which recognizes lipopolysaccharide, a component of the cell walls of some bacteria (Fig. 1). In that situation, the succinate is generated from the amino acid glutamine and acts to stabilize the transcription factor HIF-1α, which in turn leads to an increase in activity of HIF-1α-dependent genes, one of which encodes the pro-inflammatory molecule IL-1β (ref. 2). Of direct relevance to the current study are observations that implicate TLR4 (and TLR2) in IR injury in the heart[10,11]. It is possible that macrophage TLRs are bound by products of damaged tissue during ischaemia, activating the cells to produce succinate and thus contributing to IR injury.

Succinate is also elevated in other inflammatory conditions, including colitis[6] and rheumatoid arthritis[7], and it is possible that succinate generates ROS in those conditions through complex I, as shown by Chouchani and colleagues. And binding of succinate to a receptor called SUCNR1, which is expressed by dendritic cells of the immune system, has been shown to enhance the production of pro-inflammatory molecules by these cells when they are activated by TLR binding.

Chouchani and co-workers' study should therefore stimulate further analysis not only of the importance of succinate as a mediator of IR injury, but also of the molecule's broader role in inflammatory conditions and disease states involving mitochondrial ROS. Preventing succinate accumulation could bring benefits by limiting inflammation in conditions such as sepsis or rheumatoid arthritis, and may provide a new approach for limiting the damage caused by heart attack or stroke. Ultimately, the targeting of the events described here could result in much-needed therapies for patients for whom there are currently limited options. ■

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BIOGEOCHEMISTRY

Agriculture and the global carbon cycle

Evolving agricultural practices dramatically increased crop production in the twentieth century. Two studies now find that this has altered the seasonal flux of atmospheric carbon dioxide. SEE LETTERS P.394 & P.398

NATASHA MACBEAN & PHILIPPE PEYLIN

The concentration of carbon dioxide in the atmosphere undergoes seasonal, cyclic variation, the amplitude of which has increased by up to 50% in the Northern Hemisphere over the past 50 years[1,2]. Several factors have been proposed to explain this increase[3–5], including the response of the terrestrial biosphere to climate change, increased fossil-fuel emissions, and changes in oceanic fluxes and atmospheric transport of CO_2, but the relative magnitude and latitudinal contribution of each are still debated. In two studies published in this issue, Gray *et al.*[6] (page 398) and Zeng *et al.*[7] (page 394) reveal that intensification of agriculture has contributed substantially to this trend.

The atmospheric CO_2 concentration has increased at an unprecedented rate during the past few decades. We know from a global network of atmospheric CO_2 measurements that roughly only half of the emissions associated with fossil-fuel use and land-use change remain in the atmosphere[8]. The ocean and land surface must therefore act as a global carbon sink, although its magnitude and location — and the mechanisms driving it — remain uncertain because of the difficulty of measuring and modelling carbon stocks and fluxes at large scales. Improving our knowledge of the driving mechanisms is essential for accurate projections of the global carbon budget under future climate and land-use changes.

Atmospheric CO_2 data can provide an integrated, albeit indirect, measure of the global carbon budget, and so it is crucial to understand the causes of spatiotemporal variability in these data. Much focus has been put on the growth rate of the annual mean CO_2 concentration and its year-to-year variability. By contrast, less attention has been paid to the observed increase in the amplitude of the seasonal CO_2 cycle in the extratropics of the Northern Hemisphere (regions at latitudes of 30° to 90° N), which results from higher carbon uptake in the summer and greater release in the winter.

Agricultural productivity has previously been proposed as a possible cause[4]. Crops can have a stronger impact on carbon uptake than can natural vegetation, because of their high productivity. The widespread use of fertilizers, irrigation and high-yield crop cultivars has led to a threefold growth in global agricultural production in the past 50 years, with only a small expansion of cropland area[9] (Fig. 1). Gray *et al.* and Zeng *et al.* are the first to demonstrate that agricultural productivity really has affected the amplitude of the annual CO_2 cycle.

RUI DIAS-AIDOS/THINKSTOCK

Figure 1 | Agricultural revolution. The expansion of irrigation infrastructure during the twentieth century helped to intensify crop production and improve yields. Two papers[6,7] report that this intensification has increased the amplitude of seasonal variations of atmospheric carbon dioxide levels in the Northern Hemisphere.

Gray and colleagues used a carbon-accounting method and crop-production statistics published by the Food and Agriculture Organization of the United Nations to calculate how much carbon was taken up by four major crop types — maize (corn), wheat, rice and soya beans (collectively called MWRS) — in the northern extratropics each year from 1961 to 2008. They found that the annual exchange of carbon between crops and the atmosphere increased by 0.33 petagrams (1 petagram is 10^{15} grams) during this period, mainly because of farming in northern China and the midwestern United States. The authors conclude that the rise in MWRS production is responsible for 17–25% of the increase in the seasonal carbon flux required to explain observed changes in atmospheric CO_2 seasonality[2], with maize alone accounting for 66% of this increase.

Zeng and co-workers followed a more 'bottom-up' approach, adapting a terrestrial biosphere model known as VEGAS to include a simple representation of changing agricultural management practices for a generic crop functional type (a single description that represents an average of the growth characteristics of all crops). According to their study, enhanced agricultural productivity in the mid-latitudes contributes about 45% of the increasing amplitude of global net surface carbon fluxes between 1961 and 2010, compared with 29% from climate change and 26% from CO_2 fertilization (increased photosynthesis caused by rising atmospheric CO_2 levels).

Although both studies highlight the influence of agricultural intensification, they calculate considerably different values for its contribution to the increasing amplitude. Why is this? Gray *et al*. focused on the change in productivity in the extratropics, where MWRS accounts for only 68% of dry biomass production from crops — which, as they point out, may lead to a substantial underestimate in their proposed contribution. Zeng and colleagues, however, performed a global simulation with a generic crop model and assumed that crop growth is driven solely by favourable climate conditions. This may bias their results towards higher carbon uptake, because they do not account for winter wheat varieties that are commonly grown during the period of net carbon release.

So is the contribution of agriculture to the increasing seasonal amplitude of atmospheric CO_2 closer to 20%, as Gray and co-workers estimate, or around 50%, in line with Zeng and colleagues' result? The jury is still out. 'Top-down' data-driven approaches, such as those used by Gray *et al*., conceivably provide the best available crop-specific estimates. Process-based modelling frameworks are complementary; their strength lies in their potential to examine the relative influence of all possible causal mechanisms, as undertaken by Zeng and co-workers. This requires the processes to be accurately represented, but current-generation terrestrial biosphere models vary in their sensitivity to temperature, precipitation and CO_2 fertilization[8]. Moreover, the effects of nutrient limitation, and of changes in the age distribution and management of forests, are often missing or inadequately represented in models[8]. All of these issues may affect simulations of the temporal dynamics of carbon fluxes.

The terrestrial biosphere is thought to be the main driver of changes in atmospheric CO_2 seasonality in the Northern Hemisphere[2,5]. However, we have not yet clearly differentiated between the many contributory effects, such as increased growing-season length[1,10] and changing rates of respiration[11] due to warmer temperatures; enhanced plant growth caused by climate change, CO_2 fertilization and/or the deposition of nitrogen compounds from the atmosphere[4,5]; and human-induced disturbance of the natural ecosystem, for example from fire or grazing[12]. The intensification of agricultural productivity must now join the list.

Finally, an atmospheric-transport model that accounts for complex mixing processes is necessary to properly assess the different contributions to increased seasonality of atmospheric CO_2 concentrations and their spatial distribution. Shifts in the seasonal variations of fossil-fuel emissions and ocean CO_2 fluxes may have been overlooked, and the influence of tropical regions, although less seasonal, should be considered in future studies. ■

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PLANT SCIENCE

Leaf veins share the time of day

Techniques for isolating and analysing leaf cell types have now been developed, leading to the discovery that circadian clocks in the plant vasculature communicate with and regulate clocks in neighbouring cells. SEE LETTER P.419

MARÍA C. MARTÍ & ALEX A. R. WEBB

The flowering plants in our gardens and in the countryside provide us with a colourful landscape, and are often thought of as nothing more than a dormant backdrop to our lives. But beneath their attractive exteriors, plants are capable of complex behaviour, such as measuring time. In this issue, Endo *et al.*[1] (page 419) identify circadian clocks in leaf veins that signal to neighbouring cells — an indication that plant circadian clocks might be organized into a hierarchical system.

Plant leaves are sophisticated organs comprised of several cell types, each with a different function. Epidermal cells line the leaf surface, with the bulk of the leaf being composed of mesophyll cells, which are responsible for photosynthesis. In addition, the leaves and stem are infiltrated by the veins of the plant vasculature, which transports water and molecules such as sugars around the plant. Endo and colleagues developed a method for efficiently isolating epidermal, mesophyll and vasculature cells from *Arabidopsis thaliana* plants, allowing them to study spatiotemporal gene expression and circadian-clock regulation at high resolution.

Multicellular organisms ensure that cells are performing the correct processes at the right time of day through their circadian clocks, which have a period of approximately 24 hours, allowing anticipation of dawn and dusk. The timing of about 30% of gene activity in plants is modulated by circadian clocks. A clock's core consists of around 20 genes divided into two interlocking pathways — a morning loop of genes that are active during daylight hours and an evening loop active from dusk.

The researchers observed that morning-loop genes such as *CCA1* were more active in the mesophyll than in the vasculature, whereas the opposite was true of evening-loop genes such as *TOC1*. Furthermore, when