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Ratchets: the problems with boundary conditions in insulating fluids

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ABSTRACT We have constructed microfabricated devices, designed to have asymmetry in their physical structures, in order to fractionate objects under continuous-flow conditions. The fractionation of particles with the inclusion of diffusion and asymmetric structures requires a knowledge of not only statistical mechanics but also the external forces acting on the particles, since thermal Brownian fluctuations alone cannot serve to separate particles. We explicitly examine this problem in a device designed to fractionate biomolecules dissolved in water, and show that boundary conditions that influence the direction of the applied force are quite important in determining the efficiency of the device.

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1   Introduction

The concept of a rachet (in our view, an asymmetric object that would rather turn in one direction than in another) has always fascinated scientists because it seems to violate the fundamental reversibility of classical mechanics. Feynman, in his beautiful Lectures on Physics [1], considers the rachet and pawl at some finite temperature T and shows that in equilibrium the rachet and pawl cannot rotate in a unidirectional sense, but can if a temperature gradient is applied to the system so that energy flows through the system irreversibly. It is fascinating to continue this line of thought and ask how some sort of irreversible net displacement of an object can occur in an array of asymmetric microfabricated structures of such a length scale that diffusive motions in some time t are comparable to the size of the obstacles that an object passes through. Since diffusion is a function of particle size, such a device could separate particles almost magically.

Rather than speak in generalities for this paper, let us consider a very specific example which rather weakly falls under the case of ratchets, namely the passage of particles through an array of structures which are inclined at an angle to the average direction of a force applied to the particles. We stress the word 'average' here because the presence of the obstacles not only can serve to deflect the particles but also can change the local orientation of the force field acting on the particles.

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We also explicitly assume that the medium is water, an insulating fluid. The ionic flow that carries the field lines then implies that the transport is fundamentally hydrodynamic in nature and not electrostatic.

Let us first consider the ideal situation of a force field which magically can penetrate the obstacles as if they were not present. In that case the obstacles are driven straight down by the force field, but upon collision with the obstacles must move either to the right or left in order to pass around the objects. Figure 1 shows a possible configuration where molecules confined to a region in space are confined spatially in a gate and move under the influence of a force which simply makes them fall straight down in the absence of thermal diffusion, at a constant velocity v. There is a characteristic length d, which is the distance that the object must move between openings, the average distance $\langle d \rangle \sim d$ which is the mean of the asymmetric distances $d_L + d_R$ of the obstacles perpendicular to the flow (in Fig. 1 $\langle d \rangle = [d_L + d_R]/2$), and the asymmetry $\delta d = d_L - d_R$, which represents the extra distance that the object must move to the left to get around an obstacle compared to the right. Since there is no diffusion at present in the discussion, this asymmetry is irrelevant. Particles move straight down. The time t to move between holes is simply
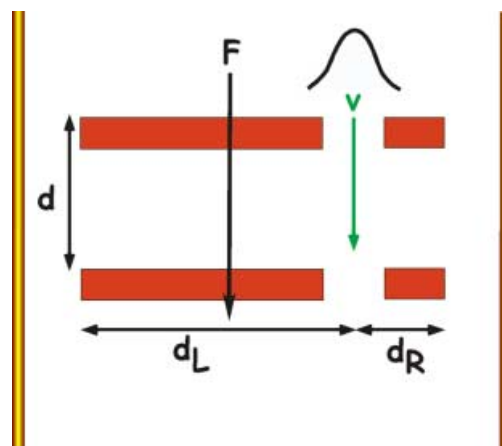
$$t = d/v. \tag{1}$$

FIGURE 1   A simple structure. Particles can move straight down in the direction v under the influence of an applied force, which can penetrate the obstacles. The initial distribution of the particles is confined to the gate. A working device would consist of a periodic array of such structures

Now, consider what happens if we allow diffusion to occur. Although the particles continue to move straight down, there is now a transverse but random displacement due to diffusion of the object. In the time that it takes the particles to move to the next hole there will be a lateral RMS displacement:

$$\delta x = \langle x^2 \rangle^{1/2} \tag{2}$$

of the particle to either side of the driving direction v. Ignoring the effects of hitting the obstacles, which we will consider shortly, one might guess that the mean displacement left or right is zero unless:

$$d_R \leq \langle x^2 \rangle^{1/2} \leq d_L, \tag{3}$$

in which case there is a good probability that the particle will move to the right. This can be viewed as a ratchet: the particle moves consistently to the right under the influence of a field pointing straight down. It violates no laws of thermodynamics because (i) it is a system not in thermal equilibrium but instead has a steady input of energy, the field driving the particle downwards; (ii) there is a spatial asymmetry to the structure. Both conditions must be met in order for this asymmetric motion to occur under the influence of a steady applied force.

Such a device can fractionate objects in principle, because the lateral displacement $\delta x \sim (2Dt >^{1/2}$ is a function of the size of the object through the diffusion coefficient D. Roughly speaking, we can say that small objects will be deflected to the right more frequently than large objects because δx is smaller for large objects than for small objects. Because the displacement δx is a function of both diffusion coefficient D and time t this sort of a fractionating device can have a large dynamic range. Discussions of such devices can be found in [2, 3] and realizations of such devices can be found in [4, 5].

There is, however, a problem with the technique that has not be explicitly addressed in any of the papers to date. There was a fundamental assumption which we put in bold face at the start of this article which we will repeat here:

Let us first consider the ideal situation of a force field which magically can penetrate the obstacles as if they were not present.

About the only force we know which can do this is gravity, although magnetic forces can approximate this if the obstacles have a very small permeability so that the induced magnetization $M \ll B$. Other common force fields in conducting liquids, typically electrophoretic or hydrodynamic, cannot penetrate obstacles. For example, suppose we microfabricate our device out of quartz, an insulating material. Then, we if use electrophoresis to move the objects down the device the electric field lines, which are determined by the paths of the ions which carry charge in an insulating liquid, must pass around the insulating obstacles rather than through, with dramatic consequences as we shall see shortly. Likewise, if we use hydrodynamic flow rather than electrophoresis, once again the fluid must pass around the obstacles rather than through them.

In fact, and this is a major point of this paper, it is possible to make an argument that in the absence of penetration of the field lines into the obstacles there can be no fractionation in an asymmetric structure for point particles. We present it here for the case of electrophoretic transport, in which case

transport occurs through electric fields E which arise from the movement of ions in the fluid:

$$v = \mu E, \tag{4}$$

where μ is the mobility of the electrophoretically transported object.

Since the electric field is due to the movement of ions in the electrically neutral fluid, and the fluid is incompressible, the divergence of the electric field E and consequently the divergence of the velocity of the particles v must be zero:

$$\nabla \bullet E = 0; \nabla \bullet v = 0. \tag{5}$$

Consider the generic asymmetric structure shown in Fig. 2, which resembles the structures we have used in our own laboratory. We have also shown the field lines around this structure if the obstacles are opaque to the force field, so that no field lines can penetrate the object. These field lines have been calculated by solving the Navier–Stokes equation in the case of a 'thin' 3-D object, where 'thin' means that the thickness h of the structure is much less than the dimensions x, y of the lateral etched structure. This is quite good an approximation in our case because the etch depth is of the order of 1 micron, while the lateral dimensions are hundreds of microns. Details of this calculation can be found in [7].

We now do the fundamental derivation for incompressible flow. Let the density of objects in the flow be ϱ. In the absence of diffusion the local flux J of the particles is then
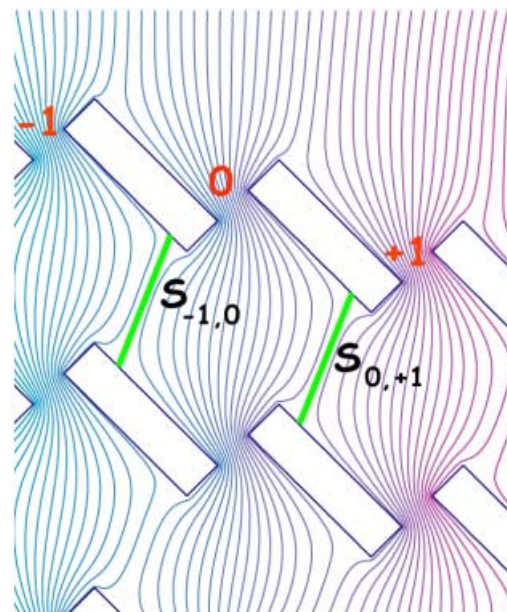
$$J = \varrho v. \tag{6}$$

FIGURE 2 Field lines in the case of a zero-divergence force field. In that case there can be no net transport by diffusion to the *right* or *left* if the particle distribution is initially symmetric around the mean coming into the array. The flux tube bounded by the $(-1, 0)$ and $(o, +1)$ surfaces is schown, and the one-dimensional surfaces which separate the $(-1, 0)$ and $(0, +1)$ flux tubes are shown

First consider the case where the diffusion coefficient D is zero. The local change in the particle density with time is

$$\frac{\partial \varrho}{\partial t} = -\nabla \bullet J = -\nabla \bullet (\varrho v). \tag{7}$$

In a steady-state flow $\frac{\partial \varrho}{\partial t} = 0$. We then find

$$0 = \frac{\partial \varrho}{\partial t} = -\varrho(\nabla \bullet v) - \nabla\varrho \bullet v. \tag{8}$$

Since $\nabla \bullet v = 0$, we get

$$\nabla\varrho \bullet v = 0. \tag{9}$$

Thus, any gradient in ϱ due to transport must be perpendicular to v. The consequence of this equation is a subtle point which we have tried to illustrate in Fig. 3. Since a streamline is a line parallel to v, we can say that ϱ cannot change along a streamline and hence any initial distribution in particles is perfectly preserved, and hence no fractionation can happen. Thus, the gradients $\nabla\varrho$ in the particle distributions that occurred with transport must be perpendicular to v, not parallel.

Now consider what happens when we turn on diffusion. The flux now has two terms:

$$J = \varrho v - D\nabla\varrho. \tag{10}$$

There are now certainly finite values to the gradient in ϱ that can occur parallel to the velocity vector, since with time diffusion can spread the initial particle distribution in any direction. But spreading of the initial distribution with distance does not represent fractionation in an asymmetric array; fractionation by ratcheting occurs by movement of the mean of the moment with distance. We consider the case where the particle distribution is symmetric around the mean coming into the array. Figure 4 contrasts this situation with the zero-diffusion situation. Once again, all gradients in the particle distribution that occurred due to diffusion must be perpendicular to v.

We next consider a distribution of particles where the mean width σ covers many gates. Label the gates with the integer i. 'Symmetric around the mean' means the following: let
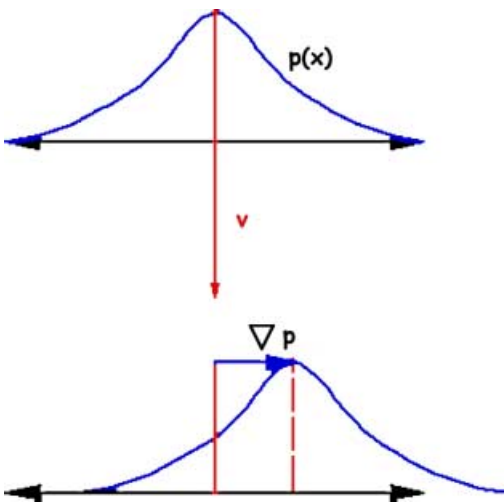

FIGURE 3 The incompressibility of the particle flux moving through structures in the case of no diffusion means that there can be no gradient in the particle flux perpendicular to the velocity v
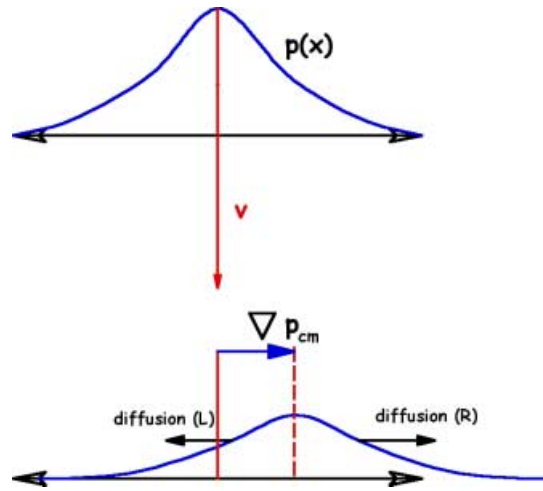

FIGURE 4 Diffusion can give rise to gradients in the particle density orthogonal to the velocity v. However, the mean position of the profile cannot change even in the presence of diffusion if the force field has zero divergence everywhere

$i = 0$ be the gate where the mean of the distribution moves. Let $\varrho_{\pm i}$ be the densities for gates $\pm i$ to the right and left of the $i = 0$ gate. The density distribution is symmetric if $\varrho_{+1} = \varrho_{-1}$. Movement of the mean can only occur if the diffusional flux across symmetrically opposed cells $\pm i$ is unequal in direction and/or magnitude.

The net flux transport ϕ_S across a streamline S which separates two flux tubes of particle flow between adjacent barriers (see Fig. 2) is

$$\phi_S = \int_S J \times dS = \int_S \varrho v \times dS - D \int_S \nabla\varrho \times dS. \tag{11}$$

Since v is parallel to dS the first term is zero and we get

$$\phi_S = -D \int_S \nabla\varrho \times dS. \tag{12}$$

However, if ϱ is symmetric around the channel labeled $i = 0$ (so that $\varrho_i = \varrho_{-i}$ and $\nabla\varrho_i = -\nabla\varrho_{-i}$ then $\phi_i = -\phi_{-i}$ and the distribution broadens, but the mean cannot shift. There is no asymmetric flux.

Does this mean these devices cannot work? No, they can work in two ways. First, if the force lines actually penetrate the obstacles rather than pass around them then there are additional terms to the force acting on the particles in addition to the field E, that is, the velocity vector v is no longer strictly proportional to E and our integrals no longer sum to zero. Figure 5 gives an example of what happens when the structure allows field lines to penetrate it due to slightly permeable obstacles. We have numerically solved Laplace's equation with a finite conductivity and you can now see penetration of the field lines into the structure. Four field lines are shown, numbered 1, 2, 4, 7. On field line 2 we show a diffuse random polymer following field line 2, impacting the structure, and then following along the structure to the first opening. In this case the object still remains within the core of stream lines associated with the original channel but now has crossed over
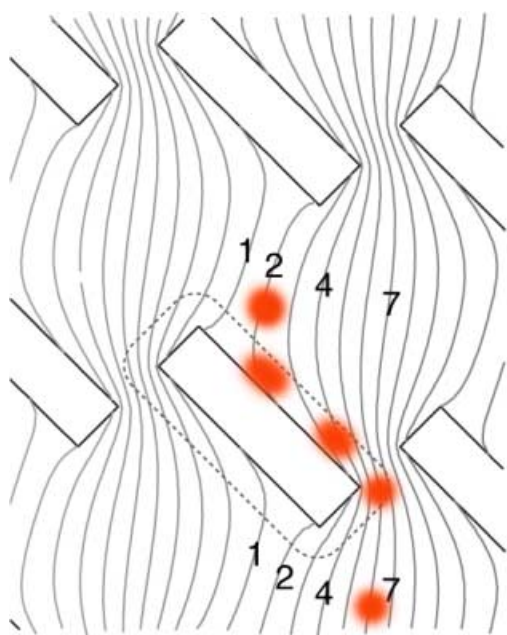
FIGURE 5 Field lines in the case of conducting structures. Four selected field lines are shown. A diffuse object is shown moving along field line 2 and then sliding along the object when the field line enters the object and exiting along the bottom along the 6th field line. Field line 7 delineates the boundary between adjacent flux bundles associated with different structures

four lines to line 6 and is close to moving over to the next obstacle set. This has to happen by diffusion, but the breaking of symmetry by the finite conductivity of the obstacle has made that more probable.

Even in the absence of field penetration there can be fractionation if the particle density ϱ is not symmetric in space to the obstacles, which we assumed in (12). An obvious example of this is the following: suppose a stream of particles is released to flow near a wall. Since there is now a spatial asymmetry to the flow the smaller particles will diffuse further from the wall than the larger ones and fractionation will occur if another set of obstacles occur which divides the stream. When we wrote ϱ_i for the ith channel we assumed that the particle density ϱ changed slowly and smoothly enough over one channel distance that it was not necessary to specify ϱ more finely. If, as we considered in the beginning example for this paper, all the particles are concentrated in one channel, then our symmetry assumption is wrong.

Finally, we can consider what happens if the objects are large compared to the obstacle gaps. In this case the object is physically excluded from a region along which the streamline would want to move it and this also acts as an additional force over the normal electrophoretic force. The fluid streamlines are not affected but the size of the obstacle is now effectively a function of the size of the particle. The net effect is to make the obstacle effectively permeable to the field and hence capable of fractionation. However, it is difficult to calculate analytically this effect. More traditional ratchet techniques which use a zero-time-average oscillating force field [6] may utilize this aspect of the boundary condition as their primary fractionating mechanism, although that is not clear at present.

2   Experiments

There are two papers in the literature that claim to have seen fractionation in asymmetric steady flow. If this is the case, they must have avoided the problems associated with incompressible flow that we discussed in Sect. 1. We will now briefly discuss how this could be.

In the case of the Boxer group's experiments [5], they made asymmetrical structures that allowed for the movement of rapidly diffusing particles to the left and slowly diffusing particles to the right. Figure 6 addresses their configuration. A wall placed on the left-hand side provided the asymmetrical boundary for the diffusional asymmetry to occur. Now, as we described above, if the fluid was entirely contained within the structures there would have been a weak fractionation due to diffusion from the wall but no fractionation due to the obstacles themselves. However, there was a trick. The liquid that was contained within the obstacles was a lipid bilayer, while on top of the lipid and the structures was an aqueous solution. The aqueous solution carried the ionic flow and generated the electric field, which presumably dragged the molecules in the lipid bilayer against the structures. Thus, in Fig. 6 we have drawn the force vectors $\boldsymbol{F}$ as penetrating the structures rather than moving around them. In that case, as we have discussed, the cancelation of the diffusive fluxes does not occur.

The second paper is the one by Chou et al. [4], which had asymmetrical rectangles inclined at an angle to the average electric fields generated by ionic flow. Unlike the case of van Oudenaarden and Boxer, this was an entirely sealed device with the liquid confined within the structures. If indeed the posts were entirely insulating then Fig. 2 would hold and the device should not fractionate. Yet there was clear evidence presented in this paper that at least statistically the DNA molecules moving through the array were deflected on the average to the right and small ones were deflected to a larger distance than the large ones.

How can this be? There are two explanations, although at this point the reasons we give are rather guesses because careful control experiments were not done at the time of
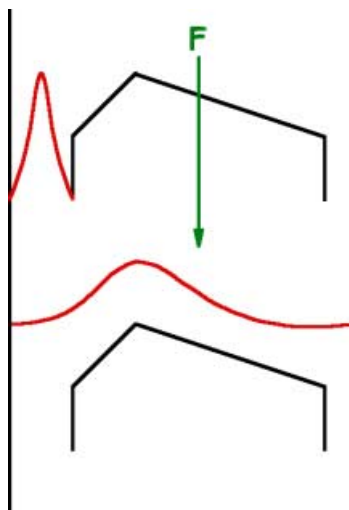

FIGURE 6 The configuration used by van Oudenaarden and Boxer [5] in their lipid-phase separations
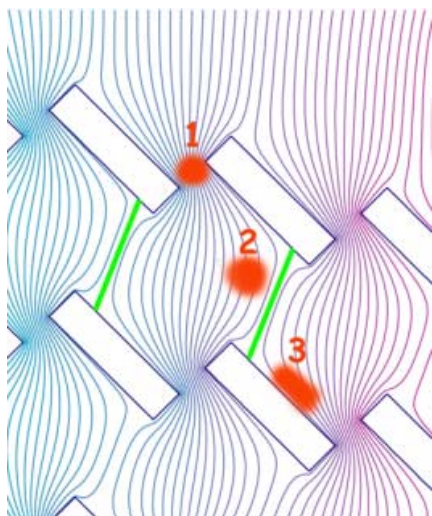
FIGURE 7   Motion of a roughly 50-kbp-long DNA molecule moving through the asymmetric lattice shown in Fig. 2. This data was taken from video images used in Chou et al. [4]. Images of the DNA molecule were taken at 0.5-s intervals, in the numbered sequence

the experiments. First, the insulating posts used were probably not entirely insulating; they were made of what is called plasma enhanced chemical vapor deposited (PECVD) quartz. PECVD quartz is well known to have a much more disordered and permeable structure than thermal quartz, which is thermally grown out of silicon. Thus, it is possible that there was substantial ionic flow through the quartz structures and hence condition (4) was not satisfied.

But our list of possible reasons for inexplicable success does not have to be mere theoretical musings, we can actually test our assumptions. Video images of single DNA molecules moving in the lattice shown in Fig. 2 show the paths that the molecules follow and can be compared to the insulating post predictions. Figure 7 shows images of a DNA molecule moving between posts. This set of data was used in the paper by Chou et al. to show that rectification of molecules could occur in such a lattice. The motion of this particular molecule is clearly not in the direction of the expected pattern for totally insulating objects, indicating that the field lines did penetrate the posts. Also, the deformation of the random coil of the DNA as it impacts an adjacent obstacle is clear. This video can be seen at the web site of the Austin group [8]. These images would indicate that this experiment did indeed work because the assumptions of the first part of the present paper were not fulfilled.

3   Close to success

We will close with a new design which should allow us to have uniform flow, discuss briefly why this design did not work because the first attempt used hydrodynamic rather than electrophoretic flow, and discuss new technologies to guarantee force penetration of the structures.

Neither the paper by van Oudenaarden and Boxer nor the paper by Austin's group showed really useful results. A useful particle-fractionation device would separate particles on a 'macroscopic' basis into clearly defined separate regions of space for later analysis. Van Oudenaarden and Boxer did not have well-formed and separated particle lines, nor did

Austin's group have well-defined particle lines. Van Oudenaarden and Boxer relied upon doing an analysis of particle-distribution means to determine if fractionation occurred, while Austin's group did a statistical analysis of individual particle trajectories, as we showed in Fig. 7.

In the case of Austin's group, one problem lay with the inability to create a well-defined initial stream of particles in a open microfabricated space of asymmetric objects. Recent papers exploiting hydrodynamic ideas of Huang and co-workers [7, 9] have, however, shown that is is possible to create extremely well-controlled jets of very narrow particle streams over large areas, even in an array of asymmetric structures. We will not repeat the details of the ideas here but rather simply point out that the key idea is to create a series of high-impedance current sources across all boundaries of the structure. Figure 8 shows the basic idea behind this current-injector scheme.

In order to test this device it was decided to run a sample of large and small fluorescent balls which are dyed different colors, making it relatively easy to track the positions of the two different-size balls. The large balls, dyed green, are 1 micron in diameter and the small balls, dyed red, are 0.1 microns in diameter. Because of optical resolution limitations, the small balls appear as a red haze while the larger green balls are resolved as separate balls.

A fatal flaw in this experiment, if you will, was the decision to use hydrostatic pressure rather than electrophoresis. The decision to use hydrostatic pressure was perfectly reasonable, since it was found that the electrophoretic mobility of the spheres was not equal and this would confound the analysis. However, in the case of hydrostatic pressure, even if the structures are made conducting, it is very unlikely that they will be equally permeable to hydrodynamic flow and most likely impermeable. In that case the divergence free flow conditions will apply and there will be no fractionation in the structure by the arguments we have given.

Figure 9 shows that the hydrodynamic flow patterns devised by Huang do indeed work: a beautiful jet is formed with
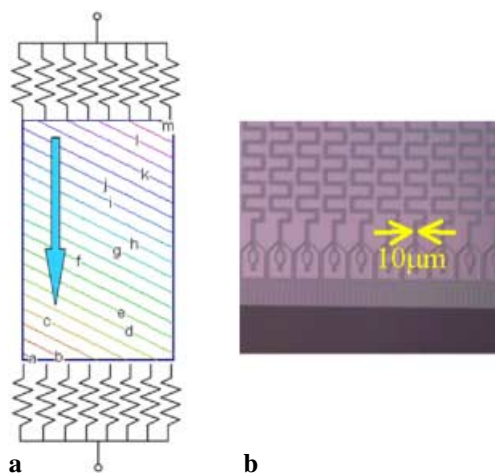

a   **b**

FIGURE 8   **a** The basic idea: in order to create contours of equal-pressure isobars across the device (isobars are shown as the *lettered lines*), a parallel series of microfluidic 'resistors' are constructed so that fluid injection effectively occurs via current sources. **b** Detail of the microfabricated device, showing the input of the high-impedance resistors into the array
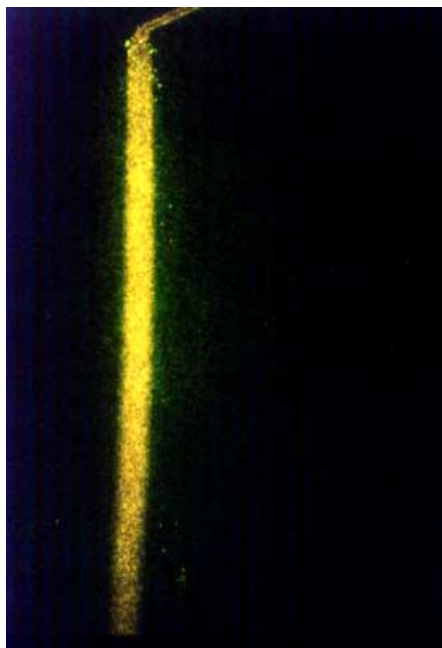
FIGURE 9   A image of a stream of fluorescent balls entering a diffusion array designed with a net of fluidic resistors. Two different ball sizes are within the stream

no bulging and straight flow down the through the array of obstacles. However, although there are two sets of balls in the jet there is no clear separation of the balls into two streams. Of course, as has been previously discussed [2, 4], there is a dimensionless ratio R of parameters which sets the resolving power of a thermal ratchet device:

$$R = \frac{D}{va}, \tag{13}$$

where D is the diffusion constant of the object, v is its transport speed through the device, and a is the characteristic diffusion length needed to cross between flux tubes. Maximum resolution is believed to occur if $R \sim 1$, so without knowledge of R it is not possible to determine the performance of the device. However, under hydrostatic flow conditions over a variety of R values ranging from 0.1 to 10 no stream separation was observed.

It was possible to observe a longitudinal fractionation that has nothing to do with ratchets, however. A pressure pulse was applied to the jet causing it to widen briefly, then the pressure was reduced. This created a burst of balls in the chip, which was etched 1 micron deep. Since this is low Reynolds number flow, the flow in the device is laminar and there is a parabolic velocity profile in the thin etched direction (see Fig. 9). The small red balls have a large diffusion constant and basically see the average of the parabolic profile, a process called 250 diffusion [10], and so they move at a common speed in the device. The larger green balls, however, do not average over the profile so rapidly and move with a heterogenous velocity distribution, some faster and some slower than the average. Thus, we would expect to see that the green-ball distribution will both lead and lag the main red-ball distribution in the array. Figure 10 shows exactly this phenomenon.
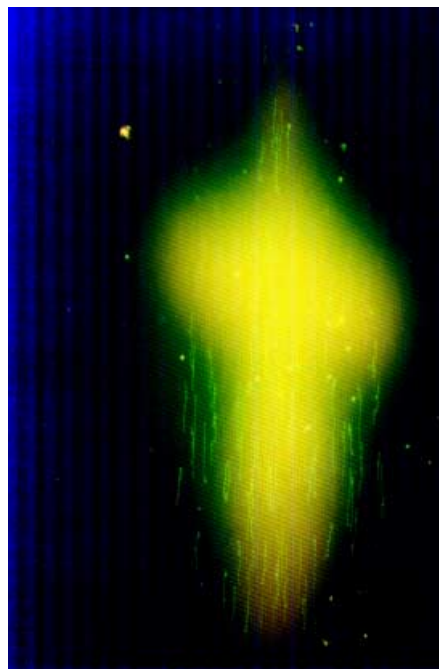

FIGURE 10   The separation of ball sizes that occurs when a pulse of balls is injected into the device. Although no lateral separation occurs, a subset of the large balls moves faster on average than the small balls, because it is centered in the parabolic profile of the flow

What to do next? It is very clear: we need to fabricate structures that are ion-permeable, run objects in electrophoretic flow using the new multi-injector system that solves the boundary values, and see if the devices can live up to the theoretical predictions. More theoretical work needs to be done also on what is the effect of finite particle size, that is, what happens when the mean particle size is comparable to the size of the gaps through which the objects flow. The averaging over the field profiles could change the performance of these devices. The devices remain fascinating, but are still rather poorly understood.

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