

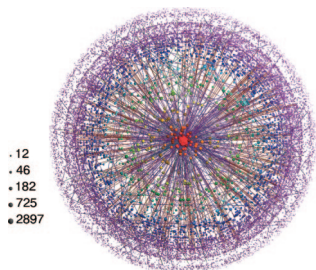
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## APPLIED PHYSICAL SCIENCES

## The topology of the Internet

The Internet has a dense core and a sparse fringe, and fractal properties in between, conclude Shai Carmi *et al.* after a mathematical analysis of Internet topology. The authors considered



Nodal representation of the Internet.

how the Internet's major nodes (Internet service providers and large organizations) are connected. They assigned each node to a “*k*-shell” according to the number of links, *k*, it has to other nodes closer to the center of the Internet. At its core, the Internet consists of a dense, heavily connected nucleus of close to 100 nodes including Google and ATT Worldnet.

Surrounding this is a region termed the “peer-connected component” and a lightly connected periphery. Within  $\approx 4$  links, it is possible to get from anywhere in the peer-connected component to anywhere else. However, nodes in the periphery are connected to others only through the nucleus. Information could therefore be routed through the peer-connected component to improve overall capacity and to avoid congestion. The authors calculated the fractal dimension of the network's outer “crust” as a function of crust thickness, *k*, and found a transition from nonfractal to fractal as *k* approaches 6. This transition is associated with a percolation threshold at *k* = 6, similar to those seen in other scale-free networks. — K.M.

“A model of Internet topology using *k*-shell decomposition” by Shai Carmi, Shlomo Havlin, Scott Kirkpatrick, Yuval Shavitt, and Eran Shir (see pages 11150–11154)

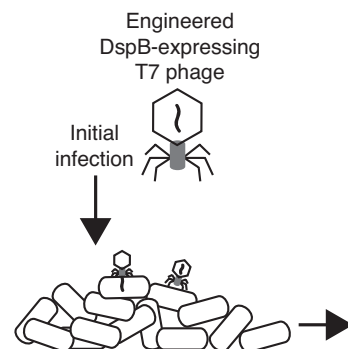
## APPLIED BIOLOGICAL SCIENCES

## Breaking up (biofilms) is no longer hard to do

Aggregated in biofilms, bacteria such as *Escherichia coli* or *Staphylococcus aureus* are resistant to antibiotics. The bacteria secrete an extracellular matrix that shields them from the environment. As a result, biofilms are often found in clinical infections that are difficult to eradicate. Timothy Lu and James Collins genetically engineered a strain of bacteriophage that is not only lethal to a specific strain of *E. coli*, but expresses an enzyme that digests a structural biofilm component. The engineered virus is much more effective

than the T7 phage at dispersing biofilms and killing bacteria. The authors began with the T7 phage and added the gene for DspB, an enzyme that hydrolyzes a key biofilm adhesin. They also added gene 1.2 from the T3 phage, which enables phages to replicate in thick biofilms. According to absorption measurements, DspB expression boosted biofilm breakup by a factor of 2.6. The engineered phage also reduced the viable bacteria count by 4.5 orders of magnitude, an improvement by a factor of 80 over control T7. The authors predict that a similar two-pronged approach to biofilm control could be customized to treat resistant bacterial infections. — K.M.

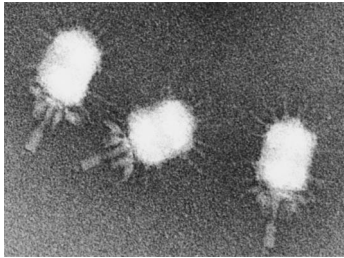
“Dispersing biofilms with engineered enzymatic bacteriophage” by Timothy K. Lu and James J. Collins (see pages 11197–11202)



Two-pronged attack strategy for biofilm removal.

## Ionic screening determines DNA packing forces in phages

The bacteriophage  $\phi 29$  enlists an ATP-powered motor protein to fill its capsid with DNA. The potential energy of the packed DNA may help the virus inject its genome into host cells during infection. Energy is stored in both the bending of DNA and electrostatic repulsion of its negatively charged backbone. Theory predicts that screening by positive ions may reduce the packing forces. Using optical tweezers to assess the force exerted by the motor



Electron micrograph of bacteriophage  $\phi 29$  viruses.

protein, Derek Fuller *et al.* explored the influence of ions on viral DNA packing. The

authors measured how the rate of packing depends on the fraction of capsid filled; they also observed how the motor velocity depends on an applied force. From these relationships, they determined the internal force resisting DNA confinement as a function of filling. Ionic content of the experimental buffer had a strong effect, confirming the influence of screening. In buffers containing  $Mg^{2+}$  or  $Co^{3+}$ , capsid pressure and, therefore, stored energy was less than when  $Na^+$  was the dominant ion. The authors note that the inferred internal forces are up to six times greater than predicted, assuming a certain DNA–DNA interaction potential and capsid volume and regular spooling of the DNA inside the capsid. — K.M.

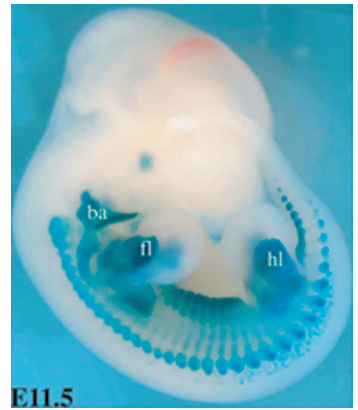
“Ionic effects on viral DNA packaging and portal motor function in bacteriophage  $\phi 29$ ” by Derek N. Fuller, John Peter Rickgauer, Paul J. Jardine, Shelley Grimes, Dwight L. Anderson, and Douglas E. Smith (see pages 11245–11250)

## DEVELOPMENTAL BIOLOGY

### Six is a lucky number for muscle development

Proper muscle development during embryogenesis requires the expression of a number of different genes. Julien Giordani *et al.* describe the interaction of several of these genes and demonstrate the crucial role of the “Six” family of proteins in the skeletal muscle of mouse limbs. Mice and humans have six *Six* genes, which are expressed in several cell types in embryo and adult and are involved in organogenesis. The authors genetically manipulated the expression of two of the *Six* genes, *Six1* and *Six4*, in mice. They

found that expression of a key myogenic regulatory factor, *Myf5*, was severely impaired in *Six1* knockouts and in a combined *Six1* knockout/*Six4* heterozygote. The two *Six* proteins appear to regulate *Myf5* expression by binding to a 145-bp regulatory region in the *Myf5* gene required for its expression in the embryonic limb buds. The results suggest that, in addition to a previously demonstrated direct regulation of another myogenic differentiation gene, *Myogenin*, the *Six* family of proteins regulates muscle development at multiple levels. — M.M.



Transgenic mouse embryo.

“Six proteins regulate the activation of *Myf5* expression in embryonic mouse limbs” by Julien Giordani, Lola Bajard, Josiane Demignon, Phillippe Daubas, Margaret Buckingham, and Pascal Maire (see pages 11310–11315)

## MEDICAL SCIENCES

### Targeting how targeted therapies work

Targeted cancer therapies, such as the kinase inhibitors Iressa and Tarceva, are showing promise in treating various types of cancer. However, it is not clear whether the drugs’ beneficial effects are related to the intended action of the drug (i.e., kinase inhibition). Accordingly, Sabrina Arena *et al.* developed an *in vitro* genetic strategy for assessing the role of kinase activity in tumor development. Using the Met receptor tyrosine kinase as a model, the authors deleted the exon encoding the catalytic domain (ATP binding site) of the enzyme from human colorectal, bladder, and endometrial cancer cells. The resulting cells expressed Met, but the enzyme lacked catalytic activity and was unresponsive to its ligand, hepatocyte growth factor (HGF). The oncogenic potential of mutant Met cells was reduced, but could be partially restored with HGF. A reportedly selective Met inhibitor also impaired growth of the mutant Met cells, indicating that the drug has actions outside its intended target. This strategy could be used to establish the oncogenic contribution of not only kinase genes but any drug/protein combination, and could help identify drugs that could be used synergistically to halt tumor progression. — M.M.

“Genetic targeting of the kinase activity of the Met receptor in cancer cells” by Sabrina Arena, Alberto Pisacane, Massimiliano Mazzone, Paolo Maria Comoglio, and Alberto Bardelli (see pages 11412–11417)