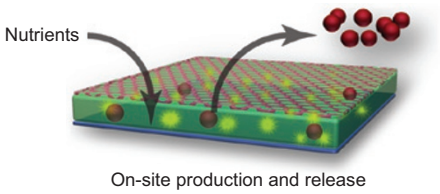
LIVING MATERIALS

A chemical factory within

Angew. Chem. Int. Ed. **51,** 11293–11296 (2012).



Materials or surfaces loaded with antibiotics typically have a limited supply of active compounds. Once these components are depleted, the antibacterial effect is lost until the active ingredients are replenished — not always a simple or feasible task. In an alternative approach to providing long-term antimicrobial activity, Wendelin J. Stark and colleagues at ETH Zürich in Switzerland have now included a microorganism capable of producing antibiotics within a sandwich structure to create a 'living material'. This material is able to synthesize antibiotics from nutrients and ensures a continuing supply of them to its surface.

The living material is structured into three layers. On the top is a nanoporous membrane. The middle layer contains agar to provide a suitable habitat for the fungus *Penicillium chrysogenum*. Mechanical support is provided from underneath by a base layer of polyacrylate. The nanoporus membrane enables nutrients to diffuse from the surface to the biological layer, and the small molecules synthesized by the fungus can make the reverse journey; however, the fungus itself — and its spores — cannot pass through the pores. The membrane also shields the biological layer from invasion by competing microorganisms. The fungus remains alive and enclosed within the material over long periods of time and proliferates when nutrients are available. It enters a hibernation state in periods when nutrients cannot be obtained, but is revived once the supply is restored.

Stark and the team showed that the fungus is capable of producing penicillin if fed from the surface. Living materials where the fungus had been grown for 10 days were capable of producing sufficient penicillin to kill penicillin-sensitive bacteria. Control experiments with penicillin-resistant bacteria or with a different fungal strain that did not produce penicillin resulted in no antibacterial effect, indicating that it arises from the production of penicillin.

This type of living material could be made from a variety of different materials and microorganisms. Tailoring the microorganism or its biochemistry offers a route to producing a wide selection of useful chemicals within a material. *RJ*

ORGANOMETALLIC CHEMISTRY

An iron-clad analogue

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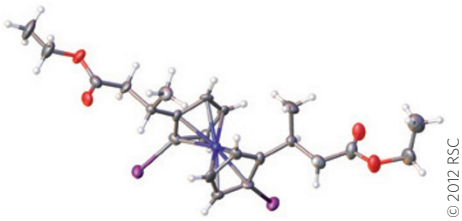


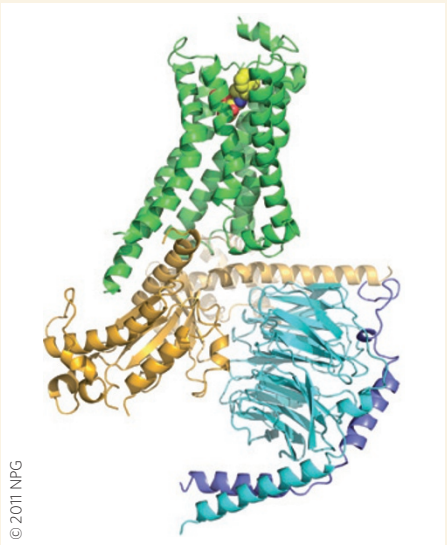
Synthetic chemists have for many years been tinkering with the structures of biomolecules to produce analogues with useful properties. Natural products with biological activity, for example, can be tailored to improve their potency and reduce any unwanted side effects. A somewhat larger target molecule that has not escaped attention is DNA, and chemists have modified each of the main structural building blocks — the sugar, the

2012 NOBEL PRIZE IN CHEMISTRY

Signalling the way

G-protein-coupled receptors (GPCRs) are a large family of proteins that span cell membranes. They sense molecules outside the cell and activate a signalling pathway within. GPCRs respond to a range of stimuli including well-known signalling molecules such as hormones and neurotransmitters (making them extremely important drug targets), as well as other triggers such as light, flavour and odour. The work of Robert J. Lefkowitz at the Howard Hughes Medical Institute and Duke University, and Brian K. Kobilka at Stanford University, has uncovered a wealth of information about the structure of GPCRs and how they work. Now Lefkowitz and Kobilka have been awarded the 2012 Nobel Prize in Chemistry in recognition of their contributions to this field of research.

In the 1960s, scientists knew about the signalling effect of hormones such as adrenaline, but the nature of the receptors they interacted with remained a mystery. Lefkowitz and colleagues used radioactivity



to trace several cell receptors and investigate their biochemistry — including the β-adrenergic receptor, which is activated by adrenaline. In the 1980s, Lefkowitz and his research group, which now included Kobilka, managed to purify enough of the β-adrenergic receptor to sequence it and clone the gene that encodes for it. When they analysed the gene they discovered a similarity to another gene that encodes for a receptor in the eye that responds to light. Lefkowitz and the team realized that these receptors formed a family — one that is now known as GPCRs.

As scientists started to understand more about the biochemistry of GPCRs, Kobilka focused on determining their three-dimensional structures. In 2007, Kobilka and his collaborators solved the structure of the β-adrenergic receptor — only the second reported structure for a GPCR. In 2011 they went one further when Kobilka and co-workers obtained the structure (pictured) of the activated β-adrenergic receptor (green) bound to an agonist (yellow spheres), and coupled to the associated G-proteins (gold, cyan and purple). *RJ*