EDITORS' CHOICE

edited by Gilbert Chin

VIROLOGY

Winding Up with New Herpes Drugs

Herpes simplex viruses (HSVs) cause a broad spectrum of diseases, ranging from oral and genital herpes in adults to life-threatening illness in newborn infants and immunocompromised individuals. HSV infections are typically treated with the antiviral drug acyclovir or other nucleoside analogs that act by inhibiting the viral DNA polymerase. Although these drugs are safe and very effective, they must be administered early in infection for maximal antiviral activity, and certain isolates of HSV have become resistant to the drugs. To circumvent these limitations, Crute *et al.* and Kleymann *et al.* used high-throughput screening assays to develop a new class of drugs that disrupt HSV replication through a different mechanism of action. These new drugs (amino-thiazolylphenyl–containing compounds and thiazole urea derivatives) act by inhibiting the HSV helicase-primase complex that normally unwinds the double-stranded viral DNA and generates primers for viral DNA synthesis. On the basis of promising results in rodent models—even when administered at a late stage of HSV infection—these new drugs, or optimized derivatives thereof, may soon be tested in clinical trials. — PAK

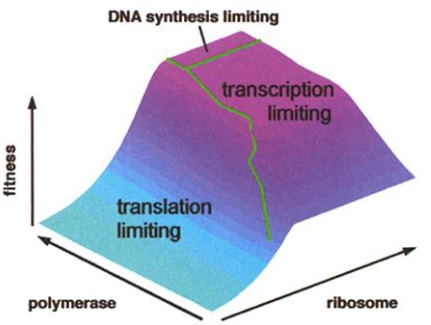
Nature Med. **8**, 386; 392 (2002).

SYSTEMS BIOLOGY

In Silico Landscaping

The development of microarray technology has powered an explosive expansion in the collection of data about the temporal and spatial expression of genes, and the soon-to-be-realized potential of similar advances in global measurement of protein levels offers the prospect of having in hand the basic parameters for building a computational model of a eukaryotic cell. In fact, the abundance of data may prove to be an embarrassment of riches because of the many ways in which the metabolic and regulatory pathways might be constructed and connected. Adding the constraints of observed interactions and laboriously gathered kinetic constants may help, particularly if analysis of simpler systems can be used as a guide.

You *et al.* have carried out experimental and computational studies on the growth of bacteriophage T7 and its host, *Escherichia coli*. The latest upgrade of their model, T7v2.5, incorporates parameters describing the host and phage nucleic acid polymerases and the host protein synthesis machinery, as well as the temporal expression of the phage genes (early and late). They find that the primary limitation on T7 growth is the number of ribosomes. In a regime of plentiful protein synthesis, the quantity of host polymerase can be limiting, but too much polymerase will result in excessive transcription of the phage early genes and diversion of the ribosomes away from making capsid proteins from late gene transcripts. Although other factors, such as host cell volume and phage polymerase processivity, are less important, they too may be limiting in certain areas of the *n*-dimensional fitness landscape. — GJC



The two-parameter fitness function for T7.

J. Bacteriol. **184**, 1888 (2002).

ENVIRONMENTAL SCIENCE

Nuclear Signatures

After the Russian nuclear submarine *Kursk* sank in August 2000 in the Barents Sea, concerns that nuclear waste might then be released into the sea and deep ocean were expressed. Matishov *et al.* explored the situation in September 2000 by sampling the local seawater, sediments, and biota (including fish) and by comparing these to earlier archival samples. They found negligible radioactivity from the *Kursk* in all of the recent samples. However, they did find anomalously high levels of iodine-129 (^{129}I) compared to samples from the early 1990s. This input is characteristic of contamination from recent fuel reprocessing efforts in the UK and France (which is controversial primarily because reprocessing can lead to production of some weapons-grade fuel). Although the levels of contamination are well below those associated with health risks, the study indicates the sensitivity of the re-

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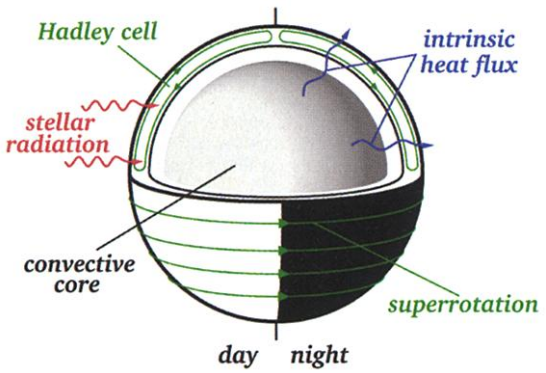


Model of extrasolar planetary dynamics; winds, green.

PLANETARY SCIENCE

Weather on the Pegasi Planets

Fifteen of the 73 extrasolar planets have nearly circular orbits and are within 0.1 astronomical unit of their solar-type star. These Pegasi planets, named after the first extrasolar planet 51 Peg b, are so close to their parent star that they are bombarded by intense stellar irradiation, which influences atmospheric dynamics and even the size of the planet.

In a pair of papers, Guillot and Showman model the radial temperature variations and atmospheric circulation of the extrasolar gas giant HD209458b, whose radius is known from direct measurement during a stellar transit. They can explain the larger-than-expected radius by proposing that 1% of the stellar radiation is converted in the planet's atmosphere into kinetic energy and then is transported as thermal energy into the convective core. This input of energy would reduce the rate at which the planet cools (and contracts) and allow for lower atmospheric temperatures, in accord with earlier calculations. In addition, the stellar flux in combination with day-night temperature asymmetries (of up to 500 K) could push the planet out of synchronous rotation with its star and generate clouds, winds (of up to 1 km per second), and other heterogeneous features. — LR

Astron. Astrophys. **385**, 156; 166 (2002).

CREDITS: (LEFT) SHOWMAN AND GUILLOT, *ASTRON. ASTROPHYS.* **385**, 156; 166 (2002); (RIGHT) LINGCHONG YOU

gion to nuclear fuel processing activity across Europe. The ^{129}I signature might also be useful as a long-distance ocean tracer, but locally influenced background levels will have to be considered. — BH

Environ. Sci. Technol. 10.1021/es0112487 (2002).

ATMOSPHERIC CHEMISTRY

Alcohol Can Impair Measurement

Oxidation reactions involving hydroxyl radical (OH) and hydrogen dioxide (HO_2)—collectively known as HO_x—play an important role in atmospheric chemistry by destroying many pollutants. However, because their concentrations are very low, on the order of parts per trillion, it has been difficult to obtain reliable data on HO_x at remote locations. Measurements of hydrogen peroxide (H_2O_2) would allow an estimate of HO_x concentration, because the reaction of two HO_2 molecules to form H_2O_2 and O_2 is the main source of H_2O_2 in the upper troposphere and the stratosphere. Unfortunately, balloon-borne measurements have produced lower H_2O_2 concentrations in the stratosphere than those predicted by models, indicating that the current understanding of the kinetics governing the production and loss of H_2O_2 is incomplete.

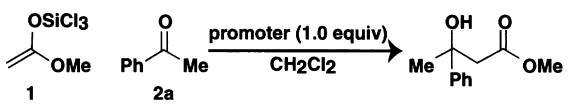
Christensen *et al.* have refined the rate constant for the H_2O_2 formation reaction from HO_2. Accounting for the effect of methanol (which often is used as a precursor for HO_2) on the formation reaction yields a rate constant lower than the one currently recommended, especially at low temperatures. When the adjusted rate constant was used in a photochemical simulation, good agreement with measured H_2O_2 was obtained. — JU

Geophys. Res. Lett. **29**, 10.1029/2001GL0114525 (2002).

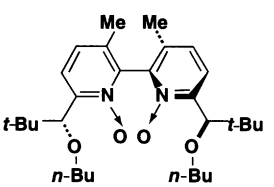
CHEMISTRY

Ketones Meet Their Match

Numerous methods exist for controlling the stereochemistry for the addition of ketones and esters to aldehydes to form an aldol (a β-hydroxy carbonyl). Methods for accomplishing the addition to the less reactive ketones, instead of aldehydes, are few and limited to α-diketones and pyruvate esters. Previous studies have shown that the trichlorosilyl enolate of methyl acetate (**1**) is highly reactive toward aldehydes, so much so that it is difficult to control the stereochemistry of the outcome. Denmark and Fan now show that **1** will add to a wide variety of ketones, such as acetophenone (**2a**), but in a highly enantioselective manner in the presence of *N*-oxide promoters. Mechanistic studies indicate that two catalyst molecules are involved in the transition state, and the authors found that bis-*N*-oxides gave yields of about 90%, with enantiomeric excesses of 80 to 85%. — PDS



The addition reaction and one of the promoter bis-*N*-oxides: Me, methyl; Ph, phenyl; *n*-Bu, *n*-butyl; and *t*-Bu, *tert*-butyl.



J. Am. Chem. Soc. 10.1021/ja025670e (2002).

HIGHLIGHTED IN *SCIENCE*'S SIGNAL TRANSDUCTION KNOWLEDGE ENVIRONMENT

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Both Sides Now

Synaptogenesis requires coordinated assembly of both pre- and postsynaptic regions. Kaufmann *et al.* show that an intracellular protein called liprin interacts with the cytoplasmic domain of the leucocyte antigen–related (LAR) tyrosine phosphatase on the presynaptic side at the *Drosophila* neuromuscular junction (NMJ). Both proteins are required for normal NMJ morphogenesis, because absence of either significantly altered both synapse size and bouton number. Consistent with the structural changes, evoked junctional potentials were reduced if either liprin or LAR was absent, although the underlying quantal machinery appeared intact because miniatures were unaltered. Wyszynski *et al.* report that liprin forms a complex with LAR and the glutamate receptor–interacting protein (GRIP) at the postsynaptic side in rat brain neurons. GRIP was also involved in clustering glutamate receptors of the AMPA (α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid) type, hinting at a role for liprin in synaptic plasticity. Hence, liprin appears central to structures at both sides of developing synapses. — LDC *Neuron* **34**, 27; 39 (2002).