To explain how variability can improve the arterial partial pressure of oxygen (pO_2), consider the pressure–volume (P–V) behaviour of an injured lung that is being mechanically ventilated with many peripheral airways closed, thereby creating large collapsed regions. Let α represent a fraction of the lung that is collapsed at the end of expiration. An uncollapsed lung will be ventilated according to a 'normal' nonlinear P–V relation[4] (see the normalized P–V curve in Fig. 1a, labelled $\alpha = 0$). Collapsed regions, however, significantly alter the P–V curve[5].

The limiting case of $\alpha = 1$ in Fig. 1a shows a model P–V curve for the first inflation of a completely collapsed lung, where V is proportional to P^N (N ranges from 10 to 16)[6]. When α is between 0 and 1, the P–V curve of the entire lung ($\alpha = 0.3$) will be a combination of the 'normal' curve and the P^N curve. Thus, for P values below 0.75, the highly nonlinear P^N term dominates, whereas, for P values above 0.75, the contribution of the 'normal' P–V curve leads to flattening of the P–V relation.

In conventional mechanical ventilation, P increases from end-expiratory pressure $P_{exp} = P_1$ (say $P_1 = 0.3$) to a fixed end-inspiratory pressure $P_{ins} = P_2$ (say $P_2 = 0.7$). The corresponding opened volume in the collapsed region increases from V_1 to V_2. We mimic variability in breathing by adding noise to P_2 so that P increases from P_1 to $P_{ins} = P_2 + \eta$, where η is a random variable changing from breath to breath and is taken from a zero-mean gaussian distribution (Fig. 1b).

Suppose that, for one inflation, P increases to $P_{ins} = 0.75$ rather than to 0.7. This results in gaining recruited volume compared with $P_{ins} = 0.7$. Suppose now that for the next inflation, P increases to only $P_{ins} = 0.65$, losing some recruited volume. Owing to the strong nonlinearity (P^N) of the P–V curve, the 'gain' of volume for $P_{ins} > P_2$ is far greater than the 'loss' of volume for $P_{ins} < P_2$. When P_{ins} samples the gaussian around P_2 many times, the mean of P_{ins} will be P_2, but the mean of the distribution of the recruited volumes will increase from V_2 to V_3. The quantity $\Delta V = V_3 - V_2$ represents the net improvement, which is more than 240%.

Hence surface area for gas exchange in the collapsed region increases, leading to an increase in arterial pO_2. In addition, as lung injury progresses, α increases, and the P–V curve of the entire lung gradually shifts towards the P^N limit. Therefore, with increasing a, adding noise to ventilation should increasingly improve the arterial pO_2, a prediction that is consistent with experiments[3].

The process of varying P around P_2 is analogous to the noise-enhanced amplification of a useful signal in a system by stochastic resonance[7]. In stochastic resonance, increasing the standard deviation (s.d.) of the noise in a nonlinear system will initially amplify a weak input so as to increase the output signal-to-noise ratio; however, further increasing the standard deviation will have the opposite effect. The output signal in our case is the arterial pO_2. When small noise is added to P_2, the surface area for gas exchange, and hence arterial pO_2, increases.

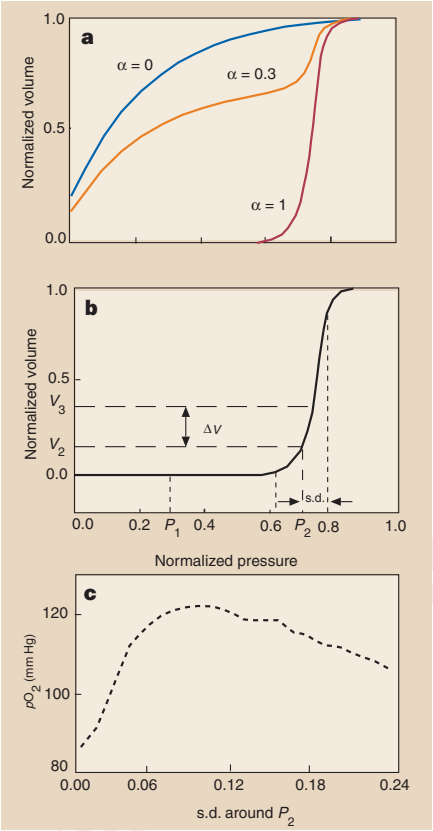

Figure 1 Variability improves arterial partial pressure of lung oxygen. **a,** Pressure–volume (P–V) curves normalized to unity at total lung capacity. $\alpha = 0$, normal P–V of a lung without collapsed regions[4]. $\alpha = 1$, P–V for a collapsed lung[6] where recruitment of volume is proportional to P^6 for $P < 0.75$. $\alpha = 0.3$, weighted average of the two limiting cases. **b,** Normalized P–V curve of a collapsed region (case $\alpha = 1$ from **a**). P_1, end-expiratory pressure; P_2, end-inspiratory pressure; V_2, corresponding recruited volume. When noise (s.d.=0.075) is added to P_2, average opened volume increases from $V_2 = 0.15$ to $V_3 = 0.363$. **c,** Predicted arterial blood oxygen partial pressure pO_2 as a function of the s.d. of the gaussian around $P_2 = 0.7$. pO_2 data obtained by calculating and averaging 1,000 normalized compliance values, C, which, using ref. 3 data, we relate to pO_2 ($pO_2 = 2.8C + 6$).

Increasing the noise amplitude too much may adversely affect the arterial pO_2. For example, as we gradually increase the standard deviation of the gaussian noise along the S-shaped nonlinearity curve ($\alpha = 0.3$ in Fig. 1a), we find that the normalized compliance, C (defined as $V_T/(P_{ins} - P_1)$, where $P_{ins} = P_2 + \eta$, and V_T is the volume inspired per breath (corresponding to $P_{ins} - P_1$), displays a maximum.

As C is linearly related to arterial pO_2 in lung injury[3] (probably because the collapse of lung regions leads to proportional changes in the area available for gas exchange), our model predicts that there is an optimum standard deviation at which pO_2 also displays a maximum (Fig. 1c). So the possibility of tuning noise for optimal gas exchange in mechanical ventilation arises, from the presence of a nonlinearity due to the competing effects of recruitment of alveoli via avalanches[8] (causing C to increase) and the gradual stiffening of the overinflated parenchymal tissues[4] (causing C to decrease).

As well as offering immediate improvement in gas exchange, noise may have long-term benefits for patients with acute lung injury and respiratory failure because, without requiring increased mean airway pressures, fewer alveolar regions will remain collapsed. This is significant, as high airway pressures cause mechanical failure of pulmonary microvasculature[9], and high shear forces on the alveolar walls increase the level of inflammation which can further propagate the inflammatory response within the alveolar compartment[10]. So including appropriately designed noise in mechanical ventilators will improve gas exchange and could have a significant effect on morbidity by breaking the chain of injury propagation in acute lung injury.

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correction

In "What's so special about figs?" (*Nature* **392**, 668; 1998) the values given in Table 1 for copper, iron, manganese and zinc should have been expressed as µg per g dry matter. Also, in ref. 1, the first author's name should read "Conklin, N. L."

strongly supports an insect–crustacean clade that excludes myriapods. Also, we anticipate that further study of the relative arrangements of the genes in metazoan mtDNA will help to clarify many other higher-level evolutionary relationships.

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What's so special about figs?

Fruit-eating animals regularly prefer to eat figs even when other food is abundant. We propose that high calcium levels contribute to the desirability of figs as food for many forest animals.

There has been debate over the nutritional significance of the fig in the diet of frugivores[1,2] and over its importance as a 'keystone' species[3–6]. We compared the mineral composition of figs and other fruits from Belize, Indonesia and Uganda, and found that there was more than three times as much calcium in figs as in other fruits.

We analysed the mineral content of figs and other non-domestic fruit species from the neotropical, African and Asian regions (Table 1), and 11 tropical and 13 temperate domestic fruit species. Regional differences were evident in the calcium, magnesium, iron, manganese, phosphorus and sodium content of all the fruits. This may have reflected varying soil fertility between collection sites.

Table 1 **Mineral analysis data**

Ash	Ca	Mg	Na	P	Cu	Fe	Mn	Zn
Belize fig								
8.13	1.91	0.40	0.040	0.18	8.79	63.1	32.3	19.6
2.04	0.70	0.14	0.016	0.05	2.29	18.8	38.2	4.3
Belize non-fig fruit								
5.99	0.39	0.47	0.063	0.17	11.6	79.1	29.8	18.6
2.78	0.35	0.29	0.037	0.12	6.38	55.6	30.4	10.4
Indonesia fig								
8.00	1.21	0.25	0.060	0.33	10.0	65.7	10.9	26.1
3.08	0.33	0.08	0.035	0.14	3.48	73.2	4.3	34.4
Indonesia non-fig fruit								
6.77	0.47	0.17	0.057	0.42	11.0	51.4	14.5	17.9
4.61	0.37	0.10	0.049	0.35	7.54	42.0	14.9	11.8
Uganda fig								
9.40	1.52	2.12	0.043	0.18	7.73	94.7	24.9	25.1
3.30	0.55	5.48	0.048	0.08	2.44	68.6	13.5	18.2
Uganda non-fig fruit								
9.69	0.48	0.36	0.014	0.14	8.43	122	42.1	22.2
6.69	0.53	0.53	0.010	0.08	3.63	71.7	57.3	16.4

Values for ash, Ca, Mg, P and Na are expressed on a % dry-matter basis. Cu, Fe, Mn and Zn expressed as mg per g dry matter. Mean values are shown, with standard deviations underneath. Sample sizes are given in Fig. 1. Species information is available from the authors.

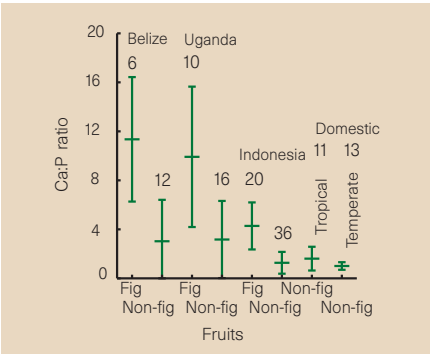

Figure 1 Mean (±s.d.) calcium-to-phosphorus ratios for fig and wild non-fig fruits from Belize, Indonesia, and Uganda, and temperate and tropical domestic fruits. Numbers indicate species per sample.

However, between fig and non-fig fruits, differences in mineral concentrations were restricted to calcium. On average, figs contained calcium levels 3.2 times higher than other fruits — levels high enough to promote eggshell deposition in birds, and bone growth in birds and mammals[7,8]. Also, the ratio of calcium to phosphorus (a measure of calcium availability[7,9]) was 3.7 times higher in figs than in other fruits (Fig. 1). Figs from Sulawesi, Indonesia contained more calcium relative to the calcium availability in the soils, indicating that fig trees may selectively absorb calcium or allocate calcium to fruits.

Previous studies have shown that the protein, carbohydrate and lipid content of figs[1,2] are variable and not exceptionally high. Our study indicates that calcium concentration relative to phosphorus may be an important criterion for selection of the fruit.

Growth processes and egg-laying are accompanied by a rise in requirements for calcium and phosphorus[7,8] to lay down eggshell, aid metabolism, construct nucleic acids and form bone. Because most non-fig fruits, as well as seeds and invertebrates, are poor sources of calcium, many birds and mammals rely on calcium supplements such as mollusc shells, bone or soil to ensure adequate dietary calcium[7,10,11]. Others consume large quantities of figs throughout the year[5,6,12]. The biological availability of calcium in figs has not been determined, but animals whose diets are rich in figs are unlikely to suffer from calcium deficiency.

Terborgh[3] and others[5,6,12] suggest that figs constitute a 'keystone' plant resource for fruit-eating birds and mammals throughout the tropics. Figs display inter- and intraspecific asynchrony in fruiting, tend to produce large crops, and show low interannual variation in fruit production[13]. These fruiting patterns make figs a reliable food source during times of general fruit scarcity.

Our results indicate that figs may be important throughout the year for maintaining an adequate balance of calcium among fruit-eating animals, thus fulfilling the role of a keystone plant resource for many animal species. These findings also suggest that the concentrations of specific minerals represent an important nutritional criterion for evaluating dietary choices across taxonomic groups and pantropical ecosystems.

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