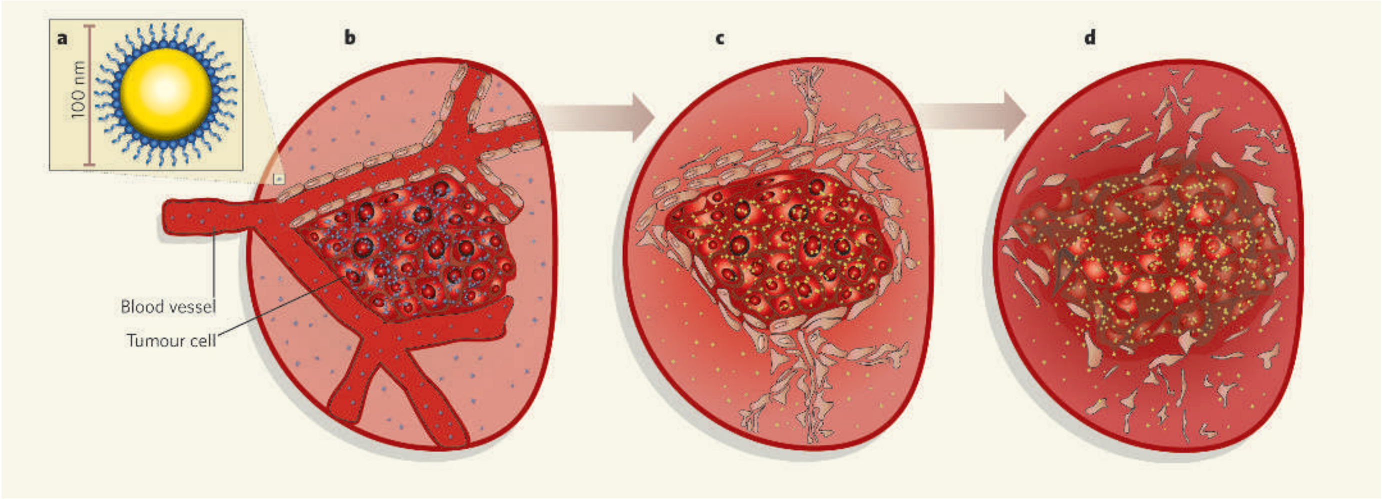

Figure 1 | Step-by-step in fighting cancer. The delivery system of Sengupta *et al.*[2] causes the sequential loss of blood vessels and the death of tumour cells. **a**, Nanometre-scale particles have an outer lipid layer (blue) and an inner core (yellow). **b**, Once injected into the bloodstream, the particle is selectively taken up into tumour tissues, where the lipid layer rapidly releases a drug that kills endothelial cells and disrupts blood vessels. **c**, The inner core gradually releases a chemotherapeutic drug to destroy the cancer cells (**d**).

humans[8]. It is promising, in this regard, that Sengupta and colleagues' system produced no increase in the expression of a factor (HIF-1α) that can link the low oxygen levels resulting from reduced blood flow with potential resistance to drug therapy and tumour invasiveness. Finally, in contrast to combretastatin, many anti-angiogenic drugs require prolonged tissue exposure to shut down the vasculature, and so may not be amenable to the particular approach described by Sengupta and colleagues.

The general concept of timing the availability of drugs aimed at specific stages or targets in cancer is widely applicable, however, and is consistent with similar efforts to promote blood-vessel formation in diseases involving insufficient blood flow[9]. Appropriate design of drugs will allow targeting of cancer cells or other specific cell types[10], and the delivery device described by Sengupta *et al.* could readily be modified for this. It may also be necessary to target multiple aspects of angiogenesis, either by using several drugs or by using a drug that interferes with several pathways (for example, MAPK inhibitors)[11], to prevent tumours from switching on alternative angiogenesis pathways. Ultimately, combining the development of advanced drug-delivery systems with the identification of early markers of cancer may allow early and highly effective intervention, and help to accomplish the US National Cancer Institute's stated goal of eliminating the suffering and death from cancer by 2015. ■

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CARBON CYCLE

The age of the Amazon's breath

Peter A. Raymond

The inorganic carbon carried in rivers of the Amazon basin seems to originate largely from the decomposition of young plant material — a finding that improves our understanding of the role of rivers in the carbon cycle.

Increases in atmospheric carbon dioxide from the burning of fossil fuels have unknown effects on the global climate and economy. Scientists aim to understand more about these effects by studying the mechanisms that control the exchange of carbon between land, the atmosphere and the oceans. Processes that remove CO_2 from the atmosphere, where it could cause global warming, and move it into long-term storage on land or in the oceans, are of particular interest in this context. Because they connect land and sea, rivers are a vital link in these processes (Fig. 1, overleaf). On page 538 of this issue, Mayorga *et al.*[1] provide insights into how this river linkage works for the world's largest river system — the Amazon.

There are two main forms of carbon: organic (such as the biomass within a tree) and inorganic (CO_2 in the atmosphere, for example). These forms are intimately coupled through photosynthesis in plants, which creates organic from inorganic carbon, and decomposition, which returns plant-produced carbon to its inorganic form. In rivers, organic and inorganic carbon exist in approximately equal proportions, and originate mainly when rainfall hits continental surfaces and either dissolves carbon, or carries it to rivers in particulate form.

A single river can drain a landscape that has a wide array of plant species, land uses, soils and climatic zones. This complexity has made it difficult to pin down exactly where most river carbon originates, how long it existed on land before being carried to a river, and how reactive it might be once in a river and, later, in the coastal ocean. Most of the carbon in rivers ultimately comes from atmospheric CO_2 and therefore represents mobile 'greenhouse carbon' that either cycles back to the atmosphere and contributes to global warming, or enters a storage compartment that is not in contact with the atmosphere (coastal sediments, for example; Fig. 1).

The Amazon basin is a central player in the global carbon balance because it stores large amounts of carbon in biomass above ground, and this carbon is being returned to the atmosphere by slash-and-burn agriculture[2]. But the

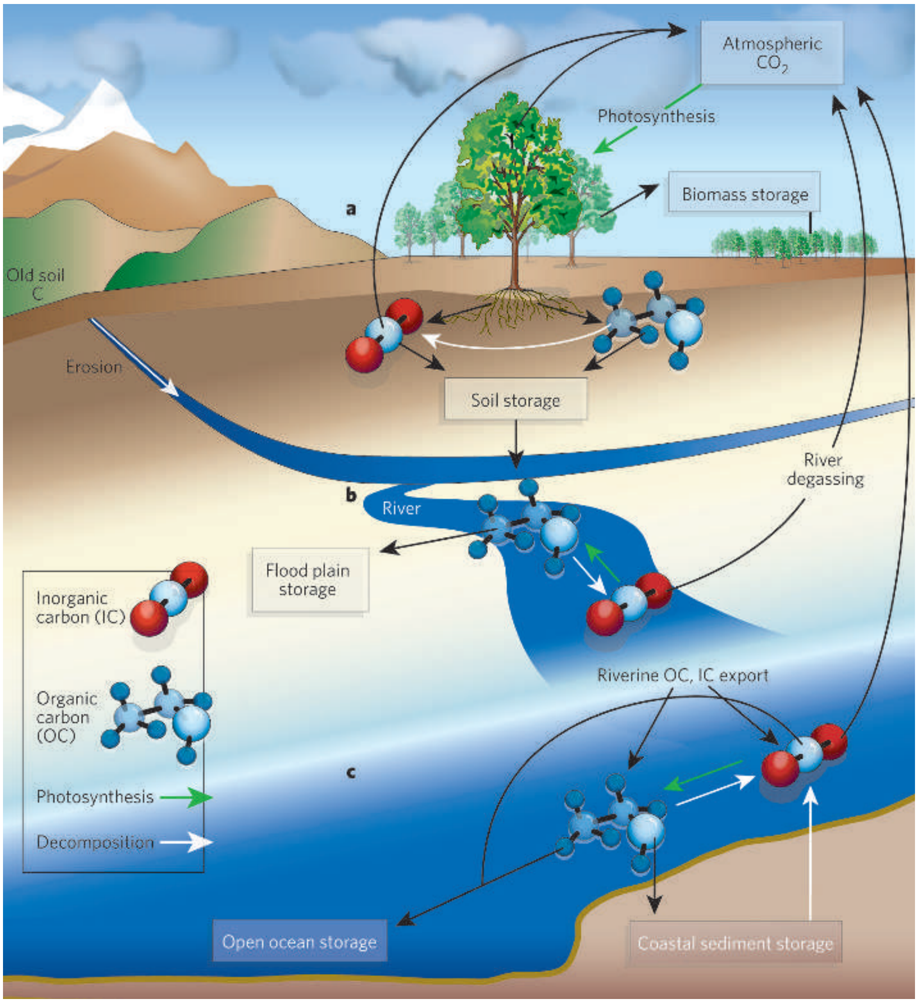

Figure 1 | **Rivers and the carbon cycle. a,** Photosynthesis in land plants fixes atmospheric CO_2 (inorganic carbon) as organic carbon, which is either stored as plant biomass or in soil, or is decomposed back to CO_2 through plant and soil respiration. This CO_2 can return to the atmosphere or enter rivers; alternatively, it can react with soil minerals to form inorganic dissolved carbonates that remain stored in soils or are exported to rivers. **b,** The transformations of organic to inorganic carbon through decomposition and photosynthesis continue in rivers; here, CO_2 will re-exchange with the atmosphere ('degassing'), or be converted to dissolved carbonates. These carbonates do not exchange with the atmosphere and are mainly exported to the coastal ocean. Organic carbon is also exported to the ocean, or stored in flood plains. **c,** In the coastal ocean, photosynthesis, decomposition and re-exchanging of CO_2 with the atmosphere still continue. Solid organic carbon (such as soil particles and phytoplankton cells) is buried in coastal sediments, where it is stored or decomposes to inorganic carbon and diffuses back into coastal waters. Dissolved inorganic and organic carbon are also exported to the open ocean, and possibly deep-ocean waters, where they are stored for many centuries.

remoteness of the Amazon and the rapid changes in land use in the region have made it difficult to determine the exact size of carbon fluxes within the basin[2]. It was only recently shown[3] that a significant amount of terrestrial organic carbon in the Amazon basin decomposes to CO_2 and is cycled back to the atmosphere through the basin's network of rivers, which 'breathe' CO_2 out in a process known as degassing. Before this, rivers had not been incorporated into the Amazon's carbon budget at all. The finding was significant, as the degassing of CO_2 from rivers occurs in many different regions of the globe[4]. The importance of understanding where this carbon comes from, and how old it is, is therefore not limited to the tropics.

Mayorga *et al.*[1] argue convincingly that the CO_2 added back to the atmosphere from the Amazonian rivers by degassing is balanced by the decomposition of organic carbon from recent plant growth. This implies that the inorganic carbon does not originate from large-scale decomposition of organic carbon previously held in long-term storage on land. The CO_2-degassing from the tropics thus simply represents the cyclical movement of the gas from the atmosphere, through land and rivers and then back to the atmosphere, and does not represent an additional input of greenhouse gas.

According to Mayorga *et al.*, this cyclical movement seems to happen, at least in the tropics, on a timescale of less than five years. They come to this conclusion by analysing the ratios of the two carbon isotopes, ^{14}C and ^{13}C, contained in both inorganic and organic carbon at different locations in the Amazon basin. The amount of ^{14}C, a radioactive isotope with a half-life of 5,730 years, can be used to determine the age of a sample (the familiar technique of carbon dating) and also provides information on the source of the carbon. The proportion of the stable carbon isotope ^{13}C supplies more clues to the origin of the carbon[5].

Although Mayorga and colleagues find that most of the organic carbon, particularly in the lowland rivers of the Amazon basin where much of the decomposition to CO_2 and degassing occurs, is indeed young, they also show that the Andean headwaters of the Amazon carry suspended particulate organic carbon that is many centuries to thousands of years old. This result is consistent with other studies on the ages of organic carbon in rivers[6–8] that also pinpoint the origin of old organic carbon in mountain headwaters as mechanically eroded old soil carbon and organic matter, known as kerogen, that is found in sedimentary rocks. Interestingly, the source of old carbon in temperate rivers is still unknown[9].

In the Mayorga study[1], the isotopic signal of the older headwater organic carbon disappears farther down the river network, the carbon presumably becoming buried or decomposed. Although the mountainous regions of the Amazon headwaters are losing soil carbon to erosion, little of this material seems to reach the coastal ocean. The small fraction of aged particulate carbon that does escape the Amazon is then reworked considerably in coastal-shelf sediments[10,11], leaving a very small amount for export and burial in the open ocean.

Mayorga and colleagues' contribution[1] provides a conceptual framework of the role of streams and rivers in tropical carbon budgets on which future studies can build. Research should now focus on how land use and climate change have altered the timescales of the connections between the atmosphere, land and water reported by Mayorga *et al.*. While we continue to burn fossil fuels, and atmospheric CO_2 concentrations continue to increase, scientists will be able to return to this benchmark study to understand how the Amazon basin continues to respond to environmental change. ■

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