

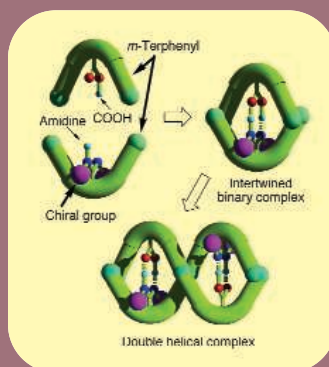
edited by Gilbert Chin

CHEMISTRY

With a Double Twist

The design of small-molecule oligomers that adopt conformations resembling the double-stranded helical structure of nucleic acids in solution has been challenging. Two strategies tried to date are to replace the phosphate ester backbone of nucleic acids with amides and to use metal ions to direct assembly of the strands.

Tanaka *et al.* describe how to build a double helix structure that relies on the formation of amidinium-carboxylate salt bridges to couple crescent-shaped backbones, which consist of *m*-terphenyl groups joined by a dialkyne linker. The right- or left-handedness of the double helices, which were characterized by circular dichroism and nuclear magnetic resonance of organic solutions and x-ray diffraction of crystals, is dictated by the chirality of the phenylethyl groups attached to the amidine. The presence of reactive trimethylsilylethynyl groups on the ends of these short strands should allow longer helices to be synthesized. — PDS



Schematic for double helix construction.

Angew. Chem. Int. Ed. 44, 3867 (2005).

coat. However, at least in these experiments, the RNAi-treated parasites appeared to be trapped in a slightly compromised coat that can be targeted successfully by the host immune system. — SMH

Proc. Natl. Acad. Sci. U.S.A. 102, 8716 (2005).

PSYCHIATRY

Correlating Variants and Variation

Genetic factors are widely believed to play a role in the etiology of schizophrenia, a debilitating psychiatric disorder that affects about 1% of the population. However, identifications of specific contributory genes and of critical sequence variants in those genes have not been unambiguous, because the disorder likely arises through the interactions of multiple genes, each exerting a weak effect.

To distinguish critical sequence variants in the *DISC1* (*disrupted-in-schizophrenia*) candidate gene from background noise, Callicott *et al.* studied whether any of the putative risk-conferring variants correlated with biological features of schizophrenia. Intriguingly, they found that in healthy people, one particular disease-associated variant of *DISC1* appears to adversely influence the anatomical structure and cognitive functioning of the hippocampal formation, which has long been a focal point of pathological studies of schizophrenia. These results thus support the hypothesis that variation in the *DISC1* gene is a contributing factor in the development of schizophrenia and likely acts, at least in part, through its effects on the hippocampus. — PAK

Proc. Natl. Acad. Sci. U.S.A. 102, 8627 (2005).

OCEAN SCIENCE

The Means of Production

The equating of new production (marine primary production fueled by nutrients supplied externally, rather than by nutrients derived from recycled organisms) to export production (primary production lost to recycling through removal to deep waters and sediments) is a common assumption in many studies of marine chemistry. This assumption has allowed numerous estimates of the hard-to-measure quantity of export production to be made, using the more easily measured new production. These quantities are then used to calculate how much CO₂ marine organisms might remove from the atmosphere, a central question in climate studies.

Plattner *et al.* investigate the strength of this assumption for annually integrated new and export production in the central Californian marine upwelling system, using an eddy-resolving, coupled physical-ecosystem-

biogeochemical model. They find that new and export production can decouple on a local scale (hundreds of kilometers), because of horizontal transport by persistent meso- and submesoscale circulation patterns, as well as by offshore flow caused by Ekman transport. Thus, although these results do not pertain to global estimates over long periods of time, they do illustrate that the concept of the equality of new and export production has to be used with care, particularly over short spatial and temporal scales. — HJS

Geophys. Res. Lett. 32, 10.1029/2005GL022660 (2005).

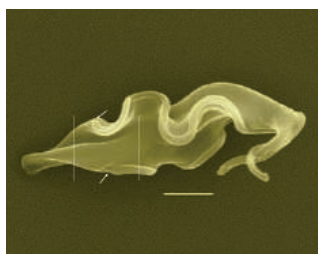
MICROBIOLOGY

Of Coats and Pockets

The protozoan parasite *Trypanosoma brucei* is responsible for African sleeping sickness. One of the interesting features of its biology is that while multiplying in the bloodstream, the parasite evades immune detection and clearance by expressing on its cell surface a dense coat of variant surface glycoprotein

(VSG); this coat is doffed periodically (internalized via the flagellar pocket) and replaced with an antigenically distinct version of VSG.

Sheader *et al.* examined how trypanosomes respond when the turnover of VSG is blocked by RNA interference. In vitro, trypanosomes deficient for VSG synthesis stalled before the cytokinesis stage of the cell cycle, when the two daughter cells normally would separate. In vivo, arrested trypanosomes were rapidly cleared from the bloodstream of infected mice, even though the total amount of surface VSG had not decreased. It appears that the ongoing manufacture of VSG is monitored by the parasite to maintain a dense surface



A trypanosome that has stalled before cytokinesis has opposing flagellar pockets.

PHYSICS**Confined to One Dimension**

In most instances, atoms in free space, either in the gas or liquid phase, can bind to form molecules only if the scattering length between the atoms is positive—that is, if the atoms attract. When the scattering length is negative, the atoms repel each other, and molecule formation does not occur. In the case of cold atoms, the scattering length can be tuned between positive and negative values by an external magnetic field.

Moritz *et al.* show that confining the atoms to a one-dimensional optical trap gives rise to quite different behavior. The reduced dimensionality in which the atoms move strongly affects the two-particle physics that subsequently determines the scattering length. They find two-particle bound molecular states irrespective of the field-tuned scattering length. This work illustrates the power of cold atoms to provide a tunable system that describes and mirrors the behavior of complex solid-state systems in which the analysis may not be as tractable. — ISO

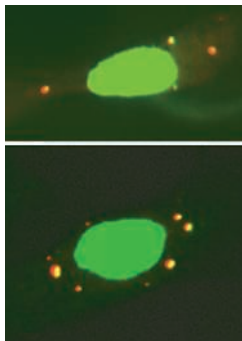
Phys. Rev. Lett. 94, 210401 (2005).

MOLECULAR BIOLOGY**RNA Traffic**

Both yeast and mammalian cells exhibit a handful of cytoplasmic sites referred to as processing bodies (P bodies), where enzymes that catalyze hydrolytic reactions, such as decapping and deadenylation, in the process of mRNA degradation can be

found. Three groups have extended the list of components that congregate at these foci.

Andrei *et al.* show that eukaryotic initiation factor 4E (eIF4E), which binds to the cap at the 5' end of the mRNA, and one of its binding partners (eIF4E-T) localize to P bodies. They suggest that these two factors combine to inhibit



Colocalization of an miRNA-targeted mRNA (green) and Argonaute 2 (red) in P bodies.

translation (the initiation stage of translation depends on eIF4E being free to interact with eIF4G) of mRNAs residing in P bodies. Sen and Blau, and Liu *et al.*, report that

P bodies contain Argonaute 2, the endonuclease of the RNA-induced silencing complex (RISC), and the latter group find microRNAs (miRNAs) in complex with their target mRNAs there, too. These observations suggest that both the cleavage of mRNAs triggered by small interfering RNAs (siRNAs) and the translational repression of mRNAs induced by miRNAs may depend on trafficking of protein-RNA complexes into P bodies. — GJC

RNA 11, 717 (2005); *Nat. Cell Biol.* 7, 633; 10.1038/ncb1274 (2005).

HIGHLIGHTED IN SCIENCE'S SIGNAL TRANSDUCTION KNOWLEDGE ENVIRONMENT**Reducing Tolerance and Dependence**

Although morphine is highly effective against pain, long-term use is problematic because it leads to tolerance and dependence—both of which are likely associated with up-regulation of cAMP signaling and adaptive changes in the expression of target genes. Morphine analgesia and tolerance are mediated through the μ opioid peptide (MOP) receptor, which is also activated by endogenous opiates and methadone; however, unlike these other ligands, morphine does not stimulate endocytosis of the MOP receptor. He and Whistler found that a concentration of methadone that did not stimulate endocytosis by itself nevertheless resulted in MOP receptor endocytosis when administered with a saturating amount of morphine. The authors propose that joint occupation of a dimeric MOP receptor by morphine and methadone can engage the endocytic machinery with much reduced activation of the cAMP pathway. In rats, this mix inhibited the development of morphine tolerance (assessed by tail-flick) and dependence (assessed by the behavioral response to pharmacologically induced opiate withdrawal) without reducing the potency of morphine analgesia. — EMA

Curr. Biol. 15, 1028 (2005).