Refining these techniques should increase our understanding of the relation between environmental fluctuations and population dynamics, in the spirit of Moran.

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Grenfell et al. *reply* — The Moran effect refers to systems of population dynamics that are linear: under these circumstances, the long-term correlation between population densities will be the same as the correlation between the random environmental perturbations. The Soay sheep exhibit significant nonlinearity in their density dependence (Fig. 2a of ref. 1). At low populations, numbers tend to increase exponentially, with mean growth rate $r = 0.24$, whereas at high densities (above a threshold of 1,172 animals), the population tends to decline, with mean $r = -0.29$. Thus, when populations on two adjacent islands are both above their thresholds, both will tend to decline, and when both are below their thresholds, both will tend to increase.

This immediately introduces a positive correlation between population dynamics on adjacent islands in the absence of any environmental forcing. When one population is above the threshold and one is below, the expectation is of no short-term correlation because the trends will tend to cancel out. Adding noise to the system has two effects. Correlated noise tends to push the dynamics into synchrony, because both populations tend to crash to low densities during the same years (for example, those with the most extreme winter weather). The nonlinearity means, however, that the same stochastic event could drive one population below the threshold but leave another population above it (for example, if initial population densities are sufficiently different). In this case, the two populations would experience different regimes of density dependence during the same year and synchrony would be reduced. Intuitively, then, in the presence of nonlinear density dependence, environmental forcing has to be stronger if it is to drive the populations into synchrony and keep them there.

Blasius and Stone have pointed out two problems with our analysis. First, they show that we had the two populations experiencing different — hence uncorrelated — noise during periods when the two populations were on opposite sides of the threshold. Correcting this mistake reduces the level of noise correlation (r_n) required to produce the observed level of population correlation (r_p) ($r_p = 0.685$) from $r_n > 0.9$ to around 0.8 for large samples. This means that the extra-Moran effect is reduced, but not abolished.

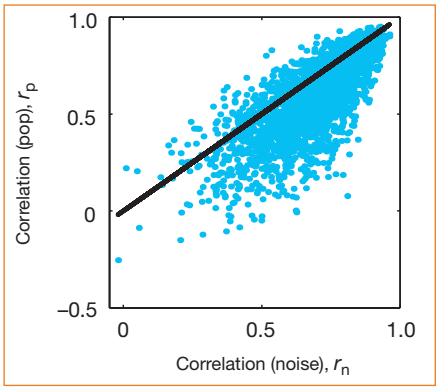

Figure 1 Scatter plot (blue) of inter-island population correlation (r_p) against true noise correlation (r_n) for 3,000 simulations (each of 18 time points) of the SETAR model, defined as in Table 1 of ref. 1, with the correction in noise realization proposed by Blasius and Stone. The black line indicates where population correlation equals the noise correlation (the expectation of the Moran effect). See ref. 2 for more details.

Their second point is that, with realistically short time series (such as our 18 points), variability in the inter-population correlation coefficient generates a relatively high expectation of observing correlations higher than Moran, leading to inflated type-I errors. We have carried out further calculations with the corrected model that agree qualitatively with this. However, even short model simulations show the imprint of nonlinearity in their aggregate correlation structure — a strong downward bias in population correlation for a given level of noise correlation, compared to various linear null models (Fig. 1; for more details, see ref. 2). Thus, the impact of nonlinearity on population correlation is apparent in the collective behaviour of short simulations, as well as in individual realizations of the model's long-term dynamics.

There are several important directions for studies on the interactions between noise and determinism in population dynamics. Most important is an increase in the realism of the underlying model. The inclusion of age- and sex-structure effects is essential, because we know that animals of different ages and sexes experience markedly different patterns of mortality[3]. A further improvement would incorporate threshold density as a random variable rather than a constant (it is intraspecific competition for food that underlies the density dependence, and food supply determines the sheep density at which competition kicks in). This would allow for island-to-island differences in the response of food availability to environmental noise, so that islands with the same population densities could experience different density-dependence regimes in the same year.

The ability to detect extra-Moran correlations depends critically on the balance between noise and density dependence (B. Blasius and L. Stone, personal communication), so any model refinement that explains more variability in terms of population processes will increase our powers of evaluation. Technically, developments in nonlinear time-series analysis need to encompass estimation of age[4] and spatial heterogeneities, as well as the dissection of process noise from measurement error. This is particularly important for the relatively short time series found in ecology, where even linear time-series models can produce a complex range of correlation behaviours[2].

A thorough understanding of spatial dynamics can only come about once the interaction between correlated noise and nonlinear density dependence is understood through long-term ecological studies, combined with models.

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Physiology

An actively controlled heart valve

Vertebrate hearts typically have cardiac valves that are thin and leaf-like and which work passively, allowing blood to move forward during systole and preventing it from flowing back during diastole. Crocodilian hearts have nodules of connective tissue, resembling opposing knuckles, or cog-teeth[1–3], in the subpulmonary conus just proximal to the pulmonary valves. Here we show that these cog-teeth act in the estuarine crocodile *Crocodylus porosus* (Fig. 1) as a valve that regulates the flow of blood between the lungs and the systemic circulation in response to a β-adrenergic mechanism. To our knowledge, this is the first report of an actively controlled intra-cardiac valve in a vertebrate.

Among the vertebrates, only the mammals, birds and crocodilians have anatomi-

cally separate ventricles that allow the complete separation of systemic and pulmonary circulations. However, shunting blood away from the lungs and into the systemic circulation is possible in the crocodilian heart because the right ventricle gives rise not only to the pulmonary arteries but also to another major vessel, the left aorta (Fig. 2a). This allows deoxygenated right-ventricular blood to bypass the lungs and to be re-circulated into the systemic circulation (pulmonary-to-systemic shunt) — that is, blood is ejected into the left aorta instead of the pulmonary arteries. For a pulmonary-to-systemic shunt to develop, the pressure in the right ventricle must exceed the pressure in the left aorta[4–8].

The cog-teeth[1–3] connective tissue nodules (Fig. 2a, b) are one of the intriguing anatomical features of the crocodilian heart. They project from the subpulmonary conus into the pulmonary outflow tract just proximal to the pulmonary leaf-like valves and fit snugly together during systole, reducing the diameter of the subpulmonary conus[3]. Indirect evidence[9–12], such as the spontaneous appearance of a biphasic pressure peak in the right ventricle, suggests that the cog-teeth might be an 'extra' valve mechanism that could help in initiating and regulating shunts.

We used a crocodile heart preparation[6] perfused *in situ* to determine the function and possible regulation of this valve. The perfused heart generated a cardiac output similar to that recorded *in vivo* and worked at physiological pressures. Using an antagonist of the β-adrenergic receptor, sotalol, we initiated a shunt where about a third of the output from the right ventricle exited through the left aorta. Injecting adrenaline or isoprenaline into the right side of the heart reduced flow to the left aorta and eventually abolished the shunt, with flow being redirected into the pulmonary artery (Fig. 2c). This indicated that control of the shunt within the heart of *C. porosus* was mediated by an intrinsic β-adrenoceptor.

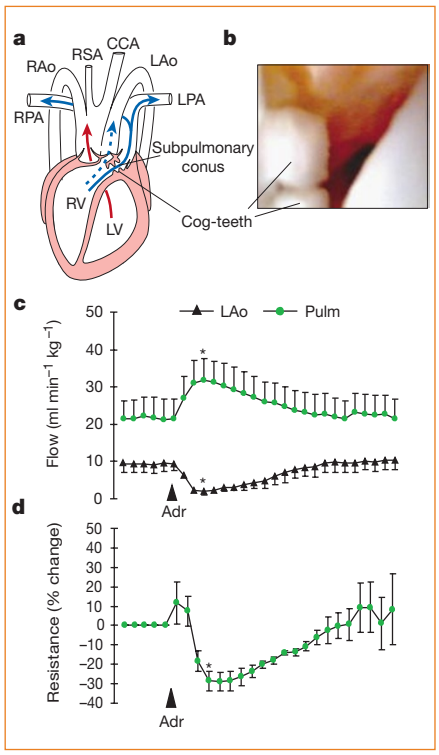

Figure 2 The 'cog-teeth' valve inside the heart of crocodilians and the flow and resistance from a perfused *Crocodylus porosus* heart preparation[6]. **a,** The crocodilian heart, outflow tract and major arteries, showing the position of the cog-teeth within the subpulmonary conus, proximal to the leaflet pulmonary valves and surrounded by cardiac muscle. During non-shunting conditions, blood is ejected from the left ventricle (LV) into the right aorta (RAo) (leading to the dorsal aorta), right subclavian artery (RSA) and the common carotid artery (CCA) (red arrow). The right ventricle (RV) ejects blood into the common pulmonary trunk which divides into the left and right pulmonary arteries (LPA and RPA) (blue arrow). During shunting, blood is ejected from the right ventricle into the left aorta (LAo) (dotted arrow). **b,** Angioscopic image[3] of the 'cog-teeth' in the subpulmonary conus in the right ventricle; pointers show individual cogs. Photo courtesy of C. Löfman. **c,** The effect of a bolus injection of adrenaline (Adr, 0.3 ml 10^{-7} M) on pulmonary and left aortic flows, and **d,** on pulmonary outflow resistance, in a *C. porosus* perfused-heart preparation pretreated with the β-adrenoceptor-antagonist sotalol. Sotalol induced a shunt in the perfused heart preparation, despite the left-aortic output pressure being set at 1.5 kPa above the pulmonary artery output pressure. A bolus injection of adrenaline eliminated the shunt, with flow in the left aorta being diverted back into the pulmonary outflow tract. The bolus injection of adrenaline resulted in a significant reduction (28.9 ± 4.9%) in pulmonary outflow resistance (means ± s.e.m.; $n = 6$; asterisks indicate a significant difference at $P < 0.05$, Wilcoxon signed rank test).

Neither heart rate nor the total power output generated by the heart preparation changed during the injection of adrenaline/isoprenaline, excluding the possibilities that the shunt was mediated by a change in the inotropic state of the heart or as the result of a change in stroke volume (Starling effect). The shunt induced by sotalol was the result of a large increase in resistance of the pulmonary outflow tract. The injected boluses of adrenaline and isoprenaline decreased the resistance of the pulmonary outflow tract, corresponding to the increased flow in the pulmonary artery (Fig. 2d). As the effects of the bolus injections wore off, the resistance of the pulmonary tract increased again and the shunt returned.

Our results demonstrate the presence and action of a regulatory intra-cardiac valve within the subpulmonary conus of the estuarine crocodile and indicate that the initiation of a shunt occurs when the β-adrenergic drive on the heart is low.

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Figure 1 The estuarine crocodile *Crocodylus porosus* has an unusual valve inside its heart that can shunt blood away from the lungs.

Erratum

A triclosan-resistant bacterial enzyme
Richard J. Heath, Charles O. Rock
Nature **406,** 145–146 (2000)
In Table 1, the third entry should have been *Streptococcus pneumoniae*, and not *Salmonella pneumoniae* as published.