

a chaperonin. The chaperonins are a family of chaperones found in all plants, animals and bacteria. They function by enclosing each individual folding chain inside a closed cavity, where the chain completes its folding into a monomer in the absence of other folding chains⁷. The closing and opening of the cavity requires ATP — the molecular source of energy used by cells. The chaperonin GroEL/ES, from the bacterium *Escherichia coli*, is sufficient to mediate the formation of active Rubisco from some cyanobacteria *in vivo*, but cannot enable the formation of active enzyme in high yield from fully unfolded subunits of either cyanobacteria or plants *in vitro*. In some cyanobacteria another chaperone, called RbcX, is also required, but this protein functions at the subunit assembly stage and does not require ATP⁸.

Liu *et al.*¹ now define the conditions necessary for the formation of active enzyme *in vitro* from purified, unfolded large subunits and folded small subunits of a cyanobacterial Rubisco. The trick is to first incubate unfolded large subunits with GroEL/ES, RbcX and ATP, to allow the large subunit to fold and bind to RbcX, and then to add folded small subunits to displace the RbcX and so bind the folded large subunits. The authors also show that the RbcX chaperone acts as a 'molecular staple' that binds to partly folded large-subunit chains in such a way that they interact correctly with small subunits, rather than aggregating with one another (see Fig. 6 on page 201).

Under their optimized conditions, the authors set up an *in vitro* system from which they obtained active Rubisco in yields up to 40%. This yield is sufficiently high to be used to screen the effects of mutations in the large-subunit chains in the hope of obtaining an improved enzyme. The advantage of such an *in vitro* screen is that the effects of mutations on enzyme activity can be studied under standardized conditions; by contrast, it is difficult to control the expression of the genes for the Rubisco subunits and the two chaperones *in vivo* in *E. coli*. Variants of the RbcX chaperone occur in plants, so Liu and colleagues' work¹ can be extended to the unsolved problem of reconstituting Rubisco isolated from chloroplasts, where this story started.

There is a more general significance to the work of Liu and colleagues. The prevailing view about chaperones, reflected in many reviews and textbooks, is that they function primarily at the protein-folding stage. Most chaperone research has also concentrated on this stage, and has led to the conclusion that such folding chaperones have many protein substrates and require ATP to function. This view ignores the fact that the first use of the term 'molecular chaperone' concerned the assembly of already-folded histone proteins with DNA⁹. Further investigations of the mechanism of action of RbcX will strengthen the less-studied view that the assembly of some oligomeric structures inside cells may also require the ministrations of

molecular chaperones that are specific for their substrates, and which do not require ATP¹⁰. ■
R. John Ellis is in the Department of Biological Sciences, University of Warwick, Coventry CV4 7AL, UK.

1. Liu, C. *et al.* *Nature* **463**, 197–202 (2010).
2. Andrews, T. J. & Lorimer, G. H. in *The Biochemistry of Plants* Vol. 10 (eds Hatch, M. D. & Boardman, N. K.) 131–218 (1987).

3. Spreitzer, R. J. & Salvucci, M. E. *Annu. Rev. Plant Biol.* **53**, 449–475 (2002).
4. Barraclough, R. & Ellis, R. J. *Biochim. Biophys. Acta* **608**, 19–31 (1980).
5. Ellis, R. J. *Nature* **328**, 379 (1987).
6. Ellis, R. J. & Minton, A. P. *Biol. Chem.* **387**, 485–498 (2006).
7. Hartl, F. U. & Hayer-Hartl, M. *Nature Struct. Mol. Biol.* **16**, 574–581 (2009).
8. Saschenbrecker, S. *et al.* *Cell* **129**, 1189–1200 (2007).
9. Laskey, R. A. *et al.* *Nature* **275**, 416–420 (1978).
10. Ellis, R. J. *Trends Biochem. Sci.* **31**, 395–401 (2006).

BEHAVIOURAL ECOLOGY

Learn to beat an identity cheat

Rebecca Kilner

Parent birds commonly face the problem of distinguishing their own brood from foreign chicks. Learnt chick-recognition evolves only when parents do not mistakenly learn to reject their own young.

Many species of cuckoo steal parental care by laying their eggs in nests belonging to other birds, but at that stage their potential victims are often well equipped to defend themselves against exploitation¹. Hosts of the common cuckoo (*Cuculus canorus*), for example, have such finely tuned powers of discrimination that they can often eject a cuckoo egg from their nest, even though it closely resembles one of their own (Fig. 1). Just two or three weeks later, however, host birds seem bizarrely incapable of identifying the monster chick that has taken over their nest (Fig. 2, overleaf), and they continue to care for the cuckoo until it becomes independent¹. Research by Shizuka and Lyon (page 223 of this issue)² helps to explain how such exquisitely adaptive host behaviour can be followed by actions that seem so absurdly maladaptive.

Previous work shows that host birds learn to recognize the appearance of their eggs the first time they breed, and thereafter reject any eggs that look odd by comparison¹. So why don't hosts similarly learn to recognize their nestlings? The following hypothesis³ provides an answer. Imagine a naive parent unlucky enough to receive a cuckoo egg the first time she breeds. The cuckoo egg is one among several host eggs in the nest, so there is a high chance that the host will correctly learn the appearance of her own eggs. However, the host is unable to learn the appearance of her own nestlings correctly because the cuckoo chick evicts all the host young from the nest soon after it hatches. Instead, she mistakenly learns to recognize the foreign nestling as her own and then, in subsequent breeding attempts, rejects her own offspring because they look odd by comparison.

Now imagine a host that doesn't learn to recognize chicks. She might similarly fall victim to the cuckoo in her first breeding attempt, but at least has the prospect of subsequently rearing her own young. So hosts that don't



M. JONES/FLPA

Figure 1 | Spot the cuckoo egg? The host bird, in this case a reed warbler, can do so and thus may reject the intruder.

learn to recognize their nestlings leave more descendants than those that do. This means that the only possible way for learnt chick-recognition to evolve is if there are safeguards against costly mistakes in the learning process^{3,4}.

In the first detailed test of this hypothesis, Shizuka and Lyon² show how hosts protect themselves against learning errors, and demonstrate that this has enabled the evolution of learnt nestling-recognition. The authors focus on the American coot, *Fulica americana*, a bird that cheats on its own kind by laying eggs in nests belonging to other American coots. In this species, the brood hatches over several days, and foreign chicks are typically among the offspring that hatch later. Coot chicks are dependent on parents in the days after hatching, and foreign chicks are raised alongside host offspring. Shizuka and Lyon suspected that hosts might be able to recognize and reject foreign coot chicks, because these offspring typically suffered higher rates of mortality than host young, even after controlling for their later position in the hatch sequence. They wondered whether hosts might learn the appearance of chicks that hatched first and then reject any later-hatching chicks that seemed foreign.



50 YEARS AGO

Under New Zealand conditions of sheep-farming, incisors of grazing sheep wear much more rapidly on improved pasture, chiefly ryegrass (*Lolium perenne*) and white clover (*Trifolium repens*), than on the finer native pastures of low carrying capacity. The cause is not nutritional in the generally accepted sense, however. It would rather seem that certain substances in the herbage of 'improved' pastures dissolve the teeth, the process being aided by the abrasive action of the plant fibre. Wear is also increased in mouths with certain undesirable anatomical characteristics which appear to be hereditary in origin.

From *Nature* 16 January 1960.

100 YEARS AGO

The Family and the Nation: a Study in Natural Inheritance and Social Responsibility. By W. C. Dampier Whetham, F.R.S., and Catherine Durning Whetham — It is the duty of preachers of eugenics, a duty conscientiously undertaken by the author ... to educate public opinion in such a way that, aided by the legislation that will then be possible, it will insist on the more rapid multiplication of the desirable components of our society, and aim at the elimination of the rotten parts which now permeate it ... It is a well-known fact that the birth-rate in Great Britain fell from 36 per 1000 in 1876 to 27 per 1000 in 1907. This in itself may give cause for alarm, but the most serious feature of the fall is that it has not been the same in all classes ... As it is, the lowest stratum is as prolific as before, therefore our birth-rate has become selective. The least valuable portions of the population are selected to produce a disproportionately large share of the next generation, by the action of the more valuable portions in bringing about at any rate a partial self-elimination.

From *Nature* 13 January 1910.



D. MIDDLETON/FLPA

Figure 2 | Spot the cuckoo fledging? Monstrous though the young cuckoo is, the reed warbler can't recognize it as an alien and continues to rear it as if it were one of its own.

To test this idea, Shizuka and Lyon presented parents with one sort of chick at the start of the nestling period (the 'referents'), and allowed them to learn the characteristics of these chicks for a day. During the next four days, parents were given test chicks, half of which were from the same brood as the referents and half of which were not, and the chicks' survival was monitored to detect evidence of learned discrimination. The experiment showed that the test offspring that were unrelated to the referents were least likely to survive to independence. A subsequent experiment ruled out the possibility that parents were simply rejecting chicks of the minority type. So parents learn to recognize their offspring by imprinting on the chicks that hatch first and they are inclined to reject any later-hatching chicks that seem odd by comparison. By using their first-hatched chicks as referents, parents are unlikely to mistakenly learn the wrong sort of offspring as their own.

The experiment therefore supports the hypothesis³ that learnt chick-recognition can evolve only when the learning process is error-free. Although the traits involved in coot chick-recognition remain to be described, classic behavioural studies suggest that both acoustic and visual cues are probably involved. For example, colonially nesting gull and swallow species are not cuckoo hosts, but they risk feeding alien young when their offspring leave the nest and intermingle with other fledglings of the same species⁵. Experiments show that parents start to discriminate against foreign chicks just before their own nestlings become mobile, and they identify offspring by the structure of their calls and by unique plumage patterns on their head⁵. Although American coots are not colonial, their chicks can swim soon after hatching and they occasionally stray onto foreign territories, where they are attacked by adults⁶. Perhaps this means that learnt chick-recognition has evolved in American coots as a general defence against feeding any alien young, rather than as a

specific defence against parasitic chicks.

Might cuckoo hosts learn to recognize their nestlings in the same way as American coots? Intriguingly, the eggs of virtually all parasitic cuckoo species hatch in advance of host young¹, and it is tempting to speculate that their shorter incubation periods have been selected to prevent the evolution of learnt nestling-recognition in their hosts. Nevertheless, there is increasing evidence that some hosts can recognize and reject cuckoo chicks⁷⁻⁹. The common theme in these diverse studies^{2,7-9} is that host discrimination against parasitic chicks can evolve as long as there are mechanisms in place to minimize the costs of accidentally rejecting host young.

Discrimination need not involve learnt chick-recognition^{4,8}: unlearned rules of thumb may enable hosts to reject foreign nestlings rather than their own. For example, hosts may avoid exploitation by abandoning offspring that are alone in the nest^{4,7}, or that take an unusually long time to fledge⁸, because these characteristics are reliably associated with cuckoo nestlings. Where there is learnt nestling-recognition, learning that is confined to a sensitive period², or guided by an innate template⁴, can reduce the chance of error. In this regard, learnt chick-recognition resembles song-learning in birds, which is often confined to periods when an appropriate tutor bird is present and which can be guided by an auditory template that prevents birds from learning the song of the wrong species¹⁰.

The sight of a tiny songbird feeding a monstrous cuckoo chick overflowing its nest (Fig. 2) is one of the most extraordinary in nature. The message emerging from the latest research is that, absurd as it may seem, such behaviour will persist as long as there are no measures to prevent hosts from routinely rejecting their own chicks.

Rebecca Kilner is in the Department of Zoology, University of Cambridge, Downing Street, Cambridge CB2 3EJ, UK.
e-mail: rmk1002@cam.ac.uk

1. Davies, N. B. *Cuckoos, Cowbirds and Other Cheats* (Poyser, 2000).
2. Shizuka, D. & Lyon, B. E. *Nature* **463**, 223–226 (2010).
3. Lotem, A. *Nature* **362**, 743–745 (1993).
4. Langmore, N. E. et al. *Behav. Ecol.* **20**, 978–984 (2009).
5. Beecher, M. D. *Behav. Genet.* **18**, 465–482 (1988).
6. Lyon, B. E. *Anim. Behav.* **46**, 911–928 (1993).
7. Langmore, N. E., Hunt, S. & Kilner, R. M. *Nature* **422**, 157–160 (2003).
8. Grim, T. *Proc. R. Soc. Lond. B* **274**, 373–381 (2007).
9. Sato, N. J., Tokue, K., Noske, R. A., Mikami, O. K. & Ueda, K. *Biol. Lett.* doi:10.1098/rsbl.2009.0540 (2009).
10. Catchpole, C. K. & Slater, P. J. B. *Bird Song: Biological Themes and Variations* (Cambridge Univ. Press, 2008).

GALAXY FORMATION

Gone with the wind?

Marla Geha

Windy weather is forecast where stars are forming. Numerical simulations show that these winds can reshape dwarf galaxies, reconciling their properties with the prevailing theory of galaxy formation.

The smallest things often cause the most trouble. The smallest galaxies are no exception: they have long caused difficulties for modern cosmology. Neither the number nor the appearance of small ‘dwarf’ galaxies conforms to the predictions of the otherwise highly successful cold dark matter (CDM) theory of galaxy formation. Such predictions, however, are usually derived from simulations that don’t include stars. This apparently glaring oversight is justified because visible matter plays a minor part in the much larger drama of galaxy formation. The hidden actor is dark matter, whose effects are felt only through gravity. On page 203 of this issue, however, Governato and colleagues¹ demonstrate that visible matter also has a key role in modifying the properties of dwarf galaxies, thereby simultaneously solving two long-standing problems with CDM galaxy formation.

The precise nature of dark matter is unknown. The favoured ‘cold’ dark matter is a hypothesized particle that became non-relativistic (slow-moving) soon after the Big Bang². Yet despite this uncertainty, the prevailing model of galaxy formation based on CDM is tremendously successful, predicting a vast range of observational data.

Dwarf galaxies are small accumulations of stars with total masses one-tenth or less that of our Galaxy. Unlike the Milky Way, with its grand spiral arms and prominent central spherical bulge, dwarf galaxies have no central bulge and have a poorly organized spiral structure³. They are also less skilled than their massive counterparts at making stars and retaining gas. Stars and gas in a dwarf galaxy typically make up less than 10% of the total mass, with the remainder composed of dark matter.

A fundamental prediction of CDM galaxy formation is that galaxies have central ‘cusps’ — the density of matter increases steeply towards a galaxy’s centre. These cusps are thought to arise because galaxies form hierarchically, with small structures merging to create larger structures^{4,5}. As merging proceeds, matter with low angular momentum sinks to a galaxy’s centre,

creating a cuspy profile. Even dwarf galaxies form out of many smaller individual objects, and should thus have steep central density profiles. This is in sharp contrast to observations. Dwarf galaxies are often seen to host large regions of nearly constant density in their centres^{6,7}: their profiles are ‘cored’. The standard CDM theory simply cannot explain cored profiles in such galaxies. Many solutions have been proposed to solve this ‘core–cusp’ dilemma⁸ — most dramatically, abandoning CDM altogether in favour of an entirely new theory.

But before such a drastic step is taken, the accuracy of the cusp prediction must be verified. Cusps are predicted from numerical simulations that include only dark matter^{3,4}. On the face of it, dwarf galaxies should be well represented by dark-matter-only simulations, because their mass is dominated by dark matter. On the other hand, these galaxies are sensitive to energetic processes such as star formation, which can release energies comparable to that binding the entire dwarf galaxy together. If star formation affects the central regions of dwarf galaxies, it might solve the core–cusp problem.

Testing this hypothesis requires simulating the dark and luminous matter in a galaxy simultaneously — a challenge for even the most powerful supercomputers.

The race to perform larger and more sophisticated galaxy formation simulations is fiercely competitive. Governato and his team¹ make a clever choice in simulating dwarf galaxies, rather than larger structures in the Universe. Simulations are severely limited by computation time, and thus the smaller size of a dwarf galaxy leaves more computational resources for resolving smaller physical scales. This is key to Governato and colleagues’ success. Their simulations follow the wider environment in which the galaxy forms, while resolving the smallest physical scales relevant to the process of star formation.

The authors’ models¹ reveal that stars and gas have an active role in shaping a dwarf galaxy. In the normal course of star formation, massive stars are produced that have very short lifetimes, ending in spectacular supernova explosions. Strong winds from these explosions remove gas from the region of star formation. If star formation takes place in the centre of a dwarf galaxy, supernova winds preferentially remove the low-angular-momentum gas that has sunk to the galaxy’s centre. The dark matter must also react to gas removal in order to maintain dynamical equilibrium — by expanding outwards.

The mark of a satisfying astrophysical solution is that it solves multiple problems with a single physical process. Governato and colleagues claim that supernova winds explain both the shallow, cored density profiles observed in dwarf galaxies and their lack of a central bulge, simultaneously overcoming two major problems in CDM galaxy formation. Still, the team has so far fully simulated only two dwarf galaxies. Simulations over a wider range of masses and environments are required to verify their bold claim that supernova winds solve the core–cusp problem. However, a strong hint that this team is heading in



Figure 1 | Which is the real galaxy? Governato and colleagues’ numerical simulations¹ produce galaxies that seem identical to images of real galaxies. (Real galaxy (right) and background image courtesy of the Sloan Digital Sky Survey Collaboration (www.sdss.org); simulated galaxy (left) and composite image courtesy of C. Brook, F. Governato and P. Jonsson.)