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From Biology to Physics and Back: The Problem of Brownian Movement

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Keywords

stochastic dynamics, thermal ratchets, bacteria motion, diffusion, optical trap, Kramers potential

Abstract

This article focuses on the history of theoretical ideas but also on the developments of experimental tools. The experiments in our laboratory are used to illustrate the various developments associated with Brownian movement. In the first part of this review, we give an overview of the theory. We insist on the pre-Einstein approach to the problem by Lord Rayleigh, Bachelier, and Smoluchowski. In the second part, we detail the achievements of Perrin, measuring Avogadro's number, quantifying the experimental observations of Brownian movement, and introducing the problem of continuous curves without tangent, a precursor to fractal theory. The third part deals with modern application of Brownian movement, escape from a fixed optical trap, particle dynamics on a moving trap, and finally development of Brownian thermal ratchets. Finally, we give a short overview of bacteria motion, presented like an active Brownian movement with very high effective temperature.

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1. INTRODUCTION TO THE THEORY OF BROWNIAN MOVEMENT

Brownian movement has an extraordinary history. It was first discovered by botanist Robert Brown (1) in 1828. Looking at the grains of pollen dispersed in water, he noticed that they had an irregular swarming motion. He thought that it was an example of life activity. Brown soon realized that it had nothing to do with biology, as the effect was independent of the particle substance. It was just a physics problem—a problem of a particle being bombarded by the surrounding water molecules.

Then experimental physicists took over. Gouy (2) in 1888 showed that the smaller the particle, the faster the activity, and he showed that the activity was independent of environmental conditions by covering the liquid with a glass plate to avoid evaporation and keeping the bath at constant temperature. Exner (3) in 1900 then showed that the motion depended on viscosity and temperature. It was simply a temperature problem. The time was free for a theoretical effort of what has been denominated Brownian movement.

Amazingly the very first paper related to this problem was by Lord Rayleigh (4) in 1891, in which, in his theory of gases, he studied the state of a free mass under bombardment by projectiles striking with velocity v and moving independently in two directions; this was, of course, posed as a one-dimensional (1D) problem.

The first theoretical interpretation came from a physicist studying speculation in the stock market in 1900, Louis Bachelier (5). A stock is seen as a Brownian object bombarded by fast buying and selling activity; it is thus a model of the fluctuations in stock price. As described by Davis & Etheridge (6), Bachelier argued that the small fluctuations in price over short times are independent of the price value and independent of past behavior, and deduced that increments are independent and normally distributed. It is the diffusion limit of a random walk. This remarkable study was essentially ignored until rediscovered in the 1960s by Savage, a mathematician, and Samuelson, an economist.

Then in 1905 came the heavy players, Smoluchowski (7) and Einstein (8). Einstein developed a bold theory in which the force on the particle comes from osmotic pressure, following the molecular theory of heat, and the particle resistance to motion from the Stokes force. Einstein was merely interested in the long-time solution and found for the solution a diffusion equation. It was a pure thermodynamic study, and he assumed elastic collisions for particles and high viscosity. The main results of that Brownian theory are that the mean-square displacement $\langle x^2 \rangle$ suffered by a spherical Brownian particle, of radius a, in time t is given by

$$\langle x^2 \rangle = \left(\frac{RT}{3\pi N_{av} a \eta} \right) t, \qquad 1.$$

where T is the temperature, η is the viscosity of the fluid, R is the gas constant and N_{av} is the Avogadro number.

The second important result was his derivation of the diffusion equation for the probability of the particle being at position x at time t:

$$\frac{\partial P}{\partial t} = D \frac{\partial^2 P}{\partial x^2}. \qquad 2.$$

The solution of the diffusion equation was given by

$$P(x,t) = \frac{1}{\left[2\pi\sigma^2(t)\right]^{1/2}} e^{-x^2/(2\sigma^2)}, \qquad 3.$$

where $\sigma^2(t) = 2Dt$, and D is the particle diffusion coefficient.

Smoluchowski was more careful using a probabilistic approach. He found that the transition from ballistic motion to diffusive motion occurs for the particle at a timescale of 10^{-8} s. The diffusion equations derived from the Einstein and Smoluchowski treatments are mathematically similar, but Smoluchowski's equation defines a concentration-dependent diffusion coefficient, whereas in Einstein's it is a constant. Also, Smoluchowski derived the diffusion equation in the presence of a force F, where f is a friction coefficient:

$$\frac{\partial P}{\partial t} = -\frac{1}{f}\frac{\partial}{\partial x}(PF) + D\frac{\partial^2 P}{\partial x^2}. \quad 4.$$

This is now called the Smoluchowski equation.

Again, and as usual in this problem, a new surprise came from a much simpler theoretical approach proposed in 1908 by Langevin (9, 10). In his one-page paper, he derived a dynamic equation with viscosity as the damping force and a necessary white noise–type fluctuating force X that was supposed to sustain the movement. This is the famous Langevin equation. Let us follow Langevin's paper.

If $\xi = \frac{dx}{dt}$ is the speed, at a given instant, of the particle in the direction that is considered, then one has, for the average, extending to many identical particles of mass m,

$$m\overline{\xi^2} = \frac{RT}{N}, \quad 5.$$

and

$$m\frac{dx^2}{dt^2} = -6\pi\mu a\frac{dx}{dt} + X. \quad 6.$$

If we consider a particle to be large with respect to the average distance between the molecules of water moving in a fluid, and the motion is caused by temperature, then the particle experiences a Stokes drag force. This value is only a mean, given the irregularities of the impact of surrounding molecules, and the fluid action oscillates. This force X is indifferently positive or negative and its magnitude maintains the agitation of the particle; otherwise the viscous resistance will make the particle stop moving. Various models have been proposed for this force X.

The fluctuating force X is an unknown that is open to many possibilities. If one follows energy equipartition, then X is a white noise force. Langevin within these premises could deduce Einstein's equation.

Finally, in 1925 Paul Levy (11) generalized the Brownian movement concept. The, by now, standard Levy walk is performed by a particle that moves in a ballistic trajectory between randomly occurring collisions and where the intercollision time is a random variable governed by a power-law distribution. It leads to

$$\langle x^2 \rangle = t^{\mu}, \quad 7.$$

where μ is larger or smaller than 1. Later, in 1947, M. Kac (12) presented a discrete approach for a random walk model for the Brownian particle.

2. JEAN PERRIN'S PRECISE EXPERIMENT AND CONCEPTS LEADING TO THE IDEA OF FRACTALS (1913)

Jean Perrin (13, p. 3) first acknowledged the acuteness of the theoretical physicists. Physicists thought that the Brownian phenomenon was

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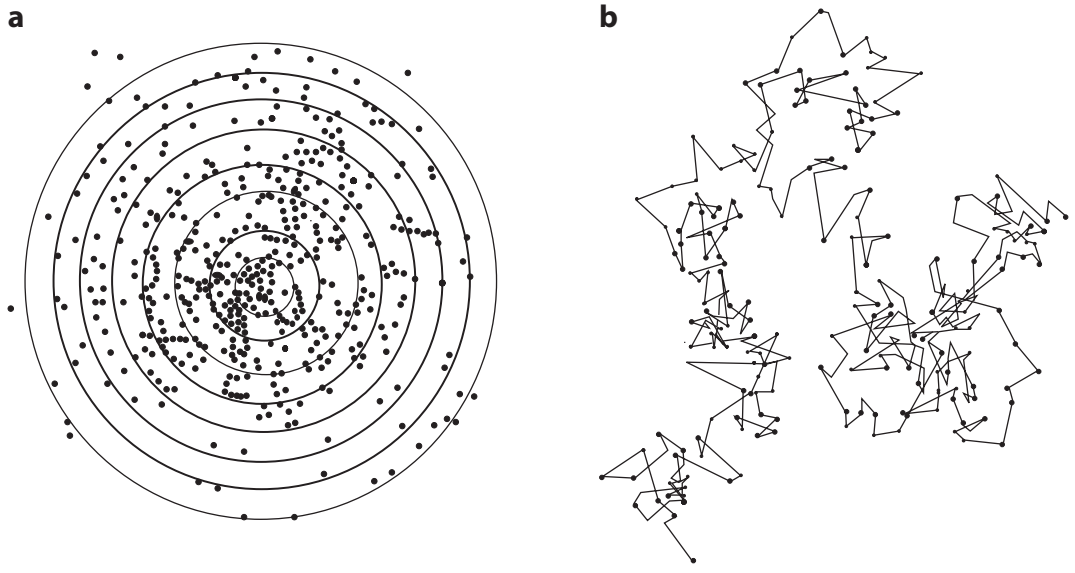

Figure 1

(*a*) Pattern obtained for the same mastic of grains by considering only grains starting from the same point. The idea of this representation came from Langevin (14). (*b*) Consecutive positions occupied by mastic grain of radius 0.53 μm. Complete irregularity of the agitation was described by Perrin. Figure adapted from Reference 14 with permission.

> analogous to the movement of the dust particles, which can be seen dancing in a ray of sun light, under the influence of feeble currents of air which set up small differences of pressure or temperature. When we reflect that this apparent explanation was able to satisfy even thoughtful minds, we ought the more to admire the acuteness of those physicists, who have recognised in this, supposed insignificant, phenomenon a fundamental property of matter.

Perrin (13) undertook a systematic study of Brownian motion (see **Figure 1**). But his aim was first to measure the Avogadro number, which is part of the theory (Equation 1).

Using the newly developed ultramicroscope, Perrin carefully observed the sedimentation of particles of gamboge, a latex, monodisperse to within 1%. This provided experimental confirmation of Einstein's equations. Perrin's observations also enabled him to estimate the size of water molecules and atoms as well as their number. He got for the Avogadro number the value

$$N_{\text{av}} = 7.05 \times 10^{23}, \qquad 8.$$

which is not far from the precise value, 6.02×10^{23}.

This was an answer to Einstein's doctoral thesis (15). There Einstein proposed to measure the Avogadro number as a confirmation of the atomic theory. This atomic theory was indeed seriously contested at that time, mainly by Mach and Ostwald.

For example, Ostwald (16, p. 471) wrote in 1909: "I have convinced myself that we have recently come into possession of experimental proof of the discrete or grainy nature of matter, for which the atomic hypothesis had vainly been sought for centuries…."

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In 1913 after Perrin's results, Poincaré (17, pp. 89–90) wrote,

> atoms are no longer a convenient fiction; it seems, so to speak, that we see them since we know how to count them.... The brilliant determinations of the number of atoms computed by Mr. Perrin have completed the triumph of atomism.... The atom of the chemist is now a reality....

This was the first time the size of atoms and molecules could be reliably calculated from visual observations. At that time, it raised atoms from useful hypothetical objects to observable entities.

Perrin then developed a systematic study of the particle trajectories and could confirm that the mean square displacement is proportional to time. But some experimental results were raising some doubts about Einstein's theory, and Perrin (14, p. 121) noticed:

> I have been very much struck by the readiness with which at that time it was assumed that the theory rested upon some unsupported hypothesis. I am convinced by this of how limited at bottom is our faith in theories; we regard them as instruments useful in discovery rather than actual demonstrations of fact.

Finally, in the introduction to his book *Atoms* (14), Perrin made some fascinating proposals. The problem of continuous curves without tangents is usually a pure mathematical problem. Perrin proposed that, in fact, in physical situations, one is dealing with continuous curves presenting no tangents. The theory was later developed by Benoit Mandelbrot (18, 19).

Perrin (14, pp. IX–X; emphasis in original) wrote:

> We must bear in mind that the uncertainty as to the position of the tangent plane at a point on the contour is by no means of the same order as the uncertainty involved, according to the scale of the map used, in fixing a tangent at a point on the coast line of Brittany. The tangent would be different according to the scale, but a tangent could always be found, for a map is a conventional diagram in which, by construction, every line has a tangent. An essential characteristic of our flake (and, indeed, of the coast line also when, instead of studying it as a map, we observe the line itself at various distances from it) is, on the contrary, that on any scale we *suspect*, without seeing them clearly, details that absolutely prohibit the fixing of a tangent.
>
> We are still in the realm of experimental reality when, under the microscope, we observe the Brownian movement agitating each small particle suspended in a fluid.... An unprejudiced observer would therefore come to the conclusion that he is dealing with an underived function, instead of a curve to which a tangent could be drawn.

This example of the coast of Brittany proposed by Perrin had an echo, 50 years later, in Mandelbrot's paper (18) entitled "How Long Is the Coast of Britain?" followed by Mandelbrot's introduction to fractal dimension (19).

3. PLAYING WITH BROWNIAN OBJECTS AFTER 1970

This is not the end of the problem but a new beginning. It restarted in the 1950s when biologists realized that several biological objects of micrometer size show, on long timescales, a Brownian behavior; the main bacterium *Escherichia coli* is micron sized and showed diffusion over long times, but over short times, up to 1 s, the movement is not diffusive. It opened the study of active Brownian movement where, through mechanical energy expenditure, not kT, a lot of active motion is present. Howard Berg's (20, 21) work is preeminent in this area. His work even opened the door to single-molecule biophysics.

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Later, starting in 1970, several new techniques were developed to greatly improve microscope techniques. In addition, forces could be applied and measured. A new probe covered the range of 1 to 100 pN; it is called optical tweezers (22, 23). To provide some scale, kT corresponds to a fluctuating force of the order of 1 pN. Later magnetic tweezers (24) were also developed.

Optical trapping is conceptually simple. A dielectric object in an electric field is polarized. In the presence of an electric field gradient, the polarized particle moves toward the region of highest field. The transverse Gaussian intensity profile across the width of the beam pulls the object toward the beam axis. To counter the destabilizing radiation pressure, one sharply focuses the laser, imposing an electric field gradient along the beam direction.

Thus, the Brownian object became again an experimental field of study, as it could be manipulated and measured with precision down to 0.1 μm, which is an ideal size for Brownian particles.

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3.1. Brownian Movement in a Force Field

With optical tweezers it is easy to trap a Brownian particle. A particle caught in a potential hole that, through the shuttling action of Brownian movement, can escape over a potential barrier yields a suitable model for elucidating chemical reaction kinetics. In his seminal work, Kramers (25) considered the escape of a particle over a potential barrier, as shown in **Figure 2**.

He found for the particle mean residence, also called Kramers time $\bar{\tau}_k$,

$$\bar{\tau}_k \cong \tau_R \, e^{Q/kT}, \qquad 9.$$

where τ_R is the relaxation time for the particle to fall into the potential well, and Q is the barrier height. Both $\bar{\tau}_k$ and τ_R can be measured, and from those measurements one can deduce the value Q

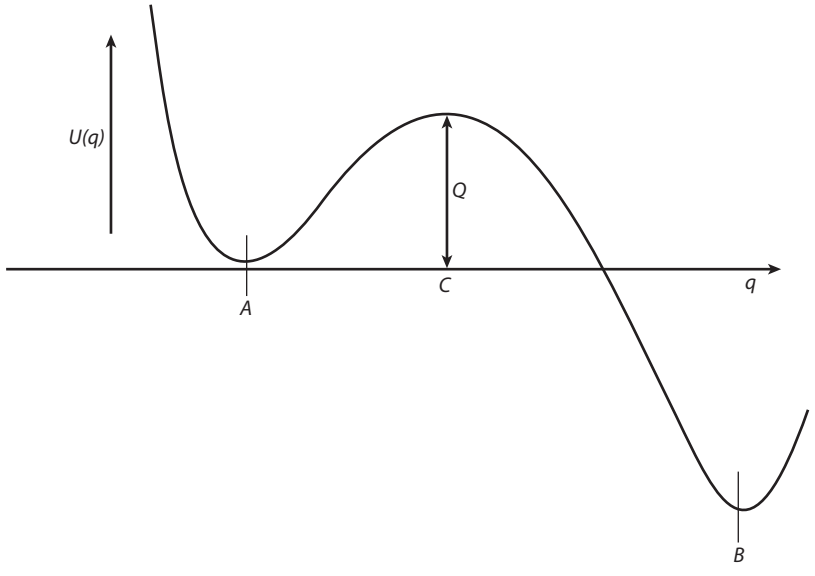

Figure 2

Potential field with smooth barrier as described by Kramers (25). To escape over the potential barrier, the particle trapped in well A must be thermally activated to overcome the barrier C of height Q and reach B. Figure adapted from Reference 25, p. 291. Copyright 1940 with permission from Elsevier.

of the barrier height. Kramers also found that the residence times in the well have an exponential distribution from which the mean Kramers time, $\bar{\tau}_k$, can be calculated.

Experiments are conceptually simple (26). Localize a Brownian particle in a double potential well and observe the thermally driven escape from one well to the other, as shown in **Figure 3*a***. The particle is trapped in a bistable potential well of interwell spacing d and barrier height Q. **Figure 3*b*** shows typical escape events, from which an exponential probability distribution is measured (**Figure 3*c***), as is, thus, a mean residence time. It is typically of the order of seconds in our setup. The relaxation time of the particle in the well τ_R is more difficult to estimate: It is on the order of 0.1 s, and in this experiment Q is of the order of a few kT. This was another direct confirmation of Kramers's theory.

The next step was to test Benzi et al.'s (28) stochastic resonance hypothesis. This occurs when the two wells are modulated asymmetrically, i.e., one up and one down and then vice versa. When the modulation time is equal to the Kramers escape time, a resonance occurs for the probability of escape. We have now three times: the mean Kramers time, $\bar{\tau}_k$; the well relaxation time, τ_R; and a modulation period, τ. One usually observes synchronization with harmonics for $\bar{\tau}_k < \tau$ (**Figure 4*a***). But when $\tau = \bar{\tau}_k$ one observes a resonance with no harmonics (**Figure 4*b***) corresponding to stochastic resonance. This experiment is the physical realization of Benzi's and Parisi's ideas (28).

3.2. Brownian Particles in a Rotating Optical Trap with Periodic Forcing

When trying to move an optical trap with a particle in it (29), as shown in **Figure 5*a***, the viscous drag, proportional to the particle velocity, will eventually cause the particle to exit from the trap. In our geometry (10- to 20-mm diameter, around 10-Hz rotation frequency), the trap always returns before the particle diffuses away (short times for the trap return, long times for the particle diffusion). It confines the particle motion to one dimension, a circle (**Figure 5*a***). The typical scenario, as the trap velocity increases, is as follows: For a small velocity the drag force is smaller than the trapping force, and the particle follows the rotating beam. It is a phase locked regime. For larger velocities, the particle escapes but does not have enough time to diffuse away from the circle; it keeps rotating, but at the smaller mean velocity than the tweezer. It is a phase slip regime (**Figure 5*b***). Finally, for much higher rotation velocity (**Figure 5*c***), no net angular motion is observed, and the particle diffuses freely on the circle. The system thus evolves from a synchronous motor to an asynchronous one and, finally, to a free diffusive motion, but always localized on the circle. So, on any closed optical trap trajectory the particle will remain in that trajectory, and this is valid for any reasonable rotation speed. This is a surprising and very explicit method for studying Brownian movement in one dimension.

3.3. The Brownian Thermal Ratchet

Starting in the 1940s, biologists discovered that some proteins are molecular machines that convert the chemical energy from ATP hydrolysis to mechanical work (30–32). They move along tracks made of actin filaments or microtubules. Intense study by physicists followed to understand the functioning of the motor proteins. Among many models, an interesting one was the Brownian thermal ratchet (33–35). It is based on Brownian particles that are diffusing and is regularly submitted to an asymmetric space periodic force, as shown in **Figure 6**.

In the absence of external forces, Brownian particles do not experience any macroscopic drift. In a similar way, a spatially periodic external potential, asymmetric or not, does not induce large-scale motion, as the associated large-scale gradient (force) is zero. However, a time modulation between the two regimes (free diffusion, applied potential) induces macroscopic drifts of Brownian

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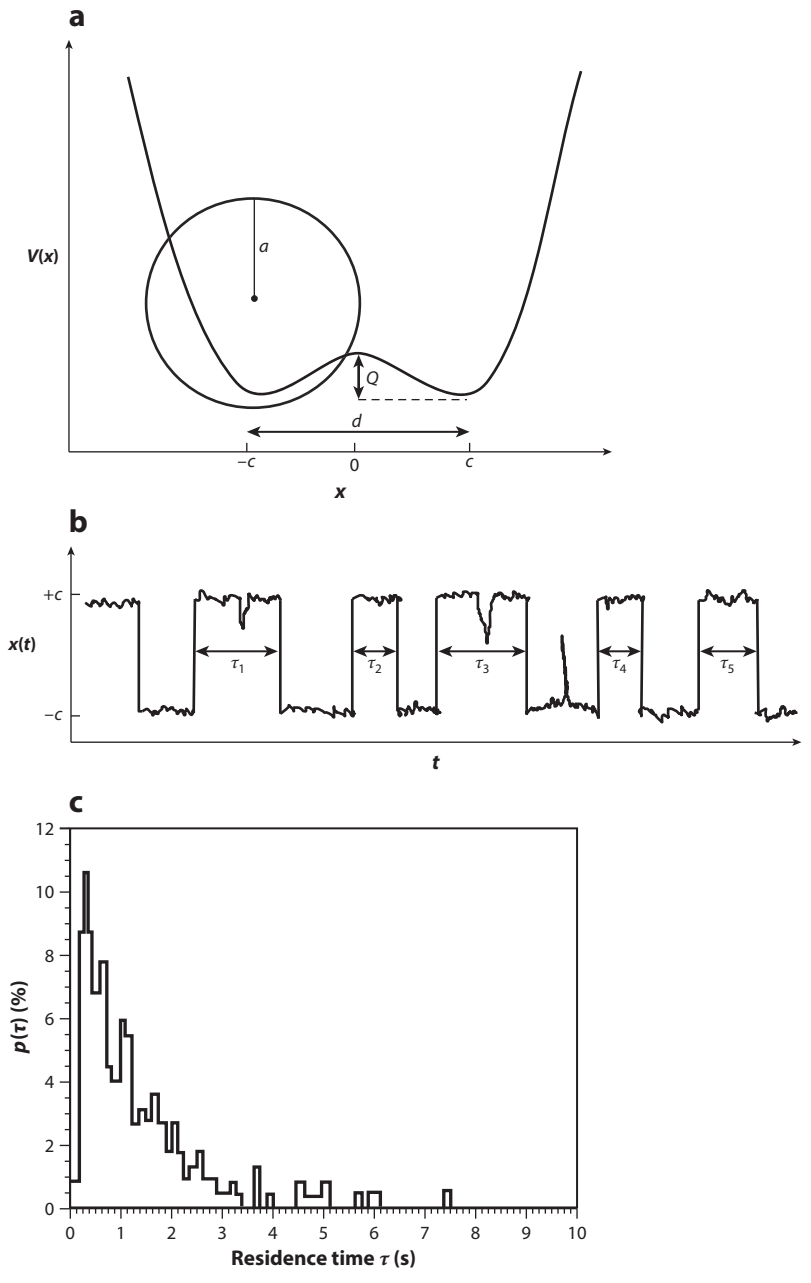

Figure 3

(*a*) Geometry and schematic of the double well. *a* is a bead radius, *Q* is the barrier height, and *d* is the distance between the wells. (*b*) The position of the particle as it escapes from $+c$ to $-c$ well. The set of first passage times $\{\tau_i\}$ between escape events determines the probability distribution. (*c*) Probability distribution for residence times in the well. Panels *a* and *c* adapted with permission from Reference 26, pp. 3376–77. Copyright 1992 by the American Physical Society. Panel *b* adapted from Reference 27 with permission.

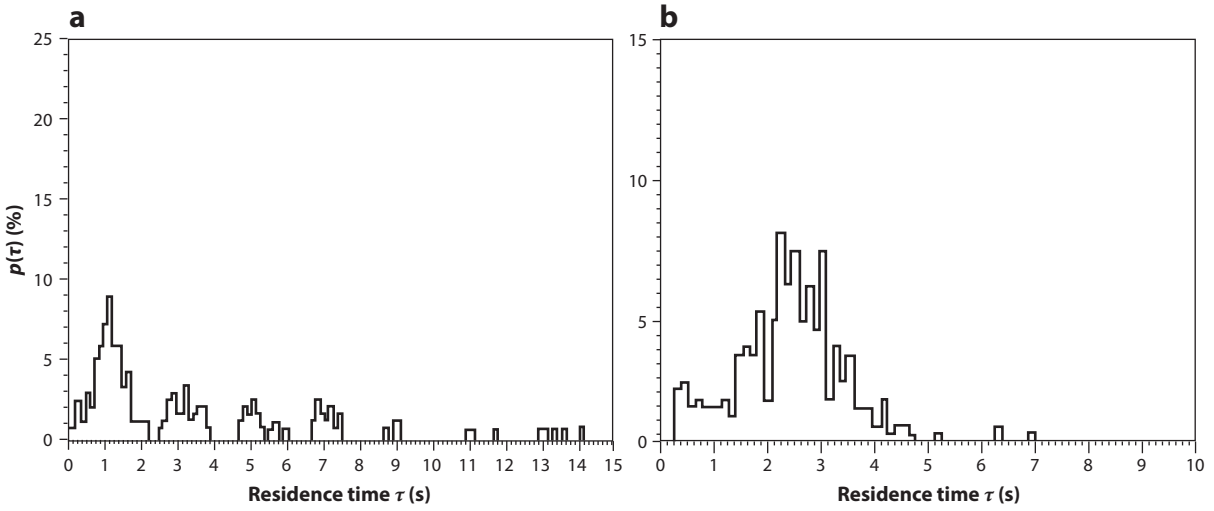

Figure 4

Probability distribution with a modulation applied to the double well. (*a*) The Kramers escape time $\bar{\tau}_k$ is smaller than the modulation time τ. This is a fundamental view of many harmonics. (*b*) Resonance, with no harmonics, for $\bar{\tau}_k = \tau$. Panel *a* adapted from Reference 27 with permission. Panel *b* adapted with permission from Reference 26, p. 3377. Copyright 1992 by the American Physical Society.

particles when the potential is asymmetric. Other mechanisms of motion have also been proposed. The principle as shown in **Figure 6** is the following: The field traps the particles in the potential minima. They freely diffuse when the field is off. When the field is switched on again after a modulation time τ_{mod}, the particles follow the local gradient of potential and get trapped in the corresponding minimum. Given the asymmetry of the potential, the particles' average diffusion time over the right-hand barrier is shorter than over the left-hand one; thus trapping into the right-hand well is preferred. Repeating this process induces a macroscopic drift of particles from left to right. The induced drift is a function of the diffusion coefficient of the particles and the modulation time of the applied field: For small τ_{mod}, the drift is zero, and the particle does not have enough time to diffuse to the next minimum. For large τ_{mod}, the particle diffuses to the forward and backward minima with equal probability ½. In between there is a maximum for the drift, which is somewhat related to stochastic resonance.

The forward and backward probabilities can be estimated as

$$P_f \approx \frac{1}{2}\exp\left(\frac{-\tau_f}{\tau_{mod}}\right) \qquad 10.$$

and

$$P_b \approx \frac{1}{2}\exp\left(\frac{-\tau_b}{\tau_{mod}}\right), \qquad 11.$$

where the characteristic diffusive times τ_f and τ_b, over the lengths λ_f and λ_b, are

$$\tau_f = \left(\lambda_f^2/2D\right) \qquad 12.$$

and

$$\tau_b = \left(\lambda_b^2/2D\right). \qquad 13.$$

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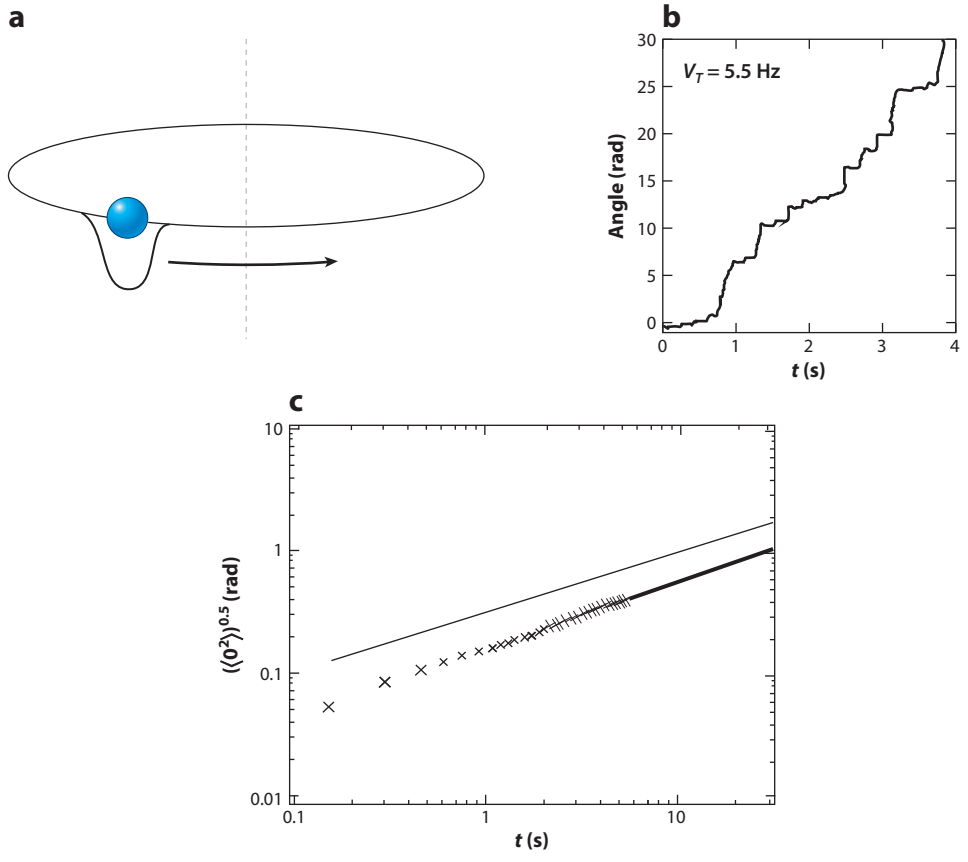

Figure 5

(*a*) Rotation of the optical trap along a circle of diameter 7 μm. The particle follows the trap. (*b*) Time series of the particle angular displacement, with trap rotation frequency of 5.5 Hz and output laser power of 700 mW. Escape times are clearly visible. (*c*) Root mean square value of the particle angular displacement as a function of time, with trap frequency of 100 Hz. The straight line indicates a power law with exponent ½ showing diffusion. Figure adapted with permission from Reference 29, pp. 5241, 5243–44. Copyright 1995 by the American Physical Society.

3.4. An Optical Thermal Ratchet

In Section 3.2, we showed how to produce a 1D Brownian motion for a trapped particle, with the trap created by an optical tweezer. If that trap is moving fast enough on a circle the particle will diffuse on the track trajectory, as shown in **Figure 5*c***. One can use this remarkable result to build an optical model based on Brownian movement. If now one modulates the tweezer light intensity with a special asymmetric amplitude modulation (**Figure 7**), the particle gets localized in a region of maximum beam intensity (37, 38).

When the modulation amplitude is off, but the light on, the particle diffuses. Giving enough time for the diffusion, τ_{off}, the particle will eventually advance in only one direction as the modulation is turned on again. Given the probabilities forward and backward, P_f and P_b (**Figure 8*a***), as a function of the time off, τ_{off}, the difference, $P_f - P_b$, will measure the motion.

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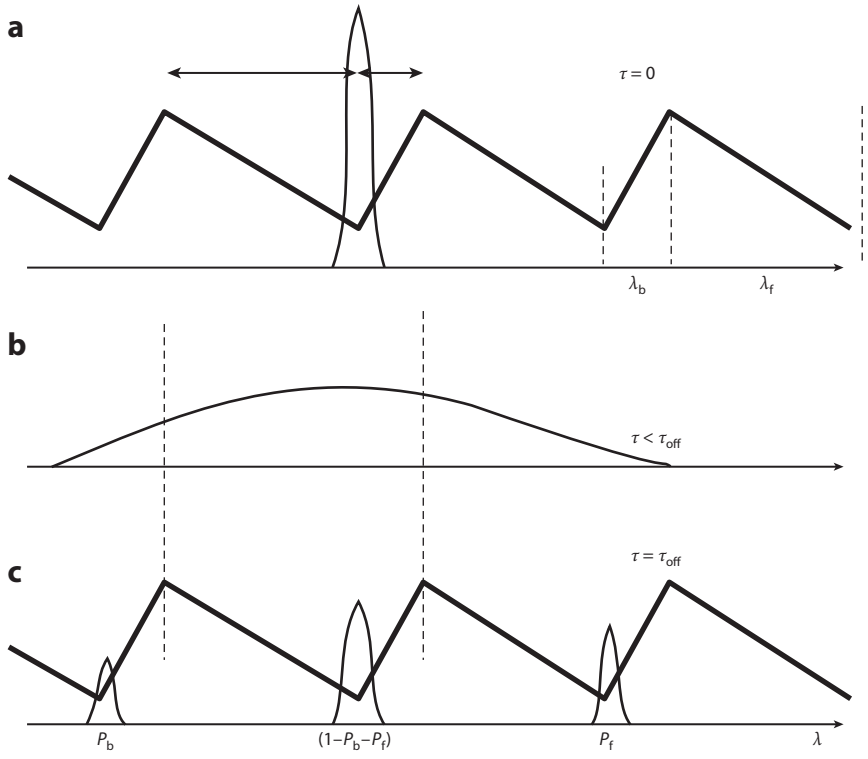

Figure 6

Illustration of asymmetric potential (*thick lines*) and particle probability densities (*thin lines*). λ_b and λ_f are the lengths of the asymmetric potential. (*a*) At time $\tau = 0$ the particle is localized, and the probability density is sharply peaked. (*b*) For times $\tau < \tau_{off}$, the potential is off and the particle diffuses freely. (*c*) At time $\tau = \tau_{off}$, the potential is back on and the particle is forced into forward and backward directions with probabilities P_f and P_b. Figure adapted with permission from Reference 37, p. 1504. Copyright 1995 by the American Physical Society.

There is an optimal τ_{off} for maximum displacement (**Figure 8*b***). We note that it is only on average that the particle motion follows the drift.

So, breaking spatial symmetry and introducing modulation in time are enough to induce direct motion from a random Brownian noise. An optical asynchronous motor functioning on Brownian noise is thus being constructed. The relationship to biological molecular motors is not clear, to say the least (34, 35).

4. ACTIVE BROWNIAN MOVEMENT

In this article, we started our description with Brown's 1828 observation of particles moving stochastically. Brown, in his first observation, attributed the motion to life activity until it became obvious that it was a physics problem of stochastic thermodynamics.

Moving now full circle, we come back to the motion of living organisms. Richards (36, p. 63) noted that there are two types of problems: "There are problems that one poses, and there are problems that pose themselves." Brownian motion was a problem that posed itself. We are now studying a problem that we pose: What about Brownian motion for living bacteria? The model

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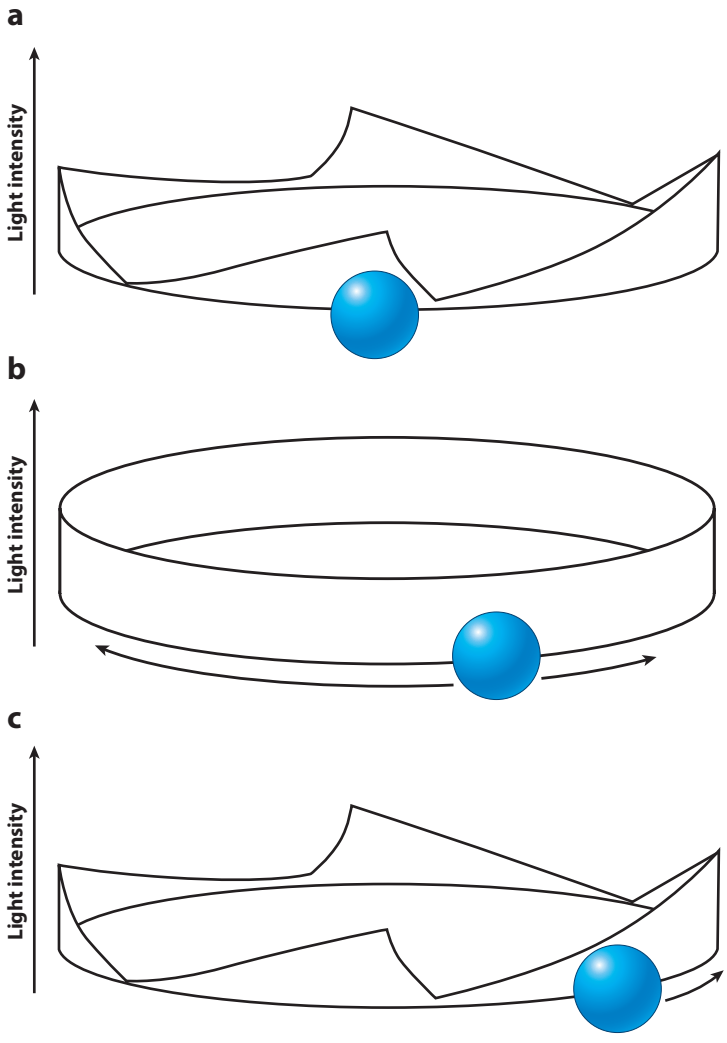

Figure 7

The spatially asymmetric modulation of the beam intensity along the circle traced by the optical trap is shown as a thin solid line (four modulations per optical trap cycle). When the modulation is on (*a*), the 1.5-μm-diameter bead is localized in a region of maximum beam intensity. When the modulation is off (*b*), the beam intensity is constant and the particle diffuses freely along the circle. Given enough off time (*c*), the next time the modulation is on the particle moves to the right. Figure adapted with permission from Reference 37, p. 1505. Copyright 1995 by the American Physical Society.

system is that of the typical *E. coli* bacterium, which is of typical Brownian size, one micrometer. A systematic study of *E. coli* dynamics was undertaken by Howard Berg and is well documented in his two books (39, 40). A quite remarkable paper by Purcell, titled "Life at Low Reynolds Number" (41), is a gem of pedagogical literature. It introduces all that is necessary to understand hydrodynamics at the micron-scale level. What was observed was that, indeed, on a long timescale of more than 1 s, bacteria behave like Brownian objects, diffusing but with an effective temperature close to 1,000 K. In the following, we describe experiments in our laboratory related to this problem.

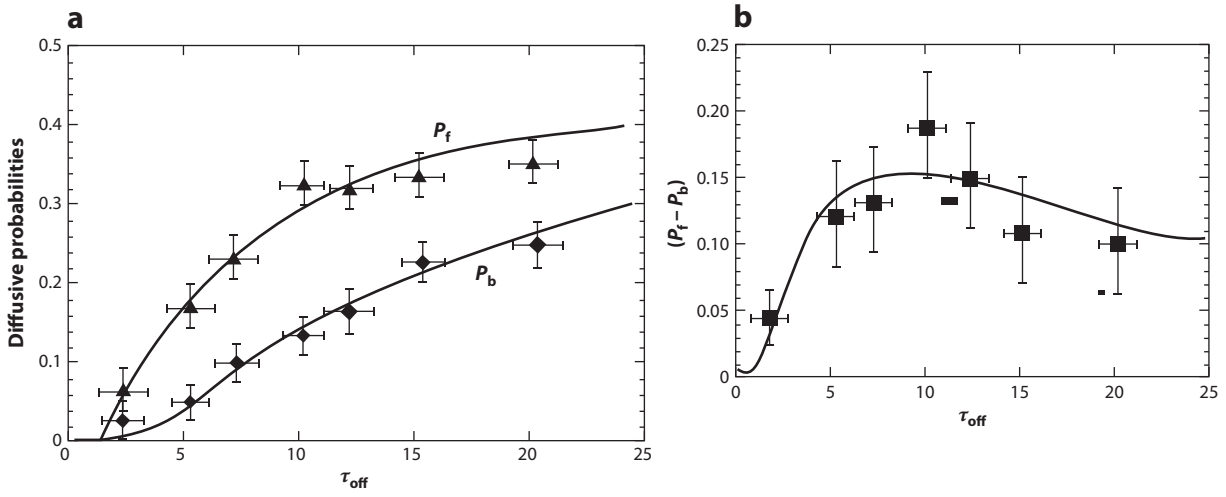

Figure 8

(*a*) The probabilities for the particle to move forward or backward as a function of τ_{off}. The two solid lines are theoretical fits. (*b*) The drift probability, i.e., the difference between the two curves in panel *a*. Figure adapted with permission from Reference 37, p. 1506. Copyright 1995 by the American Physical Society.

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4.1. Brownian Particle Diffusion in a Two-Dimensional Bacteria Bath

What happens to the Brownian movement of a particle in a sea of bacteria instead of a sea of water? This is the question we asked ourselves (42). We thus redefine Brownian movement but in a bacteria bath. We used particles of 10 μm in size so that they have essentially no visible Brownian movement. We constructed a two-dimensional (2D) setup using a free suspended horizontal soap film, where the water thickness is about a few microns. In it we suspended a small number of 10-μm beads and a high concentration of *E. coli*, $N = 510^{10}$ cell/cm^3, which is about 10% of the total volume, and we studied the beads' dynamics. For long timescales, above 10 s, normal diffusion was observed (**Figure 9**), whereas for short timescales the mean square displacement was super diffusive (**Figure 9*c***). We also observed transient formation of coherent swirls and jets in the bacteria bath. This critical time τ_c between the two regimes increases linearly with bacteria density. Also, the diffusive character of the bead was associated with an effective temperature of about 1,000 K. The bacteria velocity distribution did follow a Maxwellian velocity with mean velocity of 20 μm per second, which is a typical velocity for *E. coli*. The bacteria behaved as if they were in a three-dimensional (3D) cell. What was striking is that the positions of the 10-μm beads fluctuated strongly on distances of more than 100 μm. Thus, on short timescales, the 10-μm particle motion showed certain persistent behavior with some ballistic motion (**Figure 9*a***) and a super diffusive motion with an exponent $\propto = 1.5$. For timescales greater than 10 s, the particle motion proved to be pure diffusion with a diffusion coefficient $D_T = 10^{-9}$cm^2/s. This implies that the effective temperature of the bacteria is about 100 times greater than room temperature.

Grégoire et al. (43, 44) undertook a theoretical analysis of this stunning experiment. A Langevin equation will not suffice as it would introduce a transition between diffusion and ballistic motion that is not observed. Grégoire took a model originally proposed by Viscek et al. (45), who would

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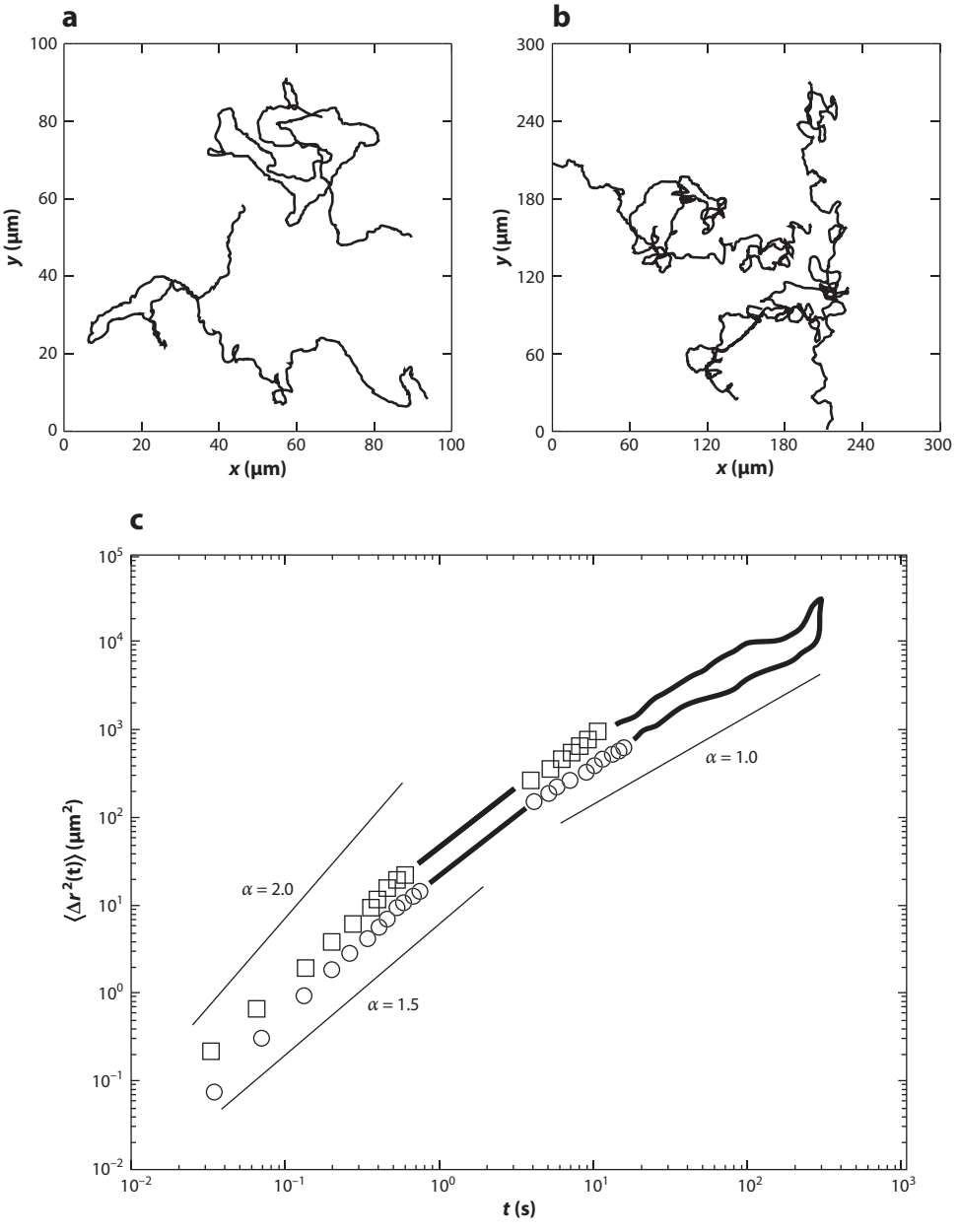

Figure 9

(*a*) Motion of two 10-μm beads followed for 20 s. (*b*) The same beads followed for 3 min. (*c*) The mean square displacement measurement for 4.5- and 10-μm beads (squares and circles, respectively). The solid lines guide the eye. Figure adapted with permission from Reference 42, p. 3018. Copyright 2000 by the American Physical Society.

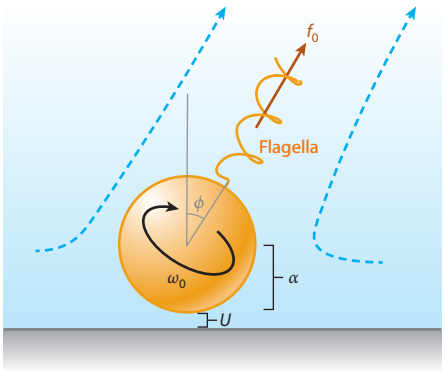

Figure 10

Cell along a glass plate positioned at a small distance U from the plate. The finite angle ϕ indicates motion. The water flow field is shown by the two dashed lines and arrows. ω_0 is the angular velocity imposed by the flagella, and f_0 is its force. Figure adapted from Reference 50 with permission.

reproduce the experimental result. It is called the self-propelled XY spin. In the experiment one could also observe collective motion in the bacteria bath such as short-lifetime swirls and jets.

4.2. Rotating Crystals of Bacteria

Let us move finally to *Thiovulum majus*, a very peculiar bacterium particularly because of its size, 10 μm in diameter, and its fast swimming velocity, up to 600 μm/s, caused by an enormously large number of flagella, around 400. It might be the fastest known living bacteria. The bacterium was purified after extraction by A. Petroff from the salt marshes near Woods Hole, Massachusetts. It is a sulfur oxidating bacterium (46). What is remarkable about this bacterium (**Figure 10**) is that when a colony of bacteria is confined between a glass slide and a coverslip, the cells localize on the glass surfaces and diffuse along the glass plate like an active Brownian object; when two bacteria are within the distance of their size, they dimerize and rotate with respect to each other. Slowly, a rotating 2D crystal grows (47). Similar phenomena have also been observed in sperms (48) and *Volvox* (49).

Figure 10 shows a sketch of the cell localized near a glass plate (50). The cell motion is characterized by the cell radius, α, the flagellar force, f_0, and the angular velocity, ω_0.

Two important parameters are the gap thickness U between the cell and wall (tens of nanometers) and the orientation of the flagella relative to the minimal ϕ. For $\phi = 0$ the cell does not move. For any change in angle, a force $f_0 \sin\phi$ is applied, causing the cell to move. As this angle keeps fluctuating, the cell develops a random motion, Brownian type (**Figure 11*b***) with an effective temperature of 410^4 K. If one bound cell approaches another within 15 μm, they are pulled into a dimer, i.e., the nucleus for crystal formation.

The physics of the problem is simple. Near a plate, at a distance U, the cell induces a large-scale flow along the plate (see **Figure 10**). This flow attracts a nearby cell. Due to the angular velocity of each cell, caused by the flagella, the particles rotate with respect to each other.

When crystallization develops (**Figure 12**) the whole crystal rotates. This active Brownian object is an interesting case of a bacterium bound to a plate, caused only by hydrodynamic interaction, and creating a small gap U between the bacterium and the plate. This is a beautiful applied mathematics question. It is a pure exercise of hydrodynamics with no apparent chemostasis or chemical attractants.

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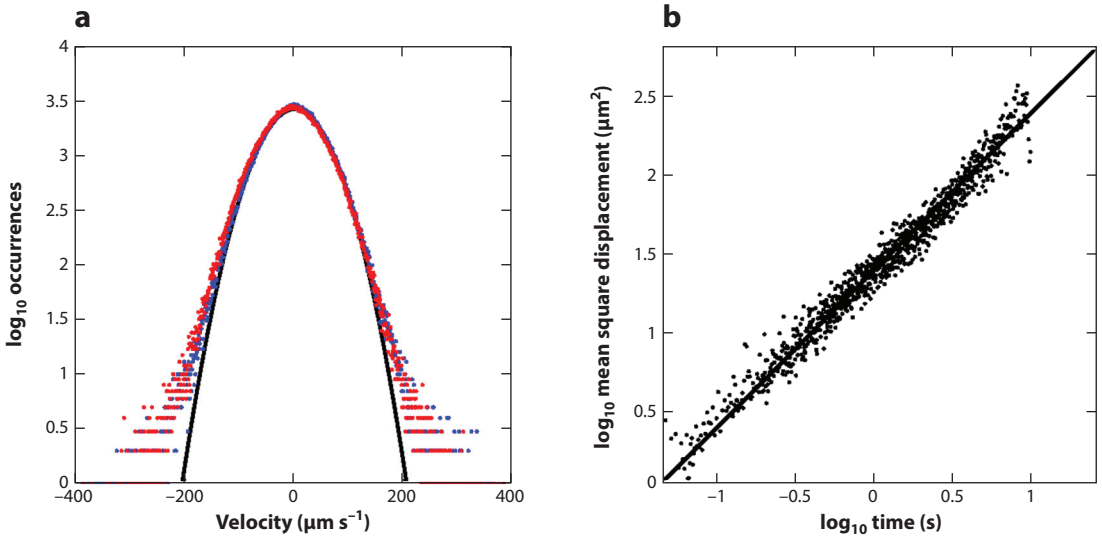

Figure 11

(*a*) Distribution of instantaneous velocities taken from 922,360 measurements. (*b*) Mean square displacement fit to linear diffusion (*black line*). Figure adapted from Reference 50 with permission.

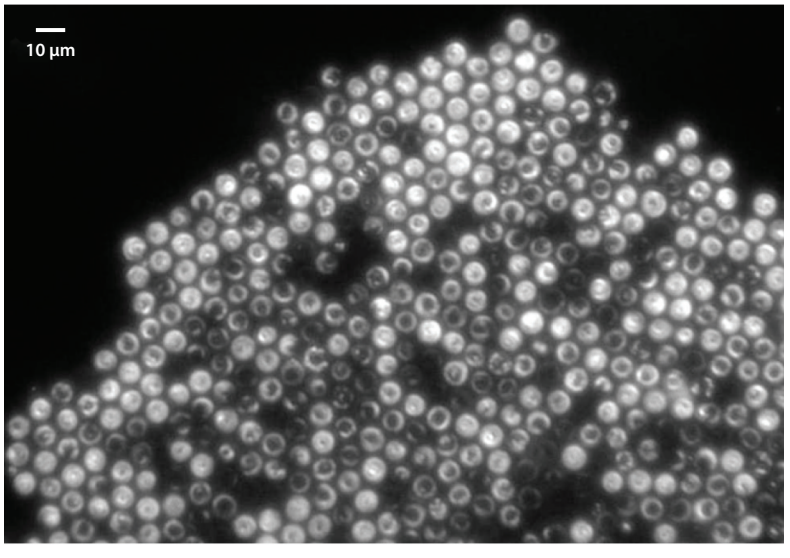

Figure 12

A large bacterial crystal in dark-field illumination. The bright glow of individual cells is caused by light scattering off the sulfur globules present inside the bacteria. Differences in cell illumination are caused by different amounts of globules. The bacterium diameter is about 8 μm. The classical six-fold symmetry of two-dimensional crystals is visible as well as are some facets. Figure adapted with permission from Reference 47, p. 2. Copyright 2015 by the American Physical Society.

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5. CONCLUSION

It is rare in physics to find a simple phenomenon not only active for almost 200 years but also still very present. This is the case with Brownian movement. Agitation of a micron-scale particle in water seems a simple phenomenon and looks trivial, but as Perrin noticed some profound scientists realized that behind the phenomenon lay a deep question of statistical physics. It also led to solving the nagging question of whether the atomic theory was just an abstract concept or a reality. Einstein's PhD thesis addressed just this problem and showed that Avogadro's number could be measured, and this would justify the atomic theory. This was one of Perrin's successful experiments, as he measured Avogadro's number in a study that was a tour de force, having to make reasonably monodisperse mastic from particles of $\sim$1 μm in size. The other beautiful remark of Perrin, following his observation of Brownian movement, was to propose that continuous functions without derivative were a common problem in physics. In doing that, and using the coast of Britanny to illustrate it, Perrin's intuition was exceptional. It opened, 50 years in advance, the theory of fractals. But the Brownian problem also brought some interesting new formalisms, like the Langevin equation and his famous fluctuating X function, white noise if equipartition but color otherwise. Let us also note that it allowed Levy & Loeve (11) to introduce another type of fluctuating motion, the Levy walks, to successfully understand foraging in biology (51). Another fascinating aspect of the problem was how Bachelier, before Einstein and Smoluchowski, proposed a close-by solution by studying the fluctuation in the stock market of a stock perturbed by bombardment of buying and selling. In doing so, Bachelier became the grandfather of mathematical finance (6).

The subject was reopened in the 1970s, when new techniques were developed to manipulate Brownian objects. The discovery of a new tool, the optical tweezer by Ashkin (22), opened a lot of possibilities, as it allowed the trapping of particles and moving them. Kramers's theory (25) of chemical reactions was easily checked by studying Brownian particle escape from an optical trap. Experiments on the synchronization of the escape led to stochastic resonance (28). The realization of stochastic thermal ratchets based on Brownian movement, as proposed by Prost et al. (34) and Magnasco (35), was also achieved.

Another development came from biology. In 1828, Brownian motion was considered a biological active phenomenon until it was understood that it was a physics problem. But now, following the pioneering work of Howard Berg (39, 40) on bacteria motion, bacteria of micron scale and even motor proteins (52, 53) have on long timescales a diffusion behavior that is Brownian-like but with an effective temperature of thousands of degrees Kelvin. To give clarity on the experimental scale, Brownian movement relates to kT energy, which is on the order of 1 pN of fluctuating force, whereas the force of bacterium flagellum is of the order of 50 to 100 pN. This explains the high effective temperature of bacteria diffusion.

Finally, following Purcell (41), let us review some relevant numbers. We are dealing here with small objects in water. In a fluid, an important characteristic force is of dimension η^2/ρ , where η is the fluid viscosity, and ρ is its density. Its value for water is 10^{-9} pN, a nanonewton. When this force is applied, the Reynolds number for the object is equal to one (equate this force to Stokes force, $\eta^2/\rho = \eta_{\text{av}}$). But, in our problem, we are dealing with objects, or bacteria, of 1 μm in size moving in water with small velocities, on the order of 10 μm/s, so their Reynolds number in water is of order 10^{-5}. We are thus dealing with much smaller forces than a nanonewton; we are in a piconewton-force range. It is a world where there is no inertia, where in order to move a bacterium must screw up its rotating flagellum into the surrounding water. Our world is very dissipative with small applied forces and very large Brownian fluctuations. Clever algorithms must be deployed to compensate for those harsh environments. This is the world described in this review.

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This opening to the bacterial world opens new directions. Soils have a high density of bacteria, about one bacterium every 10 μm. High-energy photons from the Sun allow cyanobacteria to break water and produce oxygen; purple sulfur bacteria metabolism is related to infrared absorption; sulfur-oxidation bacteria respond to the oxygen gradient by burning H_2S; and sulfur-reducing bacteria produce this H_2S from the atmosphere SO_4 gradient. All those gradients produce a stable stratification (46). This extraordinary bacteria richness will bring new phenomena as was shown by Petroff et al. studying *T. majus* crystals (47).

DISCLOSURE STATEMENT

The author is not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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