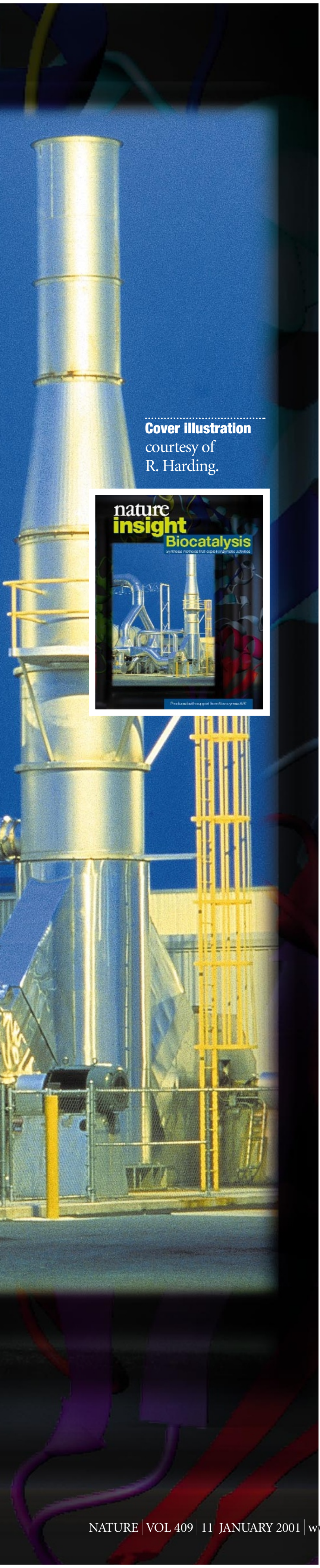

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nature insight

Biocatalysis

Synthesis methods that exploit enzymatic activities

Biocatalysis underpins some of the oldest chemical transformations known to humans, for brewing predates recorded history. The Sumerians, for instance, produced at least 19 different types of beer. This practical art was the fuse for the explosion in understanding of organic and biological chemistry that took place in the nineteenth century. Coining the word 'catalysis', Berzelius divined that it must play a central role in life's processes: "in the living plants and animals thousands of catalytic processes go on between the tissues and the fluids, and produce the amount of dissimilar chemical syntheses for whose formation from the common raw material...we could never see acceptable cause."

Studies of fermentation led to key insights into life's chemistry by Liebig, Pasteur and Emil Fischer, among others, culminating in the identification of enzymes ('in yeast') as nature's catalytic molecules and Fischer's intuitive leap of the 'lock and key' mechanism for their specificity.

It is this specificity that draws the interest of chemists seeking selective catalytic agents. But the trials of putting biocatalysis to industrial use are amply illustrated by the attempts in 1941 to produce fungal penicillin in what was basically a whole-cell process. It yielded such small amounts that the antibiotic had to be collected and recycled from the first patient's urine.

This Insight shows just how far things have progressed since then. The diversity of potentially useful enzymes at the chemist's disposal is now vast, supplemented by catalytic RNAs and antibodies. On page 226 Walsh surveys this arsenal, and discusses its deployment in applications ranging from chiral resolution to bioremediation of pollution. Koeller and Wong describe on page 232 how enzymes can become practical tools for the organic chemist, offering solutions to synthetic problems that seem intractable to artificial catalysts. Traditionally, enzymes have been regarded as catalysts designed to work in water. But on page 241 Klibanov shows how some can develop altered selectivities and enhanced thermal stability in nonaqueous solvents. On page 247 Khosla and Harbury explain how modular enzymes can be reshuffled or augmented to develop new functions in a rational manner. But 'rationality' is not the only answer to enzyme design, and Arnold shows on page 253 that *in vitro* evolution techniques provide the means to 'breed' and optimize new, non-natural enzymes. Whether or not a particular enzyme will deliver on its industrial potential depends, however, on a host of factors. On page 258 Witholt *et al.* provide an industry-wide perspective on the current successes and future challenges of using biocatalysts on a commercial scale.

We are pleased to acknowledge the financial support of Novozymes A/S in producing this Insight. As always, though, *Nature* carries sole responsibility for all editorial content and peer-review. We hope that readers will find this collection of reviews informative and thought provoking.

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