screens are already gaining popularity as a tool to determine the relationship between genotype and response to single-drug inhibitors. But, within reason, they could be expanded to evaluate the genotype relationship with multiple-kinase inhibition.

The new findings[2,3] add fuel to the argument that, using rationally chosen combinations of kinase inhibitors, successful cancer treatment can be achieved. Prior to these reports, this view had originated from the knowledge that second-site kinase mutants are a principal cause of single-agent resistance in tumours with driver mutations in kinases. Therefore, second-generation compounds must be effective against these drug-resistant proteins and should be used in combinations that prevent the emergence of resistant subclones. A good example is the proposed combined use of the ABL-kinase-inhibitor drugs imatinib and dasatinib to treat chronic myeloid leukaemia[7–9]. The kinase-switching phenomenon reported by Engelman *et al.* and Stommel *et al.* requires a broader view that incorporates drugs that target relevant bystander RTKs. So, clearly, the cocktail menu will continue to grow, but the cocktails should be mixed with appropriate molecular guidance. ■

Charles L. Sawyers is at the Memorial Sloan-Kettering Cancer Center, Human Oncology and Pathogenesis Program, 1275 York Avenue, New York, New York 10065, USA.
e-mail: sawyersc@mskcc.org

1. Sawyers, C. L. *Genes Dev.* **17,** 2998–3010 (2003).
2. Engelman, J. A. *et al. Science* **316,** 1039–1043 (2007).
3. Stommel, J. M. *et al. Science* **318,** 287–290 (2007).
4. Pao, W. *et al. PLoS Med.* **2,** e73 (2005).
5. Michor, F. *et al. Nature* **435,** 1267–1270 (2005).
6. Skaggs, B. J. *et al. Proc. Natl Acad. Sci. USA* **103,** 19466–19471 (2006).
7. Shah, N. P. *et al. Cancer Cell* **2,** 117–125 (2002).
8. Shah, N. P. *et al. J. Clin. Invest.* **117,** 2562–2569 (2007).
9. Talpaz, M. *et al. N. Engl. J. Med.* **354,** 2531–2541 (2006).

POPULATION ECOLOGY

Group living and hungry lions

Tim Coulson

Ecologists have necessarily had to simplify matters in looking at predator–prey dynamics. Study of a situation in which predator and prey live in groups reveals that a key process was previously overlooked.

Eating is a necessity of animal life. So you might expect that individuals would do everything possible to maximize their food intake. An example, often invoked, is that lions live in prides because group hunting increases food availability by allowing the lions to kill prey that would be too large for an individual to tackle. On page 1041 of this issue, however, Fryxell *et al.*[1] argue that living in groups decreases the amount of food each lion eats. Moreover, that decrease is even more severe if the lions' prey is also gregarious. How can this be explained?

Many large predators live in groups, as is dramatically seen in the familiar TV programmes that show, for example, a pack of wild dogs running down an impala or a pod of killer whales attacking a shoal of herring. Many of the prey species of these top carnivores also live in groups (Fig. 1). But there has been surprisingly little research into how group living influences individual food-intake rates, and the dynamics of the populations of predators and their prey.

A concept called the functional response[2] lies at the heart of behavioural and population ecology, and of Fryxell and colleagues' paper. This is the curve that describes the intake rate of a single predator as a function of prey density. The shape of the curve is the result of two processes — the rate at which predators encounter prey and the speed with which they consume it[3]. Much of the theory investigating the consequences of different shapes of functional response has been developed following observations and experiments from systems where both predator and prey are solitary. These systems often show dynamics in which

G. HINDE/GALLO IMAGES/GETTY

Figure 1 | Group theory. Both the wildebeest and the lioness pictured here are gregarious animals, but Fryxell and colleagues[1] conclude that the group life of both species doubly diminishes the food intake of an individual lion.

the numbers of both predator and prey increase and decrease, sometimes leading to extinction of first prey and then predator. Altering the form of the functional response can, in some circumstances, prevent extinction[4].

Fryxell *et al.*[1] examine how group living in prey, in predators and in both kinds of species influences the shape of the functional response and the interaction between predator and prey populations. They show theoretically that gregarious living in either the prey or the predator species reduces the rate of prey consumption by each predator. Intake rates are lowest when both species live in groups. If prey lives singularly, an increase in the number of prey will lead to a linear increase in the likelihood that a predator will encounter a meal on its daily wanderings. However, if the prey forms clumps, there will be large holes in the landscape through which a predator can roam without finding something to eat. Group living in prey therefore decreases intake rate. When a predator does find a group of prey, it encounters an embarrassment of riches and quickly becomes satiated. The intake rate of predators is reduced if they live gregariously because each individual searches the same area and then has to share the prey that it kills.

Fryxell *et al.* primarily use data from surveys of lions preying on wildebeest in the Serengeti National Park, Tanzania, to reach their conclusions for a system where both predator and prey live gregariously. They show that the consequence of both species living in groups is a predicted reduction in the food-intake rate per lion of 90% compared with the rate when lions forage solitarily. This is an enormous amount, and is equivalent to the decrease in food availability that results if the migratory wildebeest is present in a lion-pride territory for only a fraction of each year. The authors also examine the consequence of such a large reduction in intake rate on the dynamics of the lion and wildebeest populations. They predict that, if both species shunned group living and wandered the plains singly, the dynamics of both populations would be highly unstable, with both predator and prey likely to become extinct. In contrast, if both predator and prey live in groups, it is much more likely that both their populations will persist.

But the question of why lions live in groups remains. Fryxell *et al.* argue that the benefits primarily accrue from territory defence and the communal protection of young against males that can kill cubs when they take over a pride[5,6]. However, an argument familiar to most ecologists is that lions live gregariously because group hunting is required to bring down large prey. Fryxell *et al.* accept that group hunting does allow lions to attack and kill the formidable Cape buffalo, but they also state that: "Most individual lions refrain from contributing to group hunts." This carefully worded statement does not rule out the possibility that substantial benefits arise from group hunting, and it flags one of the problems of parametrizing functional responses. It is challenging to work out individual intake rates accurately across different sizes of predator and prey groups for a range of prey densities, especially for species with such complex social arrangements as those seen in lions. I would be interested to know whether functional responses derived entirely from observations on the feeding of individual lions would yield similar conclusions to those obtained by Fryxell *et al.* using survey data.

This work[1] shows that extending the functional response to include some realistic natural history helps to explain why the inevitable extinction of predators and prey, predicted by some simple population models, is not observed in the wild. The paper will stimulate researchers who have obtained functional responses using detailed observational data on group-living predators. And it should encourage theoreticians to examine how other aspects of animal behaviour might affect the predictions derived from simple population models. ■

Tim Coulson is in the Department of Life Science, Silwood Park Campus, Imperial College London, Ascot, Berkshire SL5 7PY, UK.
e-mail: t.coulson@imperial.ac.uk

1. Fryxell, J. M., Mosser, A., Sinclair, A. R. E. & Packer, C. *Nature* **449,** 1041–1043 (2007).
2. Holling, C. S. *Can. Entomol.* **91,** 293–320 (1959).
3. Jeschke, J. M., Kopp, M. & Tollrian, R. *Ecol. Monogr.* **72,** 95–112 (2002).
4. Abrams, P. A. & Ginzburg, L. R. *Trends Ecol. Evol.* **15,** 337–341 (2000).
5. Schaller, G. B. *The Serengeti Lion: A Study of Predator-Prey Relations* (Univ. Chicago Press, 1976).
6. Packer, C., Scheel, D. & Pusey, A. E. *Am. Nat.* **136,** 1–19 (1990).

ATTOPHYSICS

At a glance

David M. Villeneuve

Measurements on the attosecond timescale had been limited to the dynamics of electrons in an atomic gas. But a record has now been set in a quite different context — the photoemission of electrons from a surface.

The quest for faster and faster time-resolved measurements has reached a new level: Cavalieri *et al.* report (page 1029 of this issue)[1] that they have measured a delay of 100 attoseconds in the emission of electrons ejected from a surface irradiated by light. This is not just the experiment with the best time resolution yet; it is also the first time that attosecond metrology has been applied to a solid, rather than a gaseous, system.

It was only in the 1990s that the trend to ever faster measurements produced laser sources with pulse durations below 5 femtoseconds (a femtosecond is 10^{-15} seconds). This is the timescale of the motion of atoms within molecules. Femtochemistry, in which a chemical reaction is followed through its transition state, became big news[2]. But that is now old hat. The attosecond (10^{-18} seconds) is the timescale of the motion of electrons within atoms: an electron takes about 150 attoseconds to orbit a hydrogen atom.

Attosecond pulses are created when intense laser pulses of femtosecond duration are focused into a gas sample. A process known as high-harmonic generation[3] then kicks in to produce light at a range of frequencies that are precisely phased together, creating a train of very short, coherent pulses. In the past few years, the technology has evolved to the point where single pulses just 130 attoseconds long can be produced with table-top-sized laser systems[4]. These pulses are so short that their frequency (and thus energy) lies in the extreme-ultraviolet or soft-X-ray portion of the electromagnetic spectrum.

Attosecond metrology has previously been applied to samples of atomic gases to observe excitation processes of electrons such as shake-up and Auger decay[5]. These are essentially 'pump–probe' measurements: an attosecond pulse excites the system, and the intense optical laser field that generated the pulse follows it and is used to sweep up the charged products — much as an oscilloscope streaks an electron beam across the screen to resolve an electrical pulse.

Cavalieri *et al.*[1] focus their 90-electronvolt extreme-ultraviolet pulse at an angle on a tungsten metal surface (Fig. 1, overleaf). The lower-frequency optical pulse that created the attosecond pulse follows along the same path, but its passage can be delayed in steps of 300 attoseconds. Electrons liberated through the photoelectric effect by the first pulse are detected by a spectrometer that measures their kinetic energy. The optical laser field pushes these photoelectrons' energy up or down, depending on the precise position of both the attosecond pulse and the photoelectron in the laser field's cycle.

By varying the time delay between the pulse and the optical field, and measuring the shift in the up and down motion of the energy spectrum, the authors could precisely measure the emission time of the photoelectrons. They were able to distinguish electrons coming from different energy states in the surface, observing that electrons from the more deeply bound core states in the surface were emitted