fundamental quantities that are not directly related to growth, such as m_c, E_c, B_c and B_0.

Equations of the form (1) were originally proposed by von Bertalanffy[4], who suggested that growth rate is the difference between anabolic rate, B_a (biomass production, scaling as $m^{2/3}$), and catabolic rate, B_c (biomass breakdown, scaling as m): $dm/dt \propto B_a - B_c$. This case, which is considered by Banavar *et al.*, corresponds to $\alpha = 2/3$, $\beta = 1$, with a, b (and M) being 'arbitrary' parameters determined by fitting growth data. No explanation or derivation is given for any of these parameters, so the authors' version of equation (1) is simply a curve-fitting statistical description.

The assertion that $\alpha = 2/3$ by Banavar *et al.* is at odds with their earlier theoretical argument[2] for a 3/4 exponent for B. In any case, von Bertalanffy's explanation (and that of Banavar *et al.*) for the origin of equation (1) cannot be correct, as both B_a and B_c scale as $m^{3/4}$, leading to $dm/dt \propto m^{3/4}$, or $m \propto t^4$ for all times.

To reveal the universality of growth that is implied by equation (1), we showed that, by plotting $r \equiv (m/M)^{1/4}$ against $\tau \equiv at/M^{1/4} - \ln[1-(m_0/M)^{1/4}]$, all organisms conform to a predicted universal curve, $1 - e^{-\tau}$. Banavar *et al.* observe that a similar plot can be generated by using an unrealistic $\alpha = 2/3$, rather than $\alpha = 3/4$. Most data on ontogenetic growth are not of sufficient quality to distinguish between the two: we recognized this and made no claim that $\alpha = 3/4$ is a better fit than $\alpha = 2/3$. However, the statement by Banavar *et al.* that this curve is independent of α is misleading because r and τ depend explicitly on α, so the scaling curve cannot be constructed without knowing its value, as well as the values of a and b. (Indeed, Banavar *et al.* use our values based on a 3/4 power.)

Banavar and colleagues' comment misses our central point that, because equation (1) is derived from fundamental principles concerning how growth is fuelled by metabolic power at the cellular level, many important quantities can be understood quantitatively. For example, our model elegantly interprets r as the proportion of total lifetime metabolic energy that is devoted to maintenance and other activities.

We further contend that the implication made by Banavar *et al.* that their equation $dm/dt = m^{\alpha} f(m/M)$ is the most general form of the growth equation is also misleading. The function f depends on several variables, including m, M, B, m_c, E_c, B_c, cell growth and lifetime, time to maturity, and so on. Without a specific mechanistic model, why should f depend only on m/M, and what sets the fundamental timescale for growth? Our equation (1) answers these and other questions. It contains, derives and predicts many fundamental biological and physical variables that capture the essential features of ontogenetic growth, yet it yields an extraordinarily simple universal equation.

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COMMUNICATIONS ARISING

Climate change

Regional warming and malaria resurgence

Disease outbreaks are known to be often influenced by local weather, but how changes in disease trends might be affected by long-term global warming is more difficult to establish. In a study of malaria in the African highlands, Hay *et al.*[1] found no significant change in long-term climate at four locations where malaria incidence has been increasing since 1976. We contend, however, that their conclusions are likely to be flawed by their inappropriate use of a global climate data set. Moreover, the absence of a historical climate signal allows no inference to be drawn about the impact of future climate change on malaria in the region.

The findings of Hay *et al.*[1] are based on interpolation to four locations, from a 0.5°-resolution gridded climate data set[2,3], within an area of large altitudinal contrasts and sparse, geographically dispersed historical climate data. In such a region, these gridded climate anomalies are often based on data outside a particular grid cell, and their interpolation to specific sites ignores local elevational dependencies. The mean site altitudes used by Hay *et al.* (1,693 m, 1,819 m, 1,893 m and 2,031 m), compared with those of the actual input weather-station sites (506 m, 1,110 m, 1,312 m, 1,515 m, 1,624 m and 1,635 m), differ on average by 575 m, which corresponds to a temperature deviation of 3 °C. The sparse weather stations also range over a wide expanse of 5° latitude and 7° longitude. This climate data set is appropriate for up-scaling to African regions, but not for down-scaling to specific area locations; it cannot therefore support the type of analysis carried out by Hay *et al.*

Hay *et al.* focus on climate trends, but 'climate change' also applies to changes in variability. In regression analysis, a trend in covariates is not necessary; a change in variance can yield larger or more frequent responses. In the African highland, increases in the magnitude or frequency of malaria epidemics are most closely associated with short-term climate anomalies[4–6]. Because of the existence of critical climate thresholds, the association between change in malaria incidence and change in climate can be biologically meaningful, even without 'significant' climate change.

Based on an understanding of the limitations of the gridded climate data set[3] and on an examination of individual station data[7–9], we calculate that in the east African region encompassing the four study sites there was a mean warming trend of 0.15 °C per decade during 1970–98, aggregated across the 320 0.5° grid boxes (Fig. 1). This regional warming tells us little, however, about climate trends at specific sites[9], as these data[2,3] are not designed to reveal such information.

In contrast to Hay *et al.*, we have identified regional warming trends in east Africa that parallel rising trends in malaria inci-

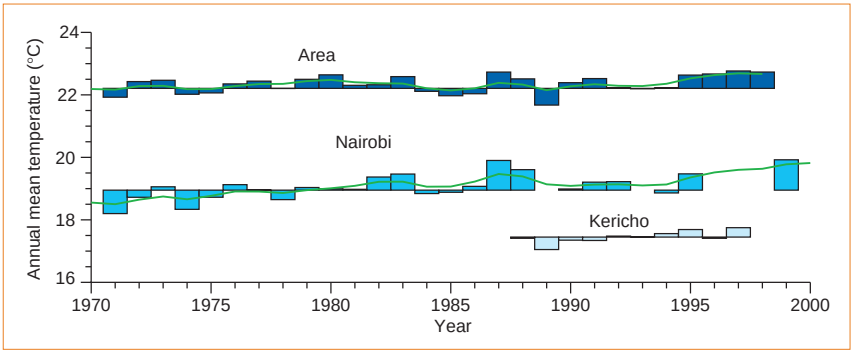

Figure 1 Annual mean temperature for Nairobi airport (WMO 63741, 1.3° S, 36.9° E, 1,624 m) and Kericho (0.37° S, 35.35° E, 2,031m) are plotted as bars to show deviations from the averages for 1961–90 (19.0 °C) and 1988–97 (17.4 °C), respectively. These station records are complemented with a large-area average from a 0.5°-gridded time-series defined by 4° S, 4° N, 28° E, 38° E (refs 2,3). The area-averaged annual mean temperature is plotted (top) as bars that display deviations from the 1961–90 average (22.2 °C). Time series for Nairobi airport and area-averaged data are also plotted after smoothing with a 10-year gaussian filter to emphasize changes on decadal timescales. In addition to the observed temperature trends, note the marked altitudinal dependency in temperatures.

dence at specific sites. But such climate and malaria data sets must be considered at comparable spatial and temporal scales. For example, in a comparison of monthly climate and malaria data in highland Kakamega, Kenya[10], we found a close association between malaria transmission and monthly maximum temperature anomalies from 1997 to 2000, using data from the same location and over the same period of time. Hay and colleagues simply compared point-incidence rates with downscaled gridded climate data, rather than coincident longitudinal malaria and climate data.

We conclude that a reliable assessment of long-term relationships between climate and malaria incidence requires increased local monitoring of appropriate climate and disease variables to establish data sets that can support long-term trend analysis. Interdisciplinary teams are needed to analyse processes as diverse as climate and human disease.

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Hay et al. *reply* — In our study[1] we did not address the impact of predicted climate change on malaria incidence because a complete global assessment is reported elsewhere[2]. Regarding the climate surfaces we used, the data set has superior spatial resolution compared with other data sets of similar temporal extent[3,4], and has been used to quantify climate change across Africa at $0.5 \times 0.5°$ spatial resolution[5] (although the resulting maps are smoothed to emphasize regional changes). It is inconsistent to assert that these same data are insufficient to demonstrate a lack of climate change.

Furthermore, these smoothed patterns[5] are at odds with the marked and variable trends in temperature identified across east Africa using long-term temperature records from meteorological stations[6]. Events occurring at the $0.5 \times 0.5°$ resolution will be less variable when averaged over wider areas, but we know of no evidence that climate surfaces interpolated from meteorological stations consistently fail to reveal trends in climate experienced at those locations.

Crucially, further work has confirmed a very high degree of correspondence between the climate surfaces[3,4] and meteorological-station data from Kericho. Moreover, these station data show no significant trend in temperature or rainfall during the 1966–95 period over which complete longitudinal hospital records show malaria incidence to have increased significantly[7].

The malaria resurgences documented at these four sites are not "point-prevalence rates", but estimates from longitudinal records of health facilities, whose catchment populations range over continuous highland areas that are similar in size to a pixel of the climate surface that we used[3,4].

The sparse coverage of meteorological stations in the data set[3,4] before 1910 in the east African region is problematic[4], and these data were excluded from our analyses. The full 1901–95 data set was used by one of the correspondents, however, in their trend analyses of African climate[5]. Moreover, our conclusions remain unaltered in the light of tests repeated for the 1970–95 period, which is coincident with the malaria resurgences and represents the most consistent meteorological-station coverage.

Patz *et al.* estimate a temperature deviation of 3 °C arising from the difference in the mean elevation of the climate surface pixels[3,4] and the elevation of meteorological station sites that contribute to them. However, the thin-plate spline procedure[8] used to generate the 1961–90 climate normals[3] that formed the basis of the entire climate data set[4] explicitly takes account of altitude to correct for the elevational dependency of temperature.

Application of our methodology[1] to the regional time-series cited by Patz *et al.* shows that the purported warming trend is not significant (details available from the authors). It is critical to test for climate changes that coincide in both space and time with the disease data[7,9], so changes on regional scales or at distant sites (such as Kakamega and Nairobi) are irrelevant, whether or not they achieve significance.

The more subtle impacts of non-significant long-term changes in climate on malaria incidence deserve to be investigated, but have not been demonstrated, so we cannot attribute significant increases in malaria incidence to non-significant changes in climate. It is because malaria incidence is related to climate that any study of long-term climate change must factor out seasonality, unlike the cited study on seasonal variability over four years[10]. Finally, windowed Fourier analysis of the meteorological station data for Kericho also showed no change in annual temperature or rainfall variability since 1966 (ref. 11), a conclusion that is corroborated by global-scale analysis of climate variability during this century[12].

Rather than climate change, variations in environmental, social and epidemiological factors are more plausible explanations for the malaria resurgences at the four sites we examined[1] and at three others in Ethiopia, Madagascar and Tanzania[13]. Evidence against the epidemiological significance of climate change in the recent malaria resurgences in Africa is mounting[7,9,13] and remains unmatched by any contrary evidence.

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