many generations as a random walk process, the analysis reduces the likelihood that the random walk is a good model of the dynamics of many insect populations. Woiwod and Hanski's work also once again emphasizes the crucial importance of long-term data collection in ecology.

In the controversy over insect population regulation, it is the more theoretically inclined ecologists who have tended to argue that density dependence is common, whereas many empiricists have been particularly attracted by theories emphasizing the unpredictability of natural systems. Empiricists look at the deterministic outcome of many theoretical models incorporating simple forms of density dependence and, knowing the world is not like that, take comfort in the unpredictable outcomes of populations modelled as random walks, and in suggestions that density dependence operates only very infrequently. Theoreticians, on the other hand, confident that density dependence must be present in persistent populations, sniff apostasy in attempts to play down the frequency with which it operates in natural populations.

The division between the two camps is probably less than it seems. There is a continuum of types of density dependence from forms that increase in severity in a simple manner across population densities, to forms that operate only over a sharp threshold[8]. Similarly, the relationships between density dependence and population density may be relatively constant, or the relationships may contain much noise and scatter. Woiwod and Hanski's results are encouraging in that they suggest that the type of density dependence occurring in natural populations of insects may not be as intractable to study as many have feared. The detection of density dependence is however only one step, albeit an important step, in understanding the dynamics of insect populations. We still need to know the biological basis of density dependence, how its strength varies with population density, and how it interacts with other sorts of mortality to determine observed population fluctuations. □

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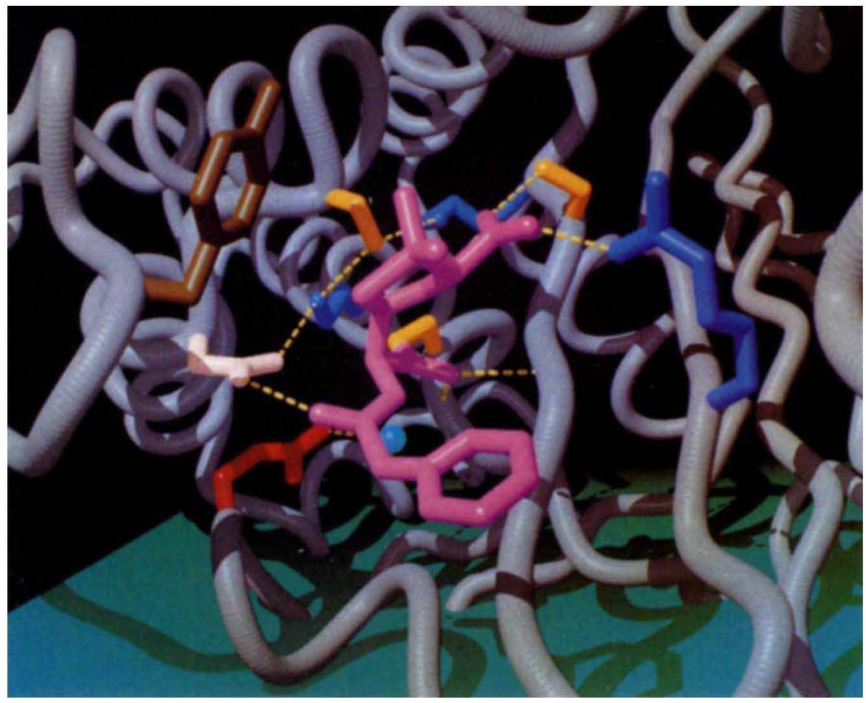
1. Woiwod, I. P. & Hanski, I. *J. anim. Ecol.* **61**, 619–630 (1992).
2. Stiling, P. *J. anim. Ecol.* **57**, 581–593 (1988).
3. Den Boer, P. J. *Oecologia* **86**, 484–491 (1991).
4. Hassell, M. P., Latto, J. & May, R. M. *J. anim. Ecol.* **58**, 883–892 (1989).
5. Holyoak, M. & Lawton, J. H. *Oecologia* (in the press).
6. Bulmer, M. G. *Biometrics* **31**, 901–911 (1975).
7. Pollard, E., Lakhani, K. L. & Rotheray, P. *Ecology* **68**, 2046–2055 (1987).
8. Strong, D. R. *Trends Ecol. Evol.* **1**, 39–42 (1986).

Drug ring bust



THIS futuristically colourful picture tells quite a story. It shows the mechanism by which the enzyme β-lactamase nullifies the antibiotic effects of penicillin, as reported by Strynadka *et al.* on page 700 of this issue.

Penicillins (and the cephalosporins) are β-lactam antibiotics which interfere with bacterial cell-wall synthesis, and consequently kill actively growing and dividing bacteria. The peptidoglycan network of the bacterial cell wall is formed by the synthesis of linear polysaccharide chains and the cross-linking of these chains with short peptides. It is this latter process of transpeptidation that is inhibited by the β-lactam antibiotics; they react irreversibly with the active site of the transpeptidases that catalyses the cross-linking.

But not all pathogenic bacteria are sensitive to these antibiotics; penicillin-resistant strains often harbour plasmids (so-called bacterial drug resistance factors) that specify β-lactamase enzymes which break down the β-lactam ring of the penicillin. The hydrolysis of the amide bond in the ring yields penicilloic acid which is devoid of antibiotic activity.

Strynadka *et al.* now provide clear insight into how these antibiotics are recognized and destroyed. They present the high-resolution crystal structures of the *Escherichia coli* RTEM class A β-lactamase and a mutant version of the same enzyme defective in deacylation, both on its own and complexed with its natural substrate, penicillin G.

Like the serine proteinases and the cell-wall synthesizing enzymes they protect from antibiotics, the β-lactamases have at the centre of their catalytic machinery a serine residue that functions as a nucleophile, attacking the carbonyl carbon of the β-lactam ring. Unlike the serine proteinases, however, distinct residues are implicated in the acylation and deacylation steps, and the two steps occur by almost completely different mechanisms.

The amino-acid residues important in catalysis are shown in this depiction of the acyl-enzyme (dashed lines are hydrogen bonds). The penicilloyl intermediate of penicillin G (pink) is covalently attached to the enzyme (α-carbon backbone in grey) via the nucleophile serine 70 (yellow, bottom).

Lysine 73 (blue tube to the left of the substrate) functions as a general base in assisting in the initial nucleophilic attack, and in combination with serine 130 (yellow, top left), in protonating the leaving group nitrogen of the β-lactam ring to form the acyl-enzyme intermediate. Glutamine 166 (red) is the general base in the deacylation reaction, assisting the nucleophilic attack by a water molecule (aquamarine sphere) on the ester carbonyl carbon of the acyl-enzyme intermediate.

The remaining residues — tyrosine 105 (brown), arginine 244 (blue, right), asparagine 132 (peach) and serine 235 (yellow, top right) among them — are involved in substrate binding.

β-lactamase enzymes are produced by many bacteria. Increased understanding of the way they work has allowed the development of resistant antibiotic analogues (for example ampillicin) and has led to the discovery of naturally occurring lactamase inhibitors (for example clavulanic acid). Strynadka *et al.* have added an extra layer of detail to knowledge of the catalytic mechanism concerned, which will no doubt guide attempts to design better inhibitors. G.R.