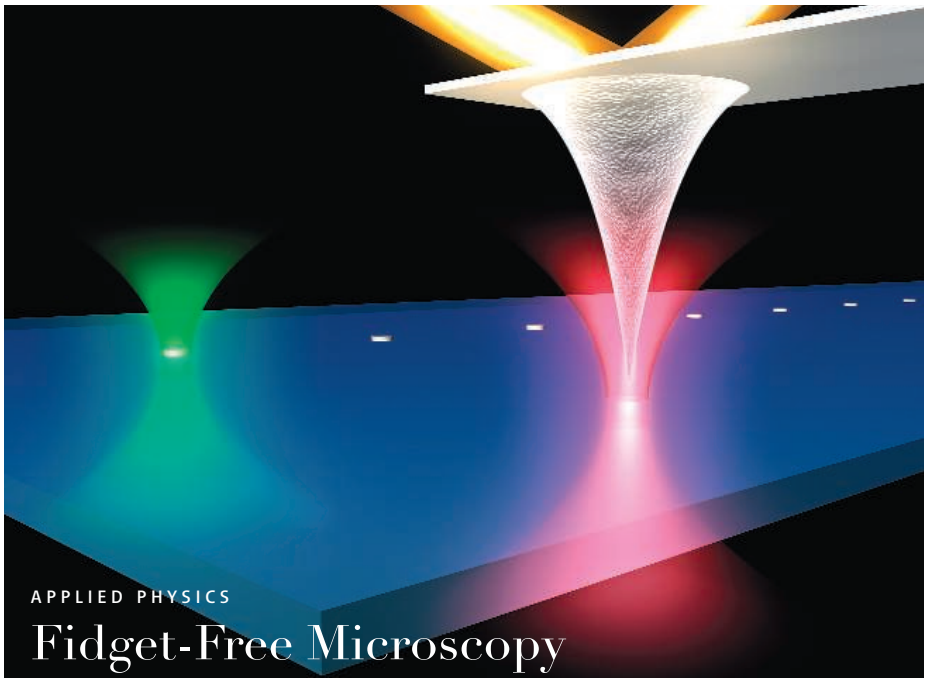


APPLIED PHYSICS

Fidget-Free Microscopy

Many people find it hard to sit still for extended periods without fidgeting and shifting about. A similar problem plagues the widely used technique of atomic force microscopy: Though the probing tip can resolve individual atoms, it is fundamentally a mechanical device and so inevitably drifts in space over time. As a result, the period available for signal-averaging to improve data quality is limited; moreover, it is often impossible to deliberately shift the tip to a different portion of the sample and then return to precisely the same starting position during the course of an imaging session (for example, to monitor slow rearrangements in two or more distinct domains of a protein). King *et al.* address this shortcoming using a laser-based feedback scheme for tip stabilization. Specifically, they detect backscattered laser light from the tip as well as a reference marker (a silicon disk) on the sample. The tip is then adjusted to remain in a fixed position relative to the marker. Studies of gold nanospheres in room-temperature air demonstrate a lateral drift rate limited to just 5 pm/min over the course of more than an hour. The method is optimized for transparent substrates, due to the backscattering detection geometry, but could potentially be extended by incorporating the reference marker into the instrument's cantilever assembly. — JSY

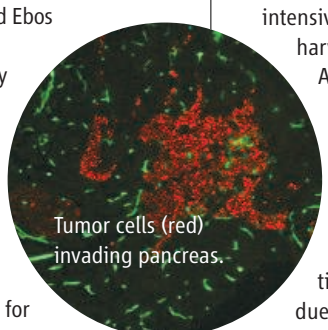
Nano Lett. **9**, 10.1021/nl803298q (2009).

BIOMEDICINE

Precipitating an Invasion

Anti-angiogenic drugs for cancer have commanded tremendous interest, especially over the past decade as they entered long-awaited clinical trials. This class of compounds inhibits the growth of tumors by cutting off their blood supply, usually by disabling cellular signaling pathways that are essential for blood vessel growth, such as the vascular endothelial growth factor (VEGF) pathway. Despite an abundance of promising preclinical data, most cancer patients have shown only a transient improvement in response to VEGF-targeting drugs, which is then followed by a progression to metastatic disease.

Two groups show that VEGF-targeting drugs have unanticipated—and undesirable—effects on tumor behavior that might explain their limited clinical efficacy. Working with four distinct mouse models, Pàez-Ribes *et al*. and Ebos *et al*. find that although the drugs initially inhibit primary tumor growth, they also appear to stimulate tumor cells to develop a more invasive and metastatic phenotype. This might occur because the drugs cause hypoxia (oxygen deficiency), which in turn selects for more malignant cells, or because the drugs increase the leakiness of blood vessels, thereby facilitating the entry of tumor cells into the circulation. — PAK



Tumor cells (red) invading pancreas.

Cancer Cell **15**, 220; 232 (2009).

GEOPHYSICS

Tossing Minerals into the Mix

Numerical models of flow in Earth's mantle have helped to constrain structural hypotheses about Earth's interior derived from seismic observations, mineral physics data on phase transitions, and geochemical data on the presence of possible distinct reservoirs. Typically, however, the models have required many simplifying assumptions—most, for example, have not explicitly used the wealth of mineral physics data. Nakagawa *et al.* have now developed a model framework that includes the phase relations, and corresponding thermodynamic properties, across five major components that dominate the major element chemistry of the mantle: the oxides of calcium, magnesium, iron, silicon, and aluminum. Models were run for the equivalent of 4.5 billion years of Earth's history, though it is still difficult to simulate the full convective vigor of Earth. The more realistic inclusion of mantle phases doesn't drastically affect many of the results as compared with prior simulations: subducting slabs, for example, are still predicted to penetrate the major phase boundary at 660 km and accumulate near the base of the mantle. The new models do show a reduced pattern of heterogeneity that is more in line with seismic data, but some of the richness of the seismic data is not as well reproduced, particularly in the complex upper mantle. — BH

Geochem. Geophys. Geosyst. **10**, 10.1029/2008GC002280 (2009).

EVOLUTION

Recovering from Stress

The evolutionary consequences of the overfishing of fish populations are generally not known, although there is evidence suggesting that fish are becoming smaller, especially in the most intensively targeted fisheries. Conover *et al.* harvested large fish from a captive Atlantic silverside population for five generations, followed by five generations without harvesting. They found that the population rebounded once culling had stopped, but that full recovery was estimated to take at least 12 generations. Hence, evolutionary changes due to selection on genetically determined traits, such as body size, are potentially reversible if the selective pressure is removed. — LMZ

Proc. R. Soc. London Ser. B **276**, 10.1098/rspb.2009.0003 (2009).

CREDITS (TOP TO BOTTOM): GREG KUEBLER/JILA; ELIZABETH ALLEN AND DOUGLAS HANAHAN