Second, there are increases in bicarbonate flux at equivalent discharge values, representing net increases in mean bicarbonate concentration. The authors assess this second effect by normalizing annual bicarbonate flux to the long-term mean annual water discharge. They conclude that more than 60% of the increased bicarbonate flux results from increased concentrations, and not mainly from increased water discharge as was previously thought[3].

Alterations in how the watersheds of the Mississippi basin work seem to have driven the increased bicarbonate discharges of the past 50 years. This period coincides with agricultural intensification, and changes in crop type and land-management practices in the basin. One must bear in mind, however, that the data from New Orleans, near the mouths of the Mississippi, provide only a highly aggregated picture. So Raymond *et al.*[4] turn to an extensive sub-watershed data set of bicarbonate discharge, land use and precipitation distribution to probe the role of cropland extent, changes in hydrology and increased precipitation.

They find that increases in discharge in agricultural — but not grassland or forested — watersheds outpaced increases in precipitation. This conclusion agrees with recent hydrological studies[6] that found that agricultural changes in the Mississippi basin, especially the expansion of soya-bean row crops, might be reducing evapotranspiration and increasing the fraction of precipitation that reaches the groundwater and flows to streams (Fig. 1). Together with practices such as liming soil to neutralize acidity, this enhanced flow through deeper mineral-rich soils results in increased bicarbonate exports from agricultural areas. The authors suggest that more than 50% of the total increase in bicarbonate export in the past 50 years results from the direct effect of land-use changes. The influence of precipitation increase and CO_2 fertilization from atmospheric CO_2 increase is comparatively small. Agriculturally driven hydrological alterations will, however, magnify the effect of precipitation increases.

Does enhanced weathering tip croplands into becoming a net sink of atmospheric CO_2 in comparison with the situation in pristine ecosystems such as forests or grasslands? The answer is complex. First, the acceleration of weathering reported by Raymond *et al.*[4] is probably limited to mineral-rich soils and particular agricultural practices. More importantly, other direct human pressures must be considered. Besides the removal of biomass during conversion from pristine ecosystems, agricultural activities commonly lead to enhanced erosion of soils and loss of associated organic carbon, providing a potential source of CO_2 to the atmosphere through oxidation downstream[2]. Sedimentation in the reservoirs that are often built to support irrigation can, on the other hand, serve as a long-term sink for eroded-soil organic carbon[2]. Consequently, the net global effect of agricultural soil erosion on atmospheric CO_2 remains contentious[2,7]. Land-management effects on river-carbon exports should be considered in parallel with the more extensively studied effects on nutrient exports. The Mississippi basin represents a notable example of both[8].

An intensification of groundwater flow and bicarbonate flux analogous to, but of smaller magnitude than, that highlighted by Raymond *et al.* seems to be occurring in some Arctic basins. Here, it is an effect of climate change on freeze–thaw cycles and permafrost coverage[9]. Thus, changes in chemical weathering caused both by direct human alterations and by the indirect effects of climate change seem to be a more significant component of regional and global perturbations of the carbon cycle than was thought.

This latest study[4] adds to mounting evidence that the levels of carbon export from developed watersheds today might not be representative of conditions before pressures such as intensive agriculture and acid deposition from industrial emissions became widespread[10]. Long biogeochemical time-series such as that from the New Orleans water-treatment stations are invaluable tools for discerning what the dominant controls on river-carbon exports are, and how they respond to large-scale human activities. ■

Emilio Mayorga is at the Institute of Marine and Coastal Sciences, Rutgers University, 71 Dudley Road, New Brunswick, New Jersey 08901-8521, USA.
e-mail: emiliomayorga@gmail.com

1. Canadell, J. G. *et al. Proc. Natl Acad. Sci. USA* **104,** 18866–18870 (2007).
2. Cole, J. J. *et al. Ecosystems* **10,** 172–185 (2007).
3. Raymond, P. A. & Cole, J. J. *Science* **301,** 88–91 (2003).
4. Raymond, P. A., Oh, N.-H., Turner, R. E. & Broussard, W. *Nature* **451,** 449–452 (2008).
5. Gaillardet, J., Dupré, B., Louvat, P. & Allègre, C. J. *Chem. Geol.* **159,** 3–30 (1999).
6. Zhang, Y.-K. & Schilling, K. E. *J. Hydrol.* **324,** 412–422 (2006).
7. Van Oost, K. *et al. Science* **318,** 626–629 (2007).
8. Donner, S. D., Kucharik, C. J. & Foley, J. A. *Global Biogeochem. Cycles* **18,** GB1028 (2004).
9. Striegl, R. G., Aiken, G. R., Dornblaster, M. M., Raymond, P. A. & Wickland, K. P. *Geophys. Res. Lett.* **32,** L21413 (2005).
10. Monteith, D. T. *et al. Nature* **450,** 537–540 (2007).

HIV/AIDS

Virus kept on a leash

Heinrich G. Göttlinger

Without its Vpu protein, the AIDS-associated virus HIV-1 becomes stuck to the surface of the human cell in which it has replicated. The mysterious factor that tethers HIV-1 is probably a cell-membrane protein.

Mammals have evolved various mechanisms to thwart the spread of intracellular pathogens. Thus, even if the infectious agent breaches the first lines of defence, the infected cells express restriction factors that suppress its further dissemination. One such restriction factor prevents HIV-1 from leaving infected cells and is counteracted by an accessory viral protein called Vpu. On page 425 of this issue, Neil and colleagues[1] characterize this factor and provide tantalizing clues about how it functions*.

To escape the infected cell, HIV-1 buds through the cell surface (thus becoming wrapped in an envelope derived from the host cell membrane) (Fig. 1a) and pinches off. But even if the virus reaches this stage of release, Vpu-deficient HIV-1 particles tend to remain trapped at the cell surface. What keeps them there has been a mystery.

The effect of Vpu on virus release has been perplexing, as it seems to be unrelated to the protein's other function of reducing cellular levels of CD4, the HIV-1 receptor on T cells of the immune system. Also, Vpu's effect on release does not seem to require other HIV-1 components, and its importance for virus release varies widely among cell lines.

*This News & Views article and the paper concerned[1] were published online on 16 January 2008.

It has emerged[2,3] that Vpu counteracts a human antiviral factor that suppresses HIV-1 release by tethering mature viral particles to the cell surface after they have completely pinched off. Such retention of HIV-1 particles at the surface of infected cells can also be induced by human interferon-α, a protein that 'jump-starts' a cell's antiviral defences[4]. Moreover, in an earlier study[5], Neil and colleagues found that Vpu counteracts the effect of interferon-α on HIV-1 release.

The authors now identify[1] an interferon-α-induced human protein that fulfils all the criteria for the tethering factor antagonized by Vpu. The protein, which they aptly name tetherin, is expressed only by cells that require Vpu for HIV-1 release. Decreasing tetherin levels in cells that normally produce this protein allows the release of Vpu-deficient viruses. Furthermore, tetherin expression in cells that normally lack this protein selectively inhibits the release of Vpu-deficient HIV-1. Neil and colleagues' findings suggest that tetherin is highly potent, with only minute quantities being enough to efficiently inhibit HIV-1 lacking Vpu.

How can tetherin entrap outgoing viral particles with such efficiency? Little is known about this small protein, but one aspect is clear — both ends of tetherin are inserted in the cell

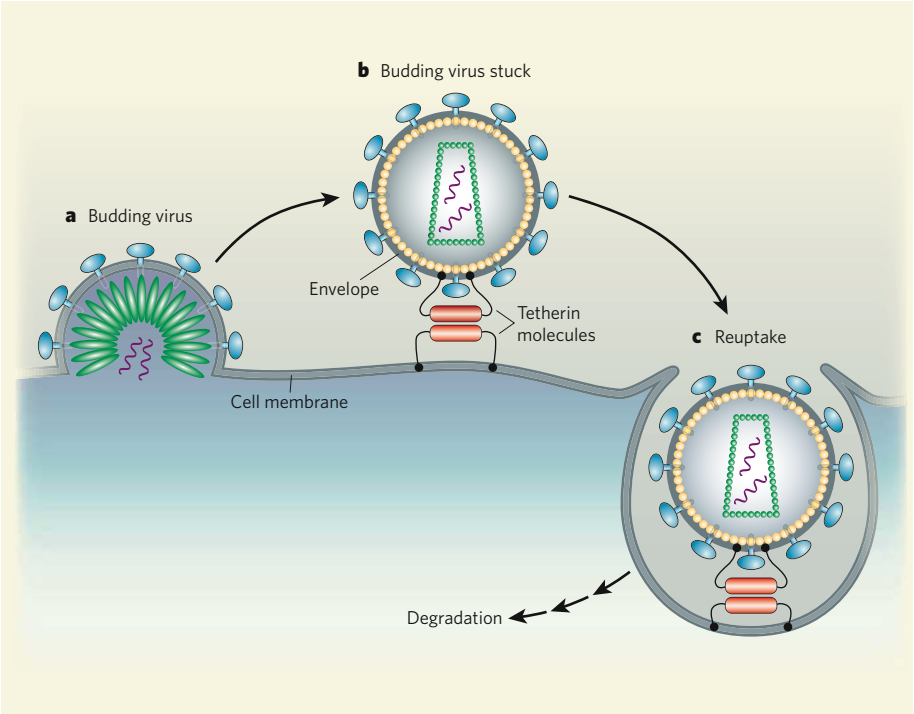


Figure 1 | Model for tetherin-mediated HIV-1 retention. **a**, HIV-1 virions assemble at the cell surface and leave infected cells by budding off from the cell membrane. Assembling virions thus become covered by a cell-membrane-derived envelope. **b**, Tetherin is localized on the outside of the cell surface, but is anchored in the cell membrane at both ends. Identifying tetherin as the cellular factor that prevents HIV-1 release, Neil *et al.*[1] speculate that this protein is also taken up by the budding virion and is firmly anchored in the viral envelope. Virion- and cell-associated tetherin could then interact, preventing the release of the mature virion from the cell surface. **c**, The authors also propose that, through one of its membrane anchors, tetherin might connect to the cell's endocytotic machinery, which engulfs extracellular material in cell-membrane invaginations and imports it into the cell. This could lead to the reuptake of mature virions by infected cells and their subsequent degradation by the cell's digestive system.

membrane through its unusual pair of membrane anchors[6]. The central portion of the protein faces the outside of the cell[6] and seems to interact with the same region of another tetherin molecule[7]. Thus, assuming that tetherin is incorporated into the membrane enveloping Vpu-deficient HIV-1 particles, Neil *et al.*[1] envisage a situation in which tetherin molecules that end up in the viral envelope hold the virus back by interacting with tetherins that are associated with the cell surface (Fig. 1b). Tetherin also interacts with the cell's endocytotic — or internalization — machinery[8], which might play a part in the reuptake of the trapped viruses into the cell and their degradation in intracellular compartments[3] (Fig. 1c).

How does Vpu counteract the effects of tetherin? Neil *et al.*[1] did not detect reduced tetherin levels in the presence of Vpu, although this could have been due to experimental overexpression of tetherin. A previous study[9], however, found that levels of the protein now identified as tetherin are reduced by an entirely unrelated human virus, Kaposi's sarcoma-associated herpesvirus (a finding that also hints at the broad antiviral activity of this protein.) The viral protein responsible in this case, K5, is a ubiquitin ligase enzyme, which adds the molecular tag ubiquitin to proteins, marking them for degradation. K5 is structurally similar to a family of human ubiquitin ligases, at least one of which can strongly reduce the cellular levels of tetherin.

With what turns out to be remarkable foresight, the authors of this earlier study[9] also tested Vpu and found that it, too, decreases the normal cellular levels of tetherin. These observations raise the possibility that Vpu uses a cellular ubiquitin ligase to dispose of tetherin, as it does for CD4. But other possibilities, such as tetherin relocalization by Vpu, rather than its degradation, are also possible.

Only HIV-1 and a handful of its cousin viruses make Vpu, which poses the question of how other related viruses deal with tetherin. For HIV-2 (the less virulent human AIDS virus), a protein that mainly facilitates viral entry substitutes for Vpu, promoting virus release[10], and we will probably soon learn whether this protein also antagonizes tetherin.

Because the amino-acid sequence of tetherin differs considerably among mammals, some HIV-1-related animal viruses might find it difficult to overcome human tetherin, preventing them from becoming human viruses. Conversely, it is worth investigating whether tetherin contributes to the inability of HIV-1 to efficiently escape from most rodent

50 YEARS AGO

"Symmetry of snow crystals" — Despite an infinite variety in the patterns which appear, there does often exist a remarkable symmetry in the six rays [of snowflakes]... Since each of the six arms of the crystal would appear to be growing independently, this symmetry poses a problem in crystal growth, for it almost seems as if each arm of the six-ray star 'knows' what the other five are doing and follows suit... I conjecture that the crystal is vibrating mechanically as a flat plate, in fact as a Chladni plate, with of course a hexagonal symmetry... When the molecules adhere to achieve growth at any particular region on one arm, this immediately introduces a localized damping action on the vibrations... But this very damping is at once felt simultaneously at the corresponding positions on the other five arms. Thus molecules arrive and adhere easily at the other five arms in precisely the same situations as on the first arm; in other words, what happens on any one arm tends to be repeated on the others...
From *Nature* 25 January 1958.

100 YEARS AGO

The product of the world's gold mines for the year 1906 could all be packed in a room 10 feet square and 9 feet high... The value of this 90 cubic feet of gold was nearly eighty-one and a half millions sterling, and its weight nearly 674 tons... Eighty-three per cent. of the total output was secured by the Anglo-Saxon world. According to calculations and estimates made in 1900 by the director of the United States mint, the gold taken from the mines of the world since the discovery of America has amounted in quantity to about 21,424 tons... Nineteen per cent., or nearly one-fifth of the whole, has been mined in the last ten years, and nearly 30 per cent. in the last twenty years.
From *Nature* 23 January 1908.

50 & 100 YEARS AGO

cells[11], which has hampered efforts to develop small-animal models of HIV-1 infection. Even in human cells, Vpu might not always be able to overcome the powerful effect of tetherin, as the release of infectious Vpu-positive HIV-1 can be inhibited with high doses of interferon-α (ref. 5). Thus, an understanding of how tetherin works, and how Vpu fends it off, could lead to strategies to limit the spread of HIV-1 and other viruses that target humans. ■

Heinrich G. Göttlinger is in the Program in Gene Function and Expression, Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, Massachusetts 01605, USA.
e-mail: heinrich.gottlinger@umassmed.edu

1. Neil, S. J. D., Zang, T. & Bieniasz, P. D. *Nature* **451,** 425–430 (2008).
2. Varthakavi, V., Smith, R. M., Bour, S. P., Strebel, K. & Spearman, P. *Proc. Natl Acad. Sci. USA* **100,** 15154–15159 (2003).
3. Neil, S. J. D., Eastman, S. W., Jouvenet, N. & Bieniasz, P. D. *PLoS Pathogens* **2,** 354–367 (2006).
4. Poli, G., Orenstein, J. M., Kinter, A., Folks, T. M. & Fauci, A. S. *Science* **244,** 575–577 (1989).
5. Neil, S. J. D., Sandrin, V., Sundquist, W. I. & Bieniasz, P. D. *Cell Host Microbe* **2,** 193–203 (2007).
6. Kupzig, S. *et al. Traffic* **4,** 694–709 (2003).
7. Goto, T. *et al. Blood* **84,** 1922–1930 (1994).
8. Rollason, R., Korolchuk, V., Hamilton, C., Schu, P. & Banting, G. *J. Cell Sci.* **120,** 3850–3858 (2007).
9. Bartee, E., McCormack, A. & Früh, K. *PLoS Pathogens* **2,** e107 (2006).
10. Bour, S., Schubert, U., Peden, K. & Strebel, K. *J. Virol.* **70,** 820–829 (1996).
11. Mariani, R. *et al. J. Virol.* **74,** 3859–3870 (2000).

MATERIALS SCIENCE

Lilliputian light sticks

Melissa Fardy and Peidong Yang

Building two different fluorescing dyes into a composite organic nanocrystal makes a tunable light generator. At just the right dye proportions, a low-cost, highly efficient source of white light is the result.

If you have ever wondered what makes that ghostly colour in the light sticks used by trick-or-treaters on a Hallowe'en night, wonder no more: a typical answer might be a fluorescing organic molecule such as 5,6,11,12-tetraphenyltetracene, also known as rubrene. Writing in *Advanced Materials*, Zhao *et al.*[1] describe how they used such organic molecules to make white-light-emitting composite nanocrystals that are visible only under a microscope. Cute as these lilliputian light sticks are, they might also point the way to a new generation of light sources.

A typical light stick contains two chemicals: hydrogen peroxide and a phenyl oxalate ester. When these two substances are mixed, energy is released. That energy excites a suitable fluorescent dye, causing it to emit a photon. The wavelength of the photon, and so the colour of the emitted light, depends on the structure of the dye (Fig. 1a). Rubrene, for example, is an orange-emitter; the related molecule 1,3,5-triphenyl-2-pyrazoline (TPP) is blue.

Zhao *et al.*[1] use a process called physical vapour deposition, which is a common way of making organic nanocrystals, to co-evaporate rubrene and TPP at 200–300 °C and condense them onto a substrate at a lower temperature. The result is a collection of uniform organic nanorods with diameters of hundreds of nanometres and lengths of several micrometres (Fig. 1b). Each nanorod functions as a tiny light stick, with its colour determined by the molecular ratio of the two organic dyes.

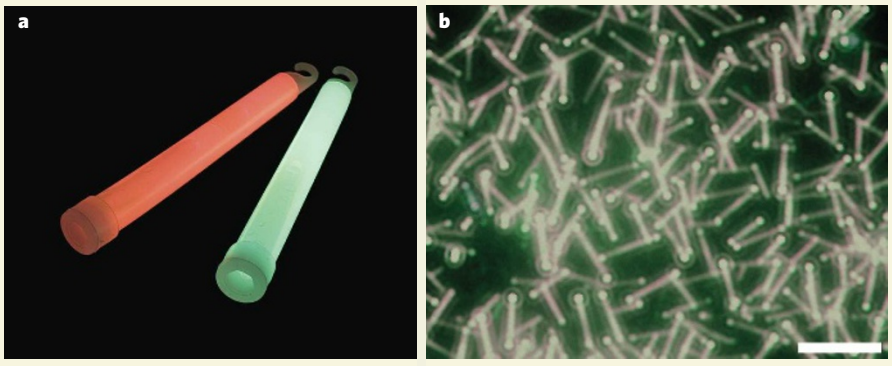
The energy-transfer mechanism in these nanorods is known as intermolecular fluorescence resonance energy transfer (IFRET), and is fundamentally different from that of a typical light stick. In a typical IFRET process[2], energy is absorbed by one fluorescent molecule (blue-emitting TPP in Zhao and colleagues' case), and transferred non-radiatively to another fluorescent molecule (orange-emitting rubrene). Consequently, the emission of the first molecule is quenched, and the emission of the second is enhanced. The efficiency of this process depends sensitively on the degree of electronic coupling between the two molecules. In an amorphous thin film, for example, where TPP and rubrene molecules are intimately mixed, the emission of TPP can be almost completely quenched with a very small amount of rubrene.

The nanorods prepared by Zhao *et al.* show an intermediate degree of IFRET owing to an unusual structural feature: as X-ray diffraction studies reveal, the rubrene nanocrystals are uniformly embedded in a crystalline TPP matrix. This results in incomplete quenching of the blue emission from TPP, even with decent levels of rubrene 'doping', leading to colour mixing of the orange and blue emissions. Importantly, at the proper molecular ratio, it becomes possible to generate stable white light.

Among researchers investigating comparable lighting devices based on inorganic semiconductors, this kind of colour tunability is often achieved by using homogeneous mixtures of different compounds. A good example is recent research into indium gallium nitride (InGaN) materials, which are considered excellent candidates for solid-state lighting applications. Here, a mixture of indium nitride and gallium nitride is used to systematically shift the emission of the materials from ultraviolet wavelengths to the near-infrared[3]. Similarly, doping has commonly been used in organic light-emitting diodes (OLEDs), both to tune their emission colour and to improve their luminescence efficiency[4].

Many of these doping studies have used amorphous thin films, in which charge carriers have low mobility. Zhao and colleagues' composite organic nanorods not only represent an unusual source of stable white light, but, because of their ordered crystalline natures, should offer better transport properties, and hence better optoelectronic performance. Single crystalline nanowires of the aromatic hydrocarbon hexathiapentacene have been shown to have charge-carrier mobilities almost ten times those of more disordered thin-film structures[5]. To sound a note of caution, however, the emission efficiency of these composite nanorods has yet to be determined. Their integration into a functional electroluminescent device must also be demonstrated.

Because of the great tunability of both their crystal and their electronic structures, inorganic semiconductor nanowires have proved to be workhorses of nanoscale science and engineering[6], finding applications in various electronic, photonic and sensing devices.



VISUALS UNLIMITED/CORBIS

WILEY-VCH

Figure 1 | Great white hope. a, Commercial light sticks containing fluorescent dyes are available in various colours. **b**, Zhao *et al.*[1] engineer similar rods on a tiny scale (scale bar, 5 μm), incorporating two dyes, TPP and rubrene, so that the rods emit white light.