T cells from either the lymph nodes or peripheral blood before HAART was discontinued in these patients, it is possible that other tissue reservoirs are responsible for the rebound in plasma viraemia. Genotypic and phenotypic studies will be required to determine the source of this rebounding virus.

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Statistical mechanics

Microscopic chaos from brownian motion?

Gaspard *et al.*[1] have analysed a time series of the positions of a brownian particle in a liquid, and claimed that it provides empirical evidence for microscopic chaos on a molecular scale. An accompanying comment[2] emphasized the fundamental nature of the experiment. Here we show that virtually identical results can be obtained by analysing a corresponding numerical time series of a particle in a manifestly microscopically non-chaotic system.

Like Gaspard *et al.*[1], we have analysed the position of a single particle colliding with many others. We used the Ehrenfest wind-tree model[3], in which the point-like ('wind') particle moves in a plane, colliding with randomly placed, fixed square scatterers ('trees') (Fig. 1a). We chose this model because collisions with the flat sides of the squares do not lead to exponential separation of corresponding points on initially nearby trajectories, so there are no positive Lyapunov exponents, which are characteristic of microscopic chaos. In contrast, Gaspard *et al.*[1] used a Lorentz model as being similar to brownian motion, a model in which the squares are replaced by hard, circular discs. This does exhibit exponential separation of nearby trajectories, leading to a positive Lyapunov exponent and hence microscopic chaos.

Nevertheless, despite being non-chaotic, the Ehrenfest model reproduces all the results presented by Gaspard *et al.*[1]. The particle trajectory segment shown in Fig. 1b is strikingly similar to that for the brownian particle (Fig. 2 of Gaspard *et al.*). Our subsequent analysis parallels that of Gaspard *et al.*[1], where further details may be found.

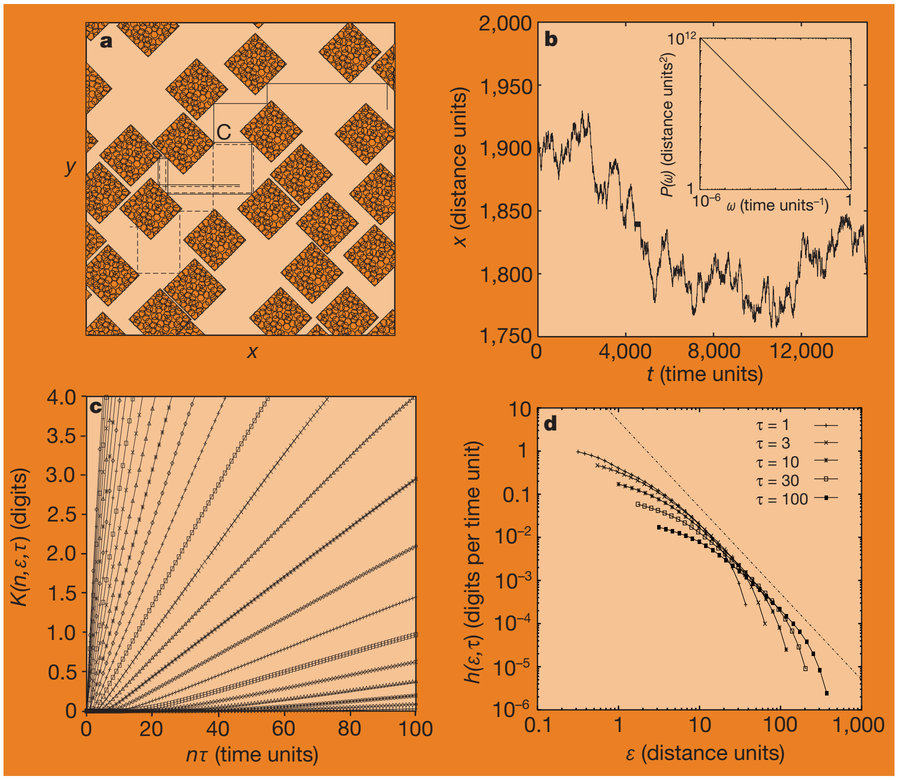

Figure 1 Brownian motion results of Gaspard *et al.*[1] numerically reproduced from the non-chaotic Ehrenfest wind-tree model (notation as in ref. 1). The square scatterers have a diagonal of two length units and fill half the area considered. The particle moves with unit velocity in four possible directions. The position on its trajectory is determined for 10^6 points separated by one time unit. **a,** Two nearby trajectories split only at a corner C; no exponential separation occurs (see Fig. 1 of ref. 1). **b,** A typical trajectory is diffusive with an ω^{-2} power spectrum (inset), where ω is the angular frequency (see Fig. 2 of ref. 1). **c,** The information entropy $K(n, \epsilon, \tau)$ for $\tau = 1$ and $\epsilon = 0.316 \times 1.21^m$, where m is an integer running from 0 to 25 (see Fig. 3 of ref. 1). **d,** The envelope of the slopes of these K curves, $h(\epsilon, \tau)$ appears to imply a positive (chaotic) h_{KS} for the Ehrenfest model, as for brownian motion (see Fig. 4 of ref. 1).

The microscopic 'chaoticity' is determined by estimating the Kolmogorov–Sinai entropy h_{KS} as described[4,5] by using the information entropy $K(n, \epsilon, \tau)$ obtained from the frequency with which the particle retraces part of its (previous) trajectory within a distance ϵ, for n measurements spaced at a time interval τ. As h_{KS} here equals the sum of the positive Lyapunov exponents, the determination of a positive h_{KS} would imply microscopic chaos. Like Gaspard *et al.*[1], we find that K grows linearly with time (Fig. 1c), giving a positive (non-zero) bound on h_{KS} (Fig. 1d). Indeed, Fig. 1b–d for a microscopically non-chaotic model are virtually identical to the corresponding Figs 2–4 of Gaspard *et al.* Thus, Gaspard *et al.* did not prove the presence of microscopic chaos in brownian motion.

The algorithm of refs 4,5 as applied here cannot determine the microscopic chaoticity of brownian motion because the time interval between measurements, 1/60 s (ref. 1), is so much larger than the microscopic timescale determined by the inverse collision frequency in a liquid, which is approximately 10^{-12} s. A decisive determination of microscopic chaos would require a time interval τ of the same order as characteristic microscopic timescales.

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Gaspard *et al.*[1] have shown that the position of a brownian particle behaves like a Wiener process with positive resolution-dependent entropy[2]. More surprisingly[3–5], they claim that this observation provides proof of 'microscopic chaos', a term they illustrate by examples of finite dimensional dynamical systems which are intrinsically unstable. We do not believe that they have provided evidence for microscopic chaos in the sense in which they use the term.

Although the recent literature finds such chaos on a molecular level quite plausible, the observed macroscopic disorder cannot be taken as direct evidence of microscopic chaos. The effectively infinite number of molecules in a fluid can generate the same macroscopic disorder without any intrinsic instability, so brownian motion can be derived for systems that would usually be called non-chaotic, such as a tracer particle in a non-interacting ideal gas. All that is needed for diffusion is 'molecular chaos' in the sense of Boltzmann, that is, the absence of observable correlations in the motion of single molecules.

Part of the confusion is due to the lack of a unique definition of microscopic chaos for systems with an infinite number of degrees of freedom. Gaspard *et al.*[1] introduced the term by extrapolating from finite dimensional dynamical systems for which chaos is well defined: on average, initially close states separate exponentially when time tends to infinity. The Lyapunov exponent, or rate of separation, is independent of the particular method used to measure 'closeness'. However, the ideas of diffusion and brownian motion involve infinitely many degrees of freedom. In this thermodynamic limit, Lyapunov exponents are no longer independent of the metric. The large system limit of a finite non-chaotic system will therefore remain non-chaotic with one particular metric and become chaotic with another.

We can illustrate this point by using an example[6] introduced in the context of cellular automata. Consider two states $\mathbf{x} = (\ldots x_{-2}, x_{-1}, x_0, x_1, x_2 \ldots)$ and $\mathbf{y} = (\ldots y_{-2}, y_{-1}, y_0, y_1, y_2 \ldots)$ of a one-dimensional bi-infinite lattice system. If the distance between $\mathbf{x}$ and $\mathbf{y}$ is defined by $d_{\max}(\mathbf{x},\mathbf{y}) = \max_i |x_i - y_i|$, it can grow exponentially only if the local differences do. This is what is usually meant by 'chaos', and what Gaspard *et al.*[1] meant by 'microscopic chaos'. This mechanism is absent in the thermodynamic limit of finite non-chaotic systems, so the limit could also be said to be non-chaotic[7–9]. However, the distance $d_{\exp}(\mathbf{x},\mathbf{y}) = \sum_i |x_i - y_i| e^{-|i|}$ can also show exponential divergence if an initially distant perturbation moves towards the origin without growing[6]. When observing a localized tracer, as Gaspard *et al.*[1] did, the latter choice may be the more appropriate.

In finite dimensional dynamical systems, chaos arises as a result of the defocusing microscopic dynamics. Positive entropy is generated by the initially insignificant digits of the initial condition brought forth by the dynamics. At the thermodynamic limit, a different mechanism also exists: perturbations coming from distant regions kick the tracer particle once and move away again to infinity. The entropy is positive because of information stored in remote parts of the initial condition. Suitable Lyapunov exponents[6] can be defined for this case as well.

To resolve the confusion, we propose letting the system size tend to infinity first, before the observation time[10]. A system observed in a particular metric μ is then described as μ-chaotic when we find a positive Lyapunov exponent using this metric. Gaspard *et al.*[1] had in mind the type of chaos that is detectable with the metric $d_{\max}$ and arises from a local instability. But they fall short of providing experimental evidence for this specific type of chaos.

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Gaspard et al. *reply* — We presented experimental evidence for the existence of microscopic chaos in the mesoscopic motion of a brownian particle in solution. We used standard techniques to analyse long trajectories of a brownian particle and inferred a dynamical entropy from this analysis. We showed that this dynamical entropy can be accessed experimentally by measuring multiple-time correlation functions for the particle. The dynamical entropy was then used to provide a positive lower bound for the sum of the Lyapunov exponents for the underlying deterministic dynamical system composed of the fluid and brownian particles. We concluded that the positive dynamical entropy, obtained experimentally, was evidence for the existence of positive Lyapunov exponents in the underlying dynamics, and hence for the existence of microscopic chaos generated by a dynamical instability.

Dettmann *et al.* and Grassberger and Schreiber argue that there may be other explanations. There is no doubt that a positive dynamical entropy could be generated by mechanisms other than a local intrinsic, dynamical instability. Illustrative models include the Rayleigh flight of a tracer particle in a non-interacting ideal gas, the motion of an impurity in a harmonic crystal, and the motion of the wind particle in the wind-tree model. In these models, an external pseudorandom generator must be involved at some stage of the simulation of the dynamics, leading to a positive dynamical entropy without a local dynamical instability.

In the Rayleigh flight and the harmonic crystal, randomness is generated repetitively by the new particles or waves continuously coming from infinity. In the wind-tree model, the scatterers are randomly located by using a pseudorandom generator before the simulation of the time evolution. As the wind particle collides with a new scatterer, it picks up new information on the location of this scatterer and the information recorded on this trajectory grows as a result. However, if the square scatterers formed a regular lattice, this growth would stop and the dynamical entropy would vanish. In contrast, for circular disks, as in the Lorentz gas, the dynamical entropy is always positive whether the lattice is regular or not. The apparent dynamical randomness of the wind-tree model therefore has its origin in the structural disorder of the model.

The models mentioned by Dettmann *et al.* and Grassberger and Schreiber fail to capture an essential feature of brownian motion: that the diffusion coefficient is inversely proportional to the viscosity of the fluid surrounding the brownian particle. The viscosity of the fluid is absent in models in which the surrounding particles either do not move or have no interaction or only harmonic interactions. These models are therefore not plausible for the interpretation of our experiment[1].

However, if the interactions between surrounding particles are generic and nonlinear, the viscosity can be positive and the dependence of the diffusion coefficient on the viscosity can be explained. In such systems with nonlinearly interacting particles, numerical and analytical studies have shown that intrinsic local instability is the dominant mechanism for generating dynamical randomness, and no external pseudorandom generator is needed[2,3]. Standard models of brownian motion are of this kind and develop chaotic dynamics with a full spectrum of positive Lyapunov exponents.

For these reasons, we believe that our explanation in terms of a randomness self-generated by the dynamical instability is the most plausible one for this experiment. We hope that further experiments will be able to distinguish more directly between different regimes of random behaviour in systems with a large number of particles, and so provide further evidence of microscopic chaos.

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