



a, Predicted net photosynthesis assuming 25°C air temperature, 2.5 kPa ambient partial pressure of water vapor, 10 mol m<sup>-2</sup> s<sup>-1</sup> boundary layer conductance, C3 and C4 V<sub>max</sub> for rubisco, respectively, of 100 and 30 μmol m<sup>-2</sup> s<sup>-1</sup>, and 1.64 mmol m<sup>-2</sup> s<sup>-1</sup> photon flux density (~80% of full sunlight). Calculated by G. J. Collatz based on models documented in refs 2 and 3. b, Atmospheric CO<sub>2</sub> concentrations from two Antarctic ice cores as related to δ<sup>13</sup>C measurements from a southern Indian peat core<sup>6</sup>. CO<sub>2</sub> data without range bars from ref. 4 and with range bars from ref. 7.

Remarkably, the data show near-pure C4 peat (-12.8‰) at the last glacial maximum (18,000 years before present).

By extension, the combination of low pCO<sub>2</sub> with hot, sunny growing seasons should yield high-δ<sup>13</sup>C peat; the implications of other atmospheric conditions can be predicted with photosynthetic models. Analogous reasoning, using lignites in place of peats, might add pieces to the puzzle of Miocene C4 expansion<sup>8,9</sup>.

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## Similarity of *met* and *trp* repressors

SIR — Lawson and Carey<sup>1</sup> describe the three-dimensional structure of a complex between *Escherichia coli* *trp* repressor and its operator, where repressors are bound in a tandem array to the DNA. The form of this array, and its functional consequences, are directly analogous to those observed for the *met* repressor system, as we have predicted<sup>2,3</sup>. We have also reported the three-dimensional structure of a tandem *met* repressor-operator complex<sup>4</sup>, and have confirmed its relevance to repression *in vivo*<sup>5</sup>.

Both *met* and *trp* repressors recognize unusual operator regions, with tandem repeats of imperfect 8-base-pair (bp) boxes. The 'met box' has consensus sequence AGACGTCT. This is an inverted repeat sequence, that is, it has an axis of 2-fold symmetry at its centre between bases C and G. Tandem strings of met boxes additionally have 2-fold axes at the junctions between boxes. This symmetry could exactly match that of a superhelical cooperative array of tandem repressors wound around the DNA, each repressor being a 2-fold symmetric protein dimer<sup>2,3</sup>. This arrangement of 2-fold axes alternating at 4-bp intervals leads to an ambiguity in assignment of the correct repressor site<sup>2,3</sup>. There is a direct similarity to *trp* repressor, which binds to arrays of 'trp boxes' (consensus AGTAACT) with identical symmetry properties<sup>6,7</sup>. Staacke *et al.*<sup>8</sup> subsequently examined this ambiguity for *trp* repressor, but did not comment on the parallels with *met* repressor.

We also noted that consensus *trp* and *met* boxes share 50% sequence identity. The two repressors are similar in controlling amino-acid biosynthesis and binding small corepressor molecules. Intriguingly, the repressors themselves have totally different polypeptide folds, and contact DNA through different secondary structure motifs, α-helices in *trp* repressor, and β-strands in *met* repressor.

In our crystal structure for the tandem *met* repressor-operator complex<sup>4</sup> (atomic coordinates available from the Brookhaven Protein Data Bank as entry 1cma), the geometric parameters describing the repressor superhelical array, and the helical order of the DNA, are almost identical to those now reported for *trp* repressor.

Lawson and Cary also raise the question of whether such tandem binding is important *in vivo*. We have shown that the cooperativity generated by the formation of the repressor array is essential to effective repression in the *met* case by changing amino-acid residues in the interface between adjacent repressors in the array

using site-directed mutagenesis, and demonstrating severe impairment of repression efficiency in an assay *in vivo* using a reporter gene. We would expect similar effects with some *trp* operators. In fact, the cooperativity generated by the tandem binding produces a very sensitive genetic switch, which may be thrown by small variations in corepressor concentration. We can expect to find further examples among gene regulatory proteins, and there are parallels with the assembly of the multiprotein complexes on the DNA before initiation of transcription by RNA polymerase.

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## Future prospects discussed

SIR — "There are lies, damn lies and statistics" is one of those colourful phrases that bedevil poor workaday statisticians who labour believing that they contribute to the advancement of scientific knowledge. In my view, the statistical methodology of Gott<sup>1</sup>, which purportedly enables one to put statistical limits on the probable lifetime of everything from human existence to *Nature* itself, breathes unfortunate new life into the saying.

Gott claims that, given the duration of existence of anything, there is a 5% probability that it is in its first or last 2.5% of existence. He uses this logic to predict, for example, the duration of publication of *Nature*. Given that *Nature* had published for 123 years when he wrote his article, he projects the duration of continued publication to be between 123/39=3.2 years and 123 × 39=4,800 years, with 95% certainty. He then goes on to predict the future longevity of our species (5,000-7.8 million years), the probability we will colonize the Galaxy and the future prospects of space travel.

This technique would be a wonderful contribution were it not based on a fallacious argument. Dubbed the "Principle