

syndrome: behavioural changes, decreased muscle strength, heart defects, annular pancreas, aganglionic megacolon, immune defects and placental vascular abnormalities.

So Arron *et al.*<sup>2</sup> looked for genes in the DSCR that could regulate NFATc. They identified *DYRK1A*, which encodes a kinase, and *DSCR1*, which encodes a known inhibitor of calcineurin. The *DYRK1A* and *DSCR1* proteins acted synergistically to block NFATc-regulated gene expression. The authors found that *DYRK1A* acts as a priming kinase that enables additional phosphorylation of NFATc by another kinase, glycogen synthase kinase 3, leading to NFATc inactivation. Furthermore, mice genetically engineered to have increased levels of *DYRK1A* alone, or of both *DYRK1A* and *DSCR1*, had abnormal heart-valve development. As expected, in these mice NFATc was mostly phosphorylated and found in the cytoplasm (Fig. 1b).

Gwack *et al.*<sup>3</sup> reached a similar conclusion on the role of *DYRK1A* in regulating NFAT signalling by using an innovative approach in fruitfly cells to identify regulators of the mammalian NFAT pathway. Although these cells do not themselves possess NFATc factors, the pathway regulating their movement is present. This provided the basis for a genome-wide screen using interfering RNAs to inhibit the expression of specific genes. The authors identified *DYRK1A* and its relative *DYRK2* as direct regulators of NFATc phosphorylation, and, like Arron *et al.*, they showed that *DYRK1A* has a priming function. Gwack *et al.* note that *DYRK1A* and *DSCR1* occur in the DSCR, and suggest that their findings might aid the understanding of the immunological and neurological defects in Down's syndrome.

But does perturbation of the NFAT system explain the many developmental abnormalities of Down's syndrome? The difficulty in establishing this, as Arron *et al.* point out<sup>2</sup>, is that the various genetically engineered mice show different developmental defects. The trisomic Ts65Dn and Ts1Cje mice, which express extra copies of *DYRK1A* and *DSCR1* (ref. 5), show few of the abnormalities found in mice deficient in the various NFATc factors. But the trisomic mice also show few of the abnormalities of Down's syndrome, although they do have cellular abnormalities that may be highly relevant in studying the condition<sup>6,7</sup>. Such discrepancies may result from subtle variations in the expression of components of the NFATc regulatory system that occur because of the ways the relevant genes have been introduced or knocked out. Similarly, the discrepancies between Down's syndrome in humans and the mouse models may derive from species differences in gene expression and regulation.

Whatever their causes, these discrepancies make it more difficult to analyse directly the components of Down's syndrome that are not replicated in the trisomic mouse models. However, one feature that occurs in the human syndrome, NFATc-deficient mice and

trisomic mice is the abnormalities of the skull and jawbone that provided the original impetus for the search by Arron *et al.*<sup>2,4</sup>. So a straightforward way to test whether increased *DYRK1A* and/or *DSCR1* expression is the cause of these defects would be to reduce the number of copies of either or both genes from three to two by mating trisomic mice with mice lacking the genes. A similar approach has already been used to explore the role of the APP protein in the brains of trisomic mice<sup>8</sup>.

Increased *DYRK1A* activity was already suspected to be a factor underlying the cognitive and muscular deficits in Down's syndrome<sup>9,10</sup>. The work of Arron *et al.*<sup>2</sup> and Gwack *et al.*<sup>3</sup> suggests another way that increased activity of *DYRK1A* and *DSCR1* may contribute not only to mental retardation, but also to many other features of Down's syndrome. ■

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1. Epstein, C. J. *The Consequences of Chromosome Imbalance: Principles, Mechanisms, and Models* (Cambridge Univ. Press, 1986).
2. Arron, J. R. *et al.* *Nature* **441**, 595–600 (2006).
3. Gwack, Y. *et al.* *Nature* **441**, 646–650 (2006).
4. Richtsmeier, J. T., Baxter, L. L. & Reeves, R. H. *Dev. Dyn.* **217**, 137–145 (2000).
5. Amano, K. *et al.* *Hum. Mol. Genet.* **212**, 1333–1340 (2004).
6. Belichenko, P. V. *et al.* *J. Comp. Neurol.* **480**, 281–298 (2004).
7. Kleschevnikov, A. M. *et al.* *J. Neurosci.* **24**, 8153–8160 (2004).
8. Cataldo, A. M. *et al.* *J. Neurosci.* **23**, 6788–6792 (2003).
9. Branchi, I. *et al.* *J. Neuropathol. Exp. Neurol.* **63**, 429–440 (2004).
10. Altafaj, X. *et al.* *Hum. Mol. Genet.* **10**, 1915–1923 (2001).

## CLIMATE CHANGE

# All in the game

Thomas Pfeiffer and Martin A. Nowak

**It is in the public interest to keep Earth's climate on an even keel — the public, in this case, being all the world's population. Are you prepared to stake your own reputation on helping to improve matters?**

Earlier this year, the German newspaper *Hamburger Abendblatt* published an advertisement<sup>1</sup> drawing attention to the impact of human activities on global climate:

Human activities have already demonstrably changed global climate, and further, much greater changes must be expected throughout this century. The emissions of CO<sub>2</sub> and other greenhouse gases will further accelerate global warming... Some future climatic consequences of human-induced CO<sub>2</sub> emissions, for example some warming and sea-level rise, cannot be prevented, and human societies will have to adapt to these changes. Other consequences can perhaps be prevented by reducing CO<sub>2</sub> emissions. Everyday measures can contribute to climate protection.

Nothing odd about that, you might think. But there was. Not only was the advert written by the director of the Max Planck Institute for Meteorology in Hamburg, Jochem Marotzke, but it was paid for by the proceeds of a 'climate game' that was designed to explore the willingness of individuals to invest in protecting Earth's climate (Fig. 1, overleaf). A paper<sup>2</sup> describing the climate game by Manfred Milinski, along with Marotzke and two other colleagues, was published simultaneously with the advert. What's the story behind that paper and the advert?

The Earth's climate is a 'public good'. It is shared by the entire human population, so it apparently does not pay for a single individual

to invest in protecting it: the direct benefit that an individual gains from his or her investment is much smaller than the costs. The Earth's climate is therefore vulnerable to overexploitation — it faces a 'tragedy of the commons'<sup>3</sup>. Experiments with public goods games are one way of exploring how such a tragedy might be avoided.

In a typical public goods game<sup>4–7</sup>, members of a group can simultaneously invest money in a group project. The group's investment is increased by the experimenter, and the return is shared equally among all members of the group. In such a setting, it typically does not pay for a player to invest, because the player's direct return will tend to be a fraction of his or her investment. Assume, for example, that the group consists of three players, and the experimenter doubles the group's investment. Then, when one player invests (say) \$1, and the others invest nothing, that player gets back only two-thirds from his or her own investment, because that investment is doubled by the experimenter but then divided among all three players. Making an investment is an altruistic act in favour of the other players. The best strategy is to invest nothing in the group project but to benefit from the others' investment. It is therefore not surprising that, if played repeatedly, the amount of money invested in the group project declines rapidly<sup>3</sup>. But if all the members of a group instead continue to invest, the entire group is better off.

Max-Planck-Institut für Meteorologie  
Max Planck Institute for Meteorology



Professor Jochem Marotzke, Geschäftsführender Direktor des Max-Planck-Instituts für Meteorologie in Hamburg:

„Der Mensch hat das globale Klima bereits nachweislich geändert und weitere, wesentlich größere Änderungen sind für dieses Jahrhundert zu erwarten. Der Ausstoß von CO<sub>2</sub> und anderen Treibhausgasen wird die globalen Erwärmung weiter verstärken. Als Folge müssen wir mit häufigerem Auftreten von Klima- und Wetterextremen über 15.000 Todesfällen allein in Frankreich, werden häufiger auftreten.“

Verantwortlich für den Text: Professor Jochem Marotzke, Max-Planck-Institut für Meteorologie, Hamburg. Diese Anzeige wurde durch Spenden finanziert. Studenten der Universität Hamburg nahmen an einem „Klimaspiel“ teil, das die Bereitschaft der Teilnehmer erforschte, eigenes Geld für den Klimaschutz auszugeben. Für weitere Informationen siehe Pressemitteilungen „Gewinn muss nicht klimpern“ auf unserer Homepage [www.mpimet.mpg.de](http://www.mpimet.mpg.de) sowie unter [www.mpg.de](http://www.mpg.de) auf der Homepage der Max-Planck-Gesellschaft.

**Figure 1 | That ad — and how it was paid for.**

Such cooperation between group members can be achieved by changing the rules of the game. For example, if players can punish or reward other players based on their behaviour in the public goods game, a high level of investment is maintained<sup>4,5,7</sup>. Players who are known to make investments in the public good gain a good reputation; and that reputation translates into direct benefits of either receiving rewards or avoiding punishment.

Maintaining cooperation in these games seems far removed from addressing such problems as global warming. But Milinski and colleagues' climate game<sup>2</sup> is a step in that direction. As in previous studies, rounds of a public goods game were alternated with rounds of an 'indirect reciprocity game'<sup>8–11</sup> in which players could reward other players based on their reputation. But in contrast to previous versions of the game, the yield from the public goods game was not given back to the group. Instead, it was paid into a 'climate fund' that was used to pay for the advert. Amazingly, the players still maintained a high level of cooperation in the public goods game, and in the indirect reciprocity game they preferentially rewarded individuals who invested in the climate fund.

The experiments revealed that reputation is essential in maintaining a high level of investment. In rounds where the investment was anonymous, the degree of cooperation was much smaller than in rounds where the investment was made public. Apparently, individuals invested in the climate game to maintain a good reputation and thereby increase the chances of being rewarded by the other players in the indirect reciprocity game. The main message of this study, then, is that whenever individual behaviour is relevant to the public good, it should be made public. Only then can an individual's regard for his or her own reputation be fully exploited.

How might these principles work in practice? Energy costs of individual households could, for example, be published by local authorities. Companies could be ranked according to their emissions and their investments in climate protection. The large costs that may arise from global climate change have to be communicated, even if the details are not yet fully understood. And even small investments in climate protection may help, such as

a slight reduction of room temperatures in winter or making the effort to use public rather than private transport, where available.

Let no one underestimate the difficulty in persuading individuals around the world, let

alone businesses and entire nations, about the necessity of putting the brakes on the human impact on climate. And cynics may sneer at the prospect of applying the principles of an academic exercise on a world stage. But like it or not, we are all involved in the very real game of climate change. It is one of the few games we cannot afford to lose. ■

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1. *Hamburger Abendblatt* 20 (9 March 2006).
2. Milinski, M., Semmann, D., Krambeck, H.-J. & Marotzke, J. *Proc. Natl Acad. Sci. USA* **103**, 3994–3998 (2006).
3. Hardin, G. *Science* **162**, 1243–1248 (1968).
4. Fehr, E. & Gächter, S. *Nature* **415**, 137–140 (2002).
5. Milinski, M. *et al. Nature* **415**, 424–426 (2002).
6. Brandt, H., Hauert, C. & Sigmund, K. *Proc. Natl Acad. Sci. USA* **103**, 495–497 (2006).
7. Panchanatan, K. & Boyd, R. *Nature* **432**, 499–502 (2004).
8. Nowak, M. A. & Sigmund, K. *Nature* **393**, 573–577 (1998).
9. Wedekind, C. & Milinski, M. *Science* **288**, 850–852 (2000).
10. Nowak, M. A. & Sigmund, K. *Nature* **437**, 1291–1298 (2005).
11. Ohtsuki, H. & Iwasa, Y. *J. Theor. Biol.* **239**, 435–444 (2006).

## PHYSICAL CHEMISTRY

# Gas in a straitjacket

Susumu Kitagawa

**Given a holding material with sufficiently small and uniform pores, gaseous oxygen can be made to form regular one-dimensional chains. That gives unprecedented insight into the properties of confined gases.**

Porous materials are invaluable 'hosts' — that is, they are useful for storing, separating and investigating various guest compounds. Typical hosts are inorganic materials called zeolites (which contain a lattice structure) or so-called granular activated carbon, which possesses a large internal surface area to accommodate guests. Just recently, a third group of materials, metal-organic frameworks known as coordination polymers, have joined this party of excellent hosts<sup>1,2</sup>. Writing in *Angewandte Chemie International Edition*, Takamizawa and colleagues<sup>3</sup> report a canny use of a coordination polymer to store molecular oxygen (strictly, dioxygen, O<sub>2</sub>) as an ordered array of three molecules (a trimer) or as a regular one-dimensional chain over a wide range of temperatures.

Molecular oxygen is a particularly welcome guest molecule, for several reasons. First, its so-called 'frontier orbitals' include unpaired electrons, and give rise to a rich array of reduction and oxidation reactions (involving the gain and loss of electrons, respectively). These electrons, through their unpaired spins, also make O<sub>2</sub> the smallest stable 'paramagnetic' molecule, meaning that it orients itself in a particular way in response to a magnetic field. Confining oxygen in an array would allow

currently unknown details of the interplay of localized atomic spins and delocalized electrons to be investigated in charge-transfer and redox reactions between the oxygen and the pore surfaces.

Second, the properties of oxygen in its ordered, solid form are particularly interesting: in various three-dimensional solid phases under different conditions, it both exhibits a form of magnetism known as antiferromagnetism (in which the spins of neighbouring electrons align pointing in opposite directions) and displays metallic conductivity and superconductivity<sup>4</sup>. In lower-dimensional, confined forms of oxygen, novel magnetic and optical properties are expected<sup>5</sup>. The problem is that oxygen is a gas under ambient conditions, and solidifies only at -218.9 °C. Investigation of ordered forms of oxygen at ambient temperatures therefore requires extremely high pressures.

Coordination polymers offer just the right tool to bring about an ordered state without applying energy in the form of pressure. The key to this capability is extremely small, regular 'ultramicro-pores' of less than 0.7 nanometres in diameter that allow guest molecules to be lined up uniformly and intimately within the polymer. Conventional hosts such as