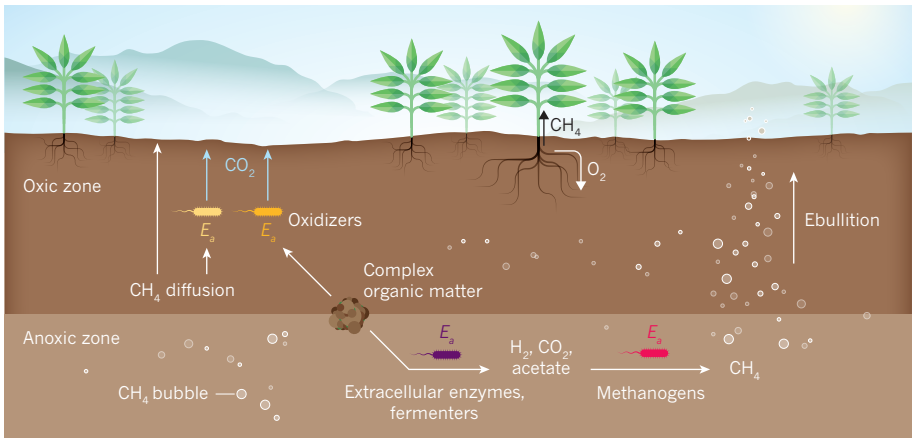

Figure 1 | Emissions network. Methane (CH_4) is generated by microorganisms (methanogens) that metabolize substrates produced through the breakdown of complex organic matter by extracellular enzymes and fermentative microorganisms. The rate of methane emission to the atmosphere is influenced by these microorganisms' individual sensitivities to temperature (indicated by E_a), and by chemical conditions, such as oxygen availability, that divert the flow of carbon to microbial competitors that oxidize organic matter to carbon dioxide. Methane emission also depends on gas transport by diffusion, by bubble ebullition and in the vasculature of plants, and on the fraction of methane that is consumed by methane-oxidizing microorganisms. Despite this complex array of factors, Yvon-Durocher *et al.*[2] report that the response of methane emissions at the ecosystem level can be described by the simple Arrhenius relationship.

and promotes methane consumption.

In their analysis of 127 studies of the ecosystem-level dependence of methane emission on temperature, Yvon-Durocher *et al.* acknowledge this complex array of factors, but conclude that the aggregate temperature response is nonetheless described by the Arrhenius equation, with an apparent activation energy (E_a) of 0.96 electronvolts, similar to the 1.10 eV observed in pure cultures of methanogens. E_a is a measure of temperature sensitivity; for example, 0.96 and 1.10 eV correspond, respectively, to a 3.5- and 4.2-fold increase in rate constant for an increase in temperature from 20 °C to 30 °C.

Statistically speaking, the large number of studies considered allows for a confident statement that the calculated mean E_a (0.96 eV) accurately reflects the mean temperature sensitivity of methane-emitting ecosystems — assuming that the sites that comprise the data set represent a random sample of all such environments. But the impact of factors other than temperature seems evident in the scatter and spread of the individual data sets considered by the authors. For example, about 40% of the studies considered had Arrhenius-plot correlation coefficients (r^2) of less than 0.5, which indicates that less than half of the variance in those emission data is explained by the Arrhenius relationship, and about 10% of the studies measured methane emissions that were higher at lower temperatures (opposite to the effect predicted by the Arrhenius equation).

The reported ecosystem-level E_a is higher than what has been called the "universal temperature dependence" of aerobic metabolism[4] — an E_a of 0.67 ± 0.15 eV that encompasses the metabolism of a wide range of plants, protozoa, invertebrates and vertebrates — and is also higher than the average E_a (0.72 eV) observed for a diverse group of 50 aerobic and anaerobic microorganisms[5]. The higher average E_a reported here for methanogenic ecosystems could reflect either that the biochemistry of methanogens (which have an average E_a of 1.10 eV) directly limits methane emissions in some ecosystems, or that the organisms that supply methanogens with substrates have similarly high temperature dependence. Nevertheless, the clear implication of these findings is that methane production will increase more steeply with temperature than would be captured by climate-change models that assume methane emission is governed by more typical (lower) values of E_a. For example, over the range of global warming projected[6] for this century (1.0–3.7 °C), an E_a of 0.96 eV suggests a 14–63% increase in methane emission compared with 10–40% for an E_a of 0.67 eV.

Yvon-Durocher and colleagues' findings constrain, and perhaps simplify, one piece of a much larger climate-change puzzle. Feedbacks from methane emissions in response to global climate change will ultimately derive from a combination of the direct temperature effects considered here and indirect effects such as thawing of permafrost (and the resultant availability of new organic matter), changes in vegetation, and large-scale inundation or drying of soils and wetlands. Moreover, methane's proportionate contribution to global warming (about 20% over the past century) may actually diminish as carbon dioxide takes an increasingly prominent role in the future[7]. But in this complex problem — unlike methane's flux to the atmosphere — every bit helps. ■

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1. Kirschke, S. *et al. Nature Geosci.* **6,** 813–823 (2013).
2. Yvon-Durocher, G. *et al. Nature* **507,** 488–491 (2014).
3. Riley, W. J. *et al. Biogeosciences* **8,** 1925–1953 (2011).
4. Gillooly, J. F. *et al. Science* **293,** 2248–2251 (2001).
5. Tijhuis, L. *et al. Biotech. Bioeng.* **42,** 509–519 (1993).
6. Stocker, T. F. *et al.* in *Climate Change 2013: The Physical Science Basis. Working Group I Contribution to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change* (eds Stocker, T. F. *et al.*) Technical Summary, 33–115 (Cambridge Univ. Press, 2013).
7. Prather, M. *et al.* (eds) in *Climate Change 2013: The Physical Science Basis. Working Group I Contribution to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change* (eds Stocker, T. F. *et al.*) Annex II, 1395–1445 (Cambridge Univ. Press, 2013).

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CLIMATE SCIENCE

A high bar for decadal forecasts of El Niño

Climate simulations suggest that multi-decadal periods of high and low variability in the phenomenon known as the El Niño–Southern Oscillation in the tropical Pacific Ocean may be entirely unpredictable.

PEDRO DINEZIO

The episodic warming and cooling of the surface temperature of the tropical Pacific Ocean, known as the El Niño–Southern Oscillation (ENSO), causes year-to-year climate fluctuations, affecting weather, ecosystems and economies around the world. The occurrence of these episodes is not regular. For example, whereas the period covering the years 1970–2000 witnessed the strongest El Niño (warming) events on record, the years since 2000 have experienced fewer and weaker such events. Writing in the *Journal of*

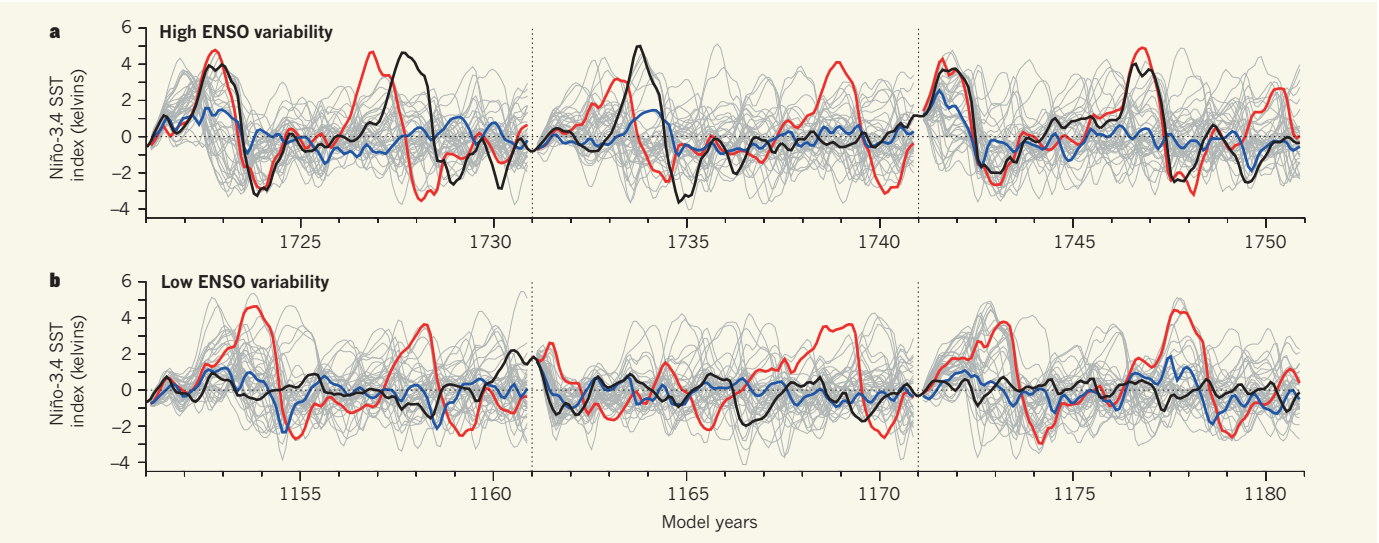

Figure 1 | Decadal forecasts of El Niño–Southern Oscillation activity. Using their GFDL-CM2.1 climate model, Wittenberg *et al.*[1] performed simulations of the variability of the El Niño–Southern Oscillation (ENSO), here quantified using the Niño-3.4 sea surface temperature (SST) index. Two distinct epochs are shown, characterized by high (**a**) or low (**b**) ENSO variability in the model's control run (black curves). For each epoch, 3 sets of 40 simulations are initialized from model years 1721, 1731 and 1741, and from 1151, 1161 and 1171, respectively (faint grey curves). Model years do not coincide with historical years. The simulations differ in only one tiny perturbation applied to the model's initial conditions. For both epochs, at least one simulation out of 40 exhibits high (red curves) or low (blue curves) ENSO variability, indicating that the level of activity is unpredictable. (Graphic courtesy of Andrew Wittenberg.)

Climate, Wittenberg *et al.*[1] make the case that these multi-decadal epochs of enhanced and subdued ENSO activity occur randomly and therefore may be unpredictable.

Changes in ENSO behaviour from decade to decade are commonly seen in historical observations and palaeoclimate proxy records[2–5]. These variations were first put into context by Wittenberg in an earlier study[6], which examined a 2,000-year simulation based on a fairly realistic climate model, known as GFDL-CM2.1. This concluded that decadal- to centennial-scale changes in ENSO behaviour can be internally generated by the model in the absence of any external forcing, such as increases in greenhouse-gas concentration or variations in solar output.

Predicting whether the coming decades will bring an onslaught of strong ENSO events — or none at all — is crucial because of the impact of such events on weather patterns around the world. Individual episodes may be predicted up to two years in advance[7], but on larger timescales our ability to forecast ENSO behaviour accurately may hinge on how ENSO responds to changes in the background climate system. This idea is supported by studies suggesting that the level of activity could be related to natural or man-made changes in the climate of the tropical Pacific[8,9].

In their latest study, Wittenberg *et al.*[1] used the same GFDL-CM2.1 model, this time to forecast epochs of high and low ENSO activity. For each epoch of activity in the model's control run, the authors performed 40 forecasts, each differing by a tiny perturbation of the size of the computer's rounding error to one of the model's numerical grid points. These 'perfect model' forecasts have the best chance of reproducing the extreme ENSO epochs seen in the control run, and permit assessment of the model's intrinsic ability to predict them.

The authors found that, beyond the first two to four years after initialization of the forecasts, the multi-decadal epochs of high and low ENSO activity are completely unpredictable. For each epoch, the model forecasts either active or quiet events with the same probability. That is, the perturbations can alter the forecasts in such a way that the model is capable of forecasting an inactive ENSO decade where it originally simulated a highly active one (Fig. 1a), or an active decade where it simulated a quiet one (Fig. 1b).

This is the 'butterfly effect' of chaos theory[10] applied to ENSO events. Seemingly small perturbations to a system, such as the flapping of a butterfly's wings, may lead to large changes in that system. It is a sobering finding, because it suggests that the changes observed in ENSO behaviour during the twentieth century could very well be random fluctuations unrelated to natural or man-made changes in the climate of the tropical Pacific.

Further research is needed to determine whether the study's conclusions can be extrapolated from the model world to the real world. During the past decade, climate models have progressed substantially in their ability to simulate ENSO events. Many models can now emulate the long-term modulation first seen in the GFDL-CM2.1 simulations, possibly owing to the inclusion of improved wind patterns[11]. But it is not known whether even the best climate models simulate the correct mix of the myriad processes that influence ENSO. One cause of uncertainty might be that the decadal fluctuations in the background climate, which are thought to be the source of ENSO predictability[12], are too weak in the models' simulations[13]. Conversely, models simulate activity that is much stronger than observed[6,14], so this too-strong ENSO might be oblivious to the too-weak changes in background climate, resulting in decreased predictability. The realism of the simulations must be improved if model-based conclusions are to be applied to the real world.

Existing observational records are not yet long enough for us to investigate whether, and how, ENSO responds to long-term climate fluctuations that could be sources of predictability. Progress on this front depends on maintaining and expanding our observational capability in the ocean, which relies on arrays of autonomous profiling floats and tropical moorings. In the meantime, results such as those of Wittenberg *et al.* are reminders of the challenges associated with forecasting ENSO changes. Future attempts to attribute the causes of individual events and their decadal variations now face a much higher bar. ■

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1. Wittenberg, A. T., Rosati, A., Delworth, T. L., Vecchi, G. A. & Zeng, F. *J. Clim.* http://dx.doi.org/10.1175/JCLI-D-13-00577.1 (2014).
2. McGregor, S., Timmermann, A., England, M. H., Timm, O. E. & Wittenberg, A. T. *Clim. Past* **9,** 2269–2284 (2013).
3. Li, J. *et al. Nature Clim. Change* **1,** 114–118 (2011).
4. Emile-Geay, J., Cobb, K. M., Mann, M. E. &

Wittenberg, A. T. *J. Clim.* **26,** 2329–2352 (2013).
5. Cobb, K. M. *et al. Science* **339,** 67–70 (2013).
6. Wittenberg, A. T. *Geophys. Res. Lett.* **36,** L12702 (2009).
7. Chen, D., Cane, M. A., Kaplan, A., Zebiak, S. E. & Huang, D. *Nature* **428,** 733–736 (2004).
8. Wang, B. & An, S. *Clim. Dyn.* **18,** 475–486 (2002).
9. DiNezio, P. N. *et al. J. Clim.* **25,** 7399–7420 (2012).
10. Lorenz, E. N. presented at *139th Annu. Meet. AAAS*, Boston, Mass. (1972); http://eaps4.mit.edu/research/Lorenz/Butterfly_1972.pdf.
11. Neale, R. B., Richter, J. H. & Jochum, M. *J. Clim.* **21,** 5904–5924 (2008).
12. Kirtman, B. P. & Schopf, P. S. *J. Clim.* **11,** 2804–2822 (1998).
13. Ault, T. R., Deser, C., Newman, M. & Emile-Geay, J. *Geophys. Res. Lett.* **40,** 3450–3456 (2013).
14. Deser, C. *et al. J. Clim.* **25,** 2622–2651 (2012).

ALZHEIMER'S DISEASE

A protective factor for the ageing brain

What guards the aged brain against neurodegeneration? A study finds that the REST protein has a central role in protecting ageing neurons from death and in maintaining cognitive capacity in the elderly. SEE ARTICLE P.448

LI-HUEI TSAI & RAM MADABHUSHI

Alzheimer's disease is the leading cause of dementia. In the United States, an estimated 13% of people aged over 65, and nearly one-third of those aged over 85, are affected by this disorder[1]. As the population ages, the number of people with the disease is expected to rise precipitously, with no effective therapeutic strategy in sight. A central question is why certain individuals who display the anatomical and molecular features of Alzheimer's disease still preserve their cognitive abilities. On page 448 of this issue, Lu *et al.*[2] provide some answers.

The authors demonstrate that a protein called repressor element 1 silencing transcription factor (REST), which is normally expressed at low levels in the neurons of young human brains, is profoundly elevated in aged brains. By contrast, they observed that REST levels are markedly reduced in the nucleus of neurons in patients with mild cognitive impairment (a condition that often precedes dementia) and Alzheimer's disease. Lu and colleagues also analysed post-mortem samples of prefrontal cortex taken from people who had previously undergone neuropsychiatric assessments[3], and found that nuclear REST levels correlated positively with cognitive function. Taken together, these findings underscore the importance of maintaining REST protein levels in the aged brain for preventing cognitive decline and Alzheimer's disease.

Previous gene-expression studies[4–6] have extensively characterized the changes that occur in the ageing brains of healthy individuals and those with Alzheimer's. Generally, in both groups, neuronal genes implicated in synaptic transmission (signalling at neural junctions), in calcium signalling and in the functioning of inhibitory neurons show decreased expression, whereas genes associated with stress responses, DNA-damage responses, immune responses and apoptotic cell death show increased expression. But there are also crucial differences. For instance, toxic stimuli that are characteristic of Alzheimer's-related neurodegeneration induce the blockage of gene expression associated with neural plasticity (changes in neural pathways and junctions) in mouse models of Alzheimer's and in the brains of people with the disease[7].

In their study, Lu *et al.* used a dazzling array of experimental approaches to demonstrate that the loss of neuroprotective REST functions contributes to neuronal vulnerability in the brains of those with Alzheimer's. The authors observed that, in the brains of healthy aged individuals, nuclear REST both targets and suppresses several pro-apoptotic genes, as well as certain genes that encode enzymes involved in the pathology of Alzheimer's. But in diseased brains this suppression is lost, resulting in the induction of genes that are likely to underlie aspects of neuronal loss and neurodegeneration (Fig. 1).

The authors also report that REST-deficient mice show no neuronal loss at 1 month old, but they do by 8 months. Similarly, the authors found that *Caenorhabditis elegans* worms deficient in *spr-1*, *spr-3* and *spr-4* (genes that evolved from the same ancestral gene as *REST*) are more sensitive to oxidative stress and have shorter lifespans than wild-type worms. Therefore, REST-mediated transcriptional repression confers resistance to neurotoxic stress in several scenarios.

When the researchers treated cultured human neurons with hydrogen peroxide (an oxidizing agent), and then administered some of the resulting culture medium to untreated cells, they observed a clear increase in the expression of REST messenger RNA by those cells. This suggests that a soluble REST-inducing factor is produced by neurons upon oxidative stress. Furthermore, the authors demonstrated that extracts of aged, but not young, human prefrontal cortex robustly induce REST expression in neural cells *in vitro*.

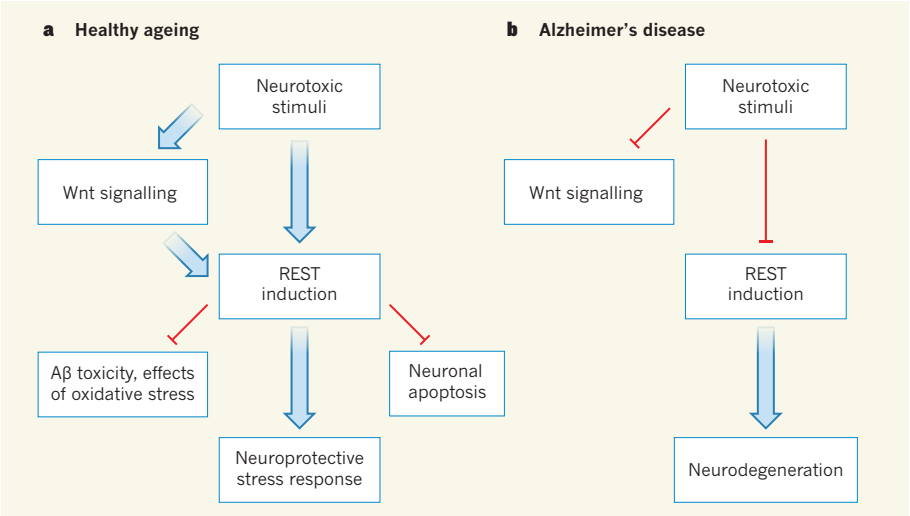

Figure 1 | REST activation distinguishes healthy aged brains from the brains of those with Alzheimer's disease. **a**, Lu *et al.*[2] report that various neurotoxic stimuli in the ageing brains of healthy people cause increased expression of the REST protein, an effect that is at least partially dependent on the Wnt-signalling pathway. REST induction activates neuroprotective stress-response pathways, while suppressing neuronal apoptotic cell death and the toxic effects of the accumulation of amyloid-β (Aβ, the main protein component of the plaques found in the brains of patients with Alzheimer's disease) and of elevated oxidative stress. **b**, In the brains of those with Alzheimer's disease, both Wnt signalling and REST induction are suppressed, leading to neurodegeneration.