Temporal Modulation of a Spatially Periodic Potential for Kinetically Governed Oriented Motion

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This theoretical paper introduces an experimental protocol derived from the concept of Brownian motors in order to selectively confer an oriented motion to given charged reactants. Instead of maintaining permanently the system in nonequilibrium conditions, we propose a simple experimental trick to restore periodically a transient out-of-equilibrium regime: the reactive medium is alternately submitted to a sawtooth potential and to a potential ramp. The model provides approximate analytical expressions for the operating conditions allowing us to design the extraction from a mixture of any desired reactant characterized by its rate constants. The orders of magnitude suggest a possible implementation in microsystems where the present approach could be used for separation and analysis.

Introduction

Purifications are ubiquitous in chemistry as well as in biology. They combine some force for motion[1] with some reaction for selectivity.[2] For instance, affinity chromatography relies on a pressure gradient and on a reaction (eq 1) in which the mixture components A_l interacts with a target B to give products C_l:

$$A_l + B \underset{k_{2l}}{\overset{k_{1l}}{\rightleftharpoons}} C_l \qquad (1)$$

where k_{1l} and k_{2l} are the forward and backward rate constants. In the simplest situations, purification arises from finding the appropriate reagent B that specifically reacts with a desired component A. Nevertheless, it is often necessary to only rely on small differences among the A_l components with regard to a given discriminative reaction such as that given in eq 1 to achieve separations.

In most of the current separative approaches, the system obeys the conditions of local and partial equilibrium[3] with regard to the reaction (eq 1).[2] Then separation relies on thermodynamics and selectivity results from the difference in equilibrium constants $K_1 = k_{1l}/k_{2l}$. This may not be sufficient for mixtures of similar compounds. In that case, it is possible to explicitly rely on kinetics, i.e., on the rate constants $\{k_{1l}, k_{2l}\}$. It increases the number of discriminating parameters: instead of only *one* thermodynamic constant, *two* rate constants characterize every reactant A_l.

A possible approach revealing kinetic properties is provided by exposing the out-of-equilibrium reactive mixture $A_l + B$ to a spatially periodic potential. When the potential is asymmetric, the latter approach is reminiscent of the field of Brownian motors.[4,5] We theoretically studied the resulting behavior in a medium with a stationary homogeneous out-of-equilibrium

profile of B concentration.[6] Upon reaction with B, any given molecule randomly exchanges between the states A_l and C_l with average lifetimes equal to $1/k_{1l}B$ and $1/k_{2l}$, respectively. We assume A_l and B to be negatively and positively charged, respectively, and C_l to be neutral. In the charged state A_l, the molecule moves toward the maxima of the sawtooth potential. In contrast, in the neutral state C_l, the molecule does not experience the potential sawtooth and exhibits a symmetric and nonoriented Brownian motion. At the macroscopic level, an oriented motion is optimized when two conditions are fulfilled. First, the average lifetime of the charged state has to be close to the duration of electrophoretic migration over the longest ramp of the sawtooth potential. Second, the average lifetime of the neutral state must be close to the duration for visiting by diffusion the distance associated with the smallest ramp. The role of diffusion is essential here, because it makes it possible to overcome the potential barrier. Thus, the velocity of the couples $\{A_l, C_l\}$ reaches a maximum for specific values of the rate constants $\{k_{1l}, k_{2l}\}$. Then, it is possible to perform the selective extraction under kinetic control of a given couple $\{A, C\}$ that exhibits the match of its rate constants and diffusion coefficient with the characteristic features of the periodic asymmetric potential. The matching relations give reasonable orders of magnitude, and the selectivity is satisfactory. In contrast, we pointed out that it was difficult to experimentally implement this approach: in the absence of specific exchanges, the profile of B concentration rapidly reaches an electrical and chemical equilibrium and the oriented motion stops.[7]

Rather than imposing permanent far-from-equilibrium conditions, which is demanding, we propose for experimental implementation to periodically drive the system out of equilibrium and to take advantage of the relaxation period during which transient nonequilibrium conditions are observed. The present paper introduces a simple way to perturb the system as often as necessary: we periodically apply the sawtooth potential during a time T_1 and turn it off during a time T_2. During T_1, we observe the oriented motion until equilibrium is reached, and then during T_2, transient out-of-equilibrium concentration profiles are periodically reset. Experimental realizations become

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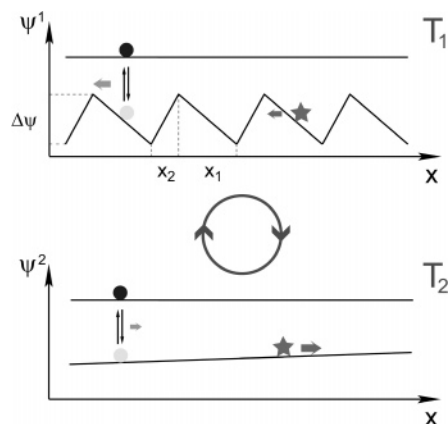‡ Université Pierre et Marie Curie.

Figure 1. Principle of the temporal modulation of a sawtooth potential for kinetically governed oriented motion. The charged mixture components are periodically submitted to (i) a one-dimensional sawtooth electric potential $\psi^1(x)$ during time T_1 and (ii) a ramp of potential $\psi^2(x)$ generating a uniform field $\bar{E}_2$ during time T_2. In contrast to the nonreactive negatively charged species $\mathbf{A}_{nr}$ (star), the resonant species exchanges between a negatively charged state, $\mathbf{A}^R$ (gray disk), and a neutral state, $\mathbf{C}^R$ (black disk), upon reacting with the $\mathbf{B}$ reagent. During T_1, $\{\mathbf{A}^R, \mathbf{C}^R\}$ covers in average a larger distance to the left than $\mathbf{A}_{nr}$ because it partially crosses the potential barrier in its neutral state. During T_2, $\{\mathbf{A}^R, \mathbf{C}^R\}$ moves to the right to a lower extent than $\mathbf{A}_{nr}$ because it spends on average less time in the charged state. The overall velocity of $\{\mathbf{A}^R, \mathbf{C}^R\}$ can be made the largest among the mixture components.

easily accessible. T_1 and T_2 are chosen to favor the couple $\{\mathbf{A}, \mathbf{C}\}$ adapted to the geometry of the sawtooth potential. In contrast to the behavior predicted upon permanent application of the latter potential, the nonreactive charged species $\mathbf{A}_{nr}$ now possess an oriented motion because of the potential stop during T_2. This interfering phenomenon could reduce the selectivity of the procedure. To suppress it, we apply during T_2 a constant field that generates a movement in the opposite direction of the motion observed during T_1. The proposed procedure is illustrated in Figure 1.

The paper is organized as follows. We first expose the theoretical model relying on electric potentials. For a given potential geometry, we determine approximate analytical values of the two parameters fixing the time period of the potential. Numerical calculations are subsequently performed to validate the analytical predictions and to evaluate the purification selectivity. Then we propose a procedure to continuously extract a given charged reactant from a mixture under kinetic control. We derive orders of magnitude showing that experimental realizations could be envisaged in microsystems. The last section is devoted to the conclusion.

The Model

We consider a mixture $\{\mathbf{A}_l\}$. To make separation at the most difficult, all these species are supposed to have the same mass m, friction γ, and charge z_A; they possess identical diffusion coefficients, $D = (k_B T/m\gamma)$ and electrophoretic mobilities $\mu = |z_A|/m\gamma$. In fact, the couples $\{\mathbf{A}_l, \mathbf{C}_l\}$ differ only by the values of the rate constants k_{1l} and k_{2l} associated with the forward and backward reactions (eq 1).

The $\mathbf{C}_l$ species are supposed to be neutral. Fulfilling electroneutrality yields $z_A = -z_B$, where z_B is the charge carried by species $\mathbf{B}$. In the following, the $\mathbf{A}_l$ are negatively charged and $\mathbf{B}$ is positively charged. Eventually, $\mathbf{B}$ is supposed to have the same mass and friction as $\mathbf{A}_l$ and $\mathbf{C}_l$ for the sake of simplicity.

Our goal is to selectively extract a given couple $\{\mathbf{A}, \mathbf{C}\}$ with predefinite rate constants, k_1 and k_2, by making use of its velocity rendered maximal among the mixture components.

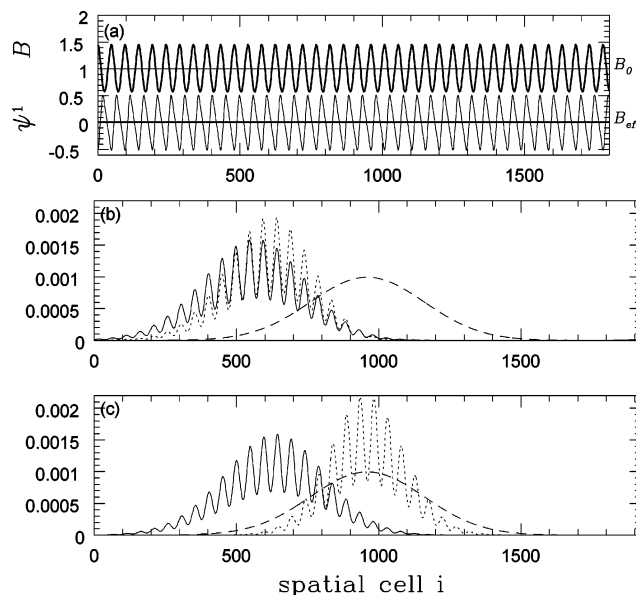**Figure 2.** (a) Spatial variation of the sawtooth potential ψ^1 (light line), spatial dependence of $\mathbf{B}$ concentration (heavy line) after 100 ($T_1^R + T_2^R$), uniform initial concentration $B_0 = 1$ (light straight line), and effective concentration $B_{eff} = 0.015$ (heavy straight line) given by eq 20. (b) Concentration profiles of the resonant couple $A^R + C^R$ (solid line), the negatively charged nonreactive species $\mathbf{A}_{nr}$ (dotted line), and the neutral nonreactive species $\mathbf{C}_{nr}$ (dashed line) after 100 ($T_1^R + T_2^R$) periods. The parameters are $\mu = 1$, $\Delta\psi = 1$, $x_1 = 32$, $x_2 = 16$, $B_0 = 1$, $D = 0.01$, $\mu = 1$, $T_1^R = 11000$, $T_2^R = 9000$, and $E_2 = 0$ in arbitrary units. (c) Same as (b) with $E_2 = 6.25 \times 10^{-4}$. The results were obtained from numerical integration of the partial differential equations (eqs 8−10).

A Permanent Sawtooth Potential. Well-known results on molecular motors suggest[4,5] to submit the mixture to a static one-dimensional sawtooth electric potential $\psi^1(x)$ such as displayed in Figures 1 and 2. Indeed, if the concentration, B, of species $\mathbf{B}$ is constant and uniform, the $\{\mathbf{A}_l, \mathbf{C}_l\}$ couples exhibit an oriented motion. Considered as a function of the rate constants (k_{1l}, k_{2l}), the corresponding velocity is extremum for the $\{\mathbf{A}^B, \mathbf{C}^B\}$ couple associated to the rate constants (k_1^B, k_2^B) fulfilling the relations below:

$$k_1^B B = \kappa_1^B = \frac{\mu \Delta\psi}{x_1^2} \qquad (2)$$

$$k_2^B = \frac{4D \ln 2}{x_2^2} \qquad (3)$$

where $\psi^1(x)$ increases over a length x_2 and decreases over a length x_1 with $x_1 > x_2$ and the height of the potential barrier is denoted as $\Delta\psi$ (Figure 1). The superscript B here emphasizes that the resonance conditions (eqs 2 and 3) are associated with a given constant and uniform $\mathbf{B}$ concentration. Equation 2 expresses that the average life time of $\{\mathbf{A}^B, \mathbf{C}^B\}$ in its charged state $\mathbf{A}^B$, $\tau_{A^B} = 1/\kappa_1^B$, is close to the duration of its electrophoretic migration over x_1, whereas eq 3 amounts to identify the average life time $\tau_{C^B} = 1/k_2^B$ of its neutral state $\mathbf{C}^B$ with the delay to visit x_2 by diffusion and overcome the potential barrier. The height of the potential barrier $\Delta\psi$ must additionally obey

$$\Delta\psi \gg \frac{2D}{\mu} \qquad (4)$$

to avoid that diffusion controls the motion of $\mathbf{A}$.[6]

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Without maintaining out-of-equilibrium the **B** concentration profile, oriented motion is only observed during a transient period before a local chemical and electric equilibrium is reached.[6] In particular, this detrimental behavior is predicted in the easiest experimental realizations that would not involve local **B** sources. For instance, it should be observed if the {A_l} mixture is simply introduced in a medium that contained **B** at a concentration only uniform before application of the $\psi^1(x)$ potential. In fact, the oppositely charged species A_l and **B** would be fast spatially separated: They could not react to yield the neutral state C_l that drives oriented motion in a steady state by overcoming the potential barrier by diffusion.

Alternation of Sawtooth and Ramp Potentials. To keep the experimental separation protocol simple and to avoid any detrimental stay in an equilibrium state, we propose the following procedure: we periodically apply (i) the preceding sawtooth potential $\psi^1(x)$ during time T_1 so that the chemical/electrical equilibrium condition is essentially reached and (ii) a ramp of potential $\psi^2(x)$ during time T_2 chosen to nullify the velocity of the nonreactive charged species A_{nr}. During the first phase, species **A** and **B** are separated, and during the second phase, diffusion enlarges the distributions of species **A** and **B** so that the neutral state **C** will be again produced. At a time scale larger than the potential period $T = T_1 + T_2$, a permanent regime is reached. We will show that the application of the preceding potential sequence confers a permanent oriented motion to the {A_l, C_l} couples that compares well with the oriented motion upon applying the permanent sawtooth potential. In particular, a maximum of velocity considered as a function of the rate constants {k_{1l}, k_{2l}} is also predicted for a resonant couple {A^R, C^R} associated with resonant rate constants, k_1^R and k_2^R.

Numerical Analysis

Adopting a macroscopic description and considering only one couple {**A**, **C**} for simplicity, the concentrations of species **A**, **B**, and **C**, respectively, denoted $A(x,t)$, $B(x,t)$, and $C(x,t)$, obey the following partial differential equations:

$$\frac{\partial A(x,t)}{\partial t} = -k_1 A(x,t)B(x,t) + k_2 C(x,t) + D\frac{\partial^2 A(x,t)}{\partial x^2} + \mu\frac{\partial E_i A(x,t)}{\partial x} \quad (5)$$

$$\frac{\partial B(x,t)}{\partial t} = -k_1 A(x,t)B(x,t) + k_2 C(x,t) + D\frac{\partial^2 B(x,t)}{\partial x^2} - \mu\frac{\partial E_i B(x,t)}{\partial x} \quad (6)$$

$$\frac{\partial C(x,t)}{\partial t} = k_1 A(x,t)B(x,t) - k_2 C(x,t) + D\frac{\partial^2 C(x,t)}{\partial x^2} \quad (7)$$

where t is time and x is the spatial coordinate. The field obeys $E_i = E_1$ that derives from the sawtooth potential during T_1, and it is uniform and equal to $E_i = E_2$ during T_2. From a theoretical point of view, the technical difficulty comes from the nonlinearity of the partial differential equations introduced by the variation of the concentration of species B. We numerically solve eqs 5−7 using the Euler method. Discrete space and time variables are introduced by $i = x/\Delta x$ and $s = t/\Delta t$ where Δx is the length of a spatial cell and Δt is the time step. The **A** concentration in cell i at discrete time s is denoted by $A_i(s)$. We

consider a sufficiently long medium of length equal to 40 periods of the sawtooth potential, i.e., of $40(x_1 + x_2)$ cells. To prevent numerical instabilities, the potential is slightly smoothed and the initial profiles of **A** and **C** are not Dirac distributions but Gaussian centered in the middle cell $i = 20(x_1 + x_2)$ and of variance equal to 10 cells. Initially, we impose a uniform **B** concentration, $B_i(0) = B_0$, and equilibrium concentrations for **A** and **C**, i.e., $\sum_i A_i(0) = k_2 N/(k_1 + k_2)$ and $\sum_i C_i(0) = k_1 N/(k_1 + k_2)$ where N is a constant. The discretized equations read

$$A_i(s + 1) = A_i(s) - k'_1 A_i(s)B_i(s) + k'_2 C_i(s) + D'(A_{i+1}(s) + A_{i-1}(s) - 2A_i(s)) - \frac{\mu'}{2}[(A_{i+1}(s) + A_i(s))(\psi^i_{i+1} - \psi^i_i) - (A_{i-1}(s) + A_i(s))(\psi^i_i - \psi^i_{i-1})] \quad (8)$$

$$B_i(s + 1) = B_i(s) - k'_1 A_i(s)B_i(s) + k'_2 C_i(s) + D'(B_{i+1}(s) + B_{i-1}(s) - 2B_i(s)) + \frac{\mu'}{2}[(B_{i+1}(s) + B_i(s))(\psi^i_{i+1} - \psi^i_i) - (B_{i-1}(s) + B_i(s))(\psi^i_i - \psi^i_{i-1})]$$

$$C_i(s + 1) = C_i(s) + k'_1 A_i(s)B_i(s) - k'_2 C_i(s) + D'(C_{i+1}(s) + C_{i-1}(s) - 2C_i(s)) \quad (9)$$

where we introduced scaled parameters obeying $k'_1 = k_1\Delta t$, $k'_2 = k_2\Delta t$, $D' = D\Delta t/(\Delta x)^2$, and $\mu' = \mu\Delta t/(\Delta x)^2$.

In particular, we determine the mean value $\bar{x}$ and the variance σ^2 of position x, considered as a random variable distributed according to $A_i(s) + C_i(s)$:

$$\bar{x} = \sum_i x(A_i(s) + C_i(s)) \quad (10)$$

$$\sigma^2 = \sum_i (x - \bar{x}(s))^2 (A_i(s) + C_i(s)) \quad (11)$$

At a time scale larger than the period $T_1 + T_2$, $\bar{x}$ and σ^2 grow linearly with time, allowing us to define the velocity of the profile displacement, v, as the slope of the line $\bar{x}$ versus t and an apparent diffusion coefficient D_{app} obeying

$$\sigma^2 = 2D_{app}t \quad (12)$$

Results and Discussion

To selectively maximize the velocity v^R of the desired couple {A^R, C^R} among the mixture components, we adopt a stepwise approach to identify the values of the different parameters: the potential barrier $\Delta\psi$, the characteristic lengths of the sawtooth potential x_1 and x_2, the characteristic times of the potential, T_1^R and T_2^R, the value of the electric field E_2, and the initial concentration B_{eff} of **B** species seen by A^R. We then perform numerical calculations to validate the preceding analytical results and to identify interfering mixture components during the sorting procedure. In the last subsection, we explain a protocol to selectively extract a given couple {**A**, **C**} with predefinite rate constants, k_1 and k_2, by maximizing its velocity within a mixture of similar components.

Approximate Analytical Derivation. The approximate analytical derivation relies on introducing an effective **B** concentration, B_{eff}, defined as the apparent uniform **B** concentration seen by the resonant couple {A^R, C^R} in a steady-state.

Definition of the Resonant Rate Constants k_1^R, k_2^R. The physical origin of the present oriented motion does not depend on the application of a uniform field during T_2 but only on the

coupling between the reaction given in eq 1 and the $\psi^1(x)$ potential. Thus, selective sorting out of the $\{\mathbf{A}^R, \mathbf{C}^R\}$ couple will rely on fulfilling eq 2- and 3-like relations that here are written as

$$k_1^R B_{\text{eff}} = \kappa_1^R = \frac{\mu \Delta \psi}{x_1^2} \tag{13}$$

$$k_2^R = \frac{4D \ln 2}{x_2^2} \tag{14}$$

Equations 13 and 14 are assumed to be fulfilled in the following.

Expression of $T_1^{\mathbf{R}}$. We choose T_1^R as the time necessary for the mean position $\bar{x}$ of the profile of $[A^R(x,t) + C^R(x,t)]$ to travel over a distance x_1 in the presence of a constant field $-\Delta\psi/x_1$ and for a constant concentration B_{eff} of species $\mathbf{B}$. Too large a T_1 would diminish v^R because electrophoretic motion is stopped once $\{\mathbf{A}^R, \mathbf{C}^R\}$ is located in the maxima of the $\psi^1(x)$ potential. Too short a T_1 would also reduce v^R by enlarging the relative contribution of nonoriented diffusion during T_2 to the overall $\{\mathbf{A}^R, \mathbf{C}^R\}$ motion. The equations governing the evolution of the system are

$$\frac{\partial A^R(x,t)}{\partial t} = -\kappa_1^R A^R(x,t) + k_2^R C^R(x,t) + D\frac{\partial^2 A^R(x,t)}{\partial x^2} -$$
$$\frac{\mu \Delta \psi}{x_1}\frac{\partial A^R(x,t)}{\partial x} \tag{15}$$

$$\frac{\partial C^R(x,t)}{\partial t} = \kappa_1^R A^R(x,t) - k_2^R C^R(x, t) + D\frac{\partial^2 C^R(x,t)}{\partial x^2} \tag{16}$$

$\mathbf{A}^R$ and $\mathbf{C}^R$ are supposed to be originally at chemical equilibrium and deposited at the coordinate $x = 0$:

$$A^R(x,0) = \frac{Nk_2^R \delta(x)}{\kappa_1^R + k_2^R} \tag{17}$$

$$C^R(x,0) = \frac{N\kappa_1^R \delta(x)}{\kappa_1^R + k_2^R} \tag{18}$$

Multiplying eqs 15 and 16 by x, integrating over space, and summing them, we find a differential equation for $\bar{x}$ that readily gives

$$\bar{x} = \frac{\mu \Delta \psi}{x_1}\frac{k_2^R}{\kappa_1^R + k_2^R}t \tag{19}$$

Using eq 13 and our definition of T_1^R, we eventually find

$$T_1^R = \frac{1}{k_1^R B_{\text{eff}}} + \frac{1}{k_2^R} \tag{20}$$

T_1^R is the sum of the respective average effective lifetimes of $\mathbf{A}^R$ and $\mathbf{C}^R$, $\tau_{A^R} = (1/k_1^R B_{\text{eff}})$ and $\tau_{C^R} = (1/k_2^R)$. It is the average time for $\{\mathbf{A}^R, \mathbf{C}^R\}$ to spend τ_{A^R} in its charged state. T_1^R is larger than the time $\tau_\chi^R = 1/(k_1^R B_{\text{eff}} + k_2^R)$ associated to the relaxation of the reaction given in eq 1 for $\{\mathbf{A}^R, \mathbf{C}^R\}$. Thus T_1^R can be seen as the time necessary for the resonant couple $\{\mathbf{A}^R, \mathbf{C}^R\}$ to reach both local chemical and electric equilibrium in the

sawtooth potential ψ^1. Using eqs 13 and 14, we can rewrite T_1^R as

$$T_1^R = \frac{x_1^2}{\mu \Delta \psi} + \frac{x_2^2}{4D \ln 2} \tag{21}$$

Expression of $T_2^{\mathbf{R}}$. After application of the sawtooth potential $\psi^1(x)$, the distributions of $\{\mathbf{A}^R, \mathbf{C}^R\}$ and $\mathbf{B}$ are narrow and separated by a gap as shown in Figure 2b. The basic role of T_2^R is to enlarge the distribution of $\mathbf{A}^R$ and $\mathbf{B}$ thanks to diffusion so that they are able to react again. Taking into account that $x_1 > x_2$ and assuming B_{eff} is uniform, we choose T_2^R as the time necessary for the width at half-height of an initial δ-distribution $[A^R(x,t) + C^R(x,t)]$ to reach $2x_2$ by diffusion. Too large a T_2 would diminish v^R by enlarging the relative contribution of nonoriented diffusion to the $\{\mathbf{A}^R, \mathbf{C}^R\}$ overall motion. The equations controlling the dynamics are given by eqs 15 and 16 where the field $-\Delta\psi/x_1$ has been replaced by E_2. Considering that the ramp potential during T_2^R acts as a small perturbation, we neglect the E_2 field contribution in eqs 15 and 16 for deriving the T_2^R value. More precisely, we use the following equations to analyze the dynamics

$$\frac{\partial A^R(x,t)}{\partial t} = -\kappa_1^R A^R(x,t) + k_2^R C(x, t) + D\frac{\partial^2 A^R(x,t)}{\partial x^2} \tag{22}$$

$$\frac{\partial C^R(x,t)}{\partial t} = \kappa_1^R A^R(x,t) - k_2^R C^R(x,t) + D\frac{\partial^2 C^R(x,t)}{\partial x^2} \tag{23}$$

We use the same initial conditions as in eqs 17 and 18. Multiplying eqs 22 and 23 by x^2, integrating over space, and summing them, we find a differential equation for the variance of the position σ^2. With our definition of T_2^R, we get

$$T_2^R = \frac{1}{k_2^R} \tag{24}$$

T_2^R identifies with the average lifetime of the neutral state $\mathbf{C}^R$. Using eq 14, we find

$$T_2^R = \frac{x_2^2}{4D \ln 2} \tag{25}$$

Expression of E_2. In the absence of any field during T_2^R, the nonreactive charged species $\mathbf{A}_{\text{nr}}$ exhibits an oriented motion with a velocity that is comparable to the one of the resonant species $\{\mathbf{A}^R, \mathbf{C}^R\}$ as shown in Figure 2b. In order to keep a good selectivity for the present separation procedure, we introduce a uniform field E_2 during time T_2^R, chosen to nullify the velocity of the nonreactive species $\mathbf{A}_{\text{nr}}$ (see Figures 1 and 2c). After application of the sawtooth potential $\psi^1(x)$ during T_1^R, the distribution of $\mathbf{A}_{\text{nr}}$ is composed of narrow peaks located in the maxima of the sawtooth potential. During T_2^R, these peaks enlarge under the effect of diffusion and translate due to the field E_2. We consider for example such a peak located at $x = 0$ after T_1^R. After T_2^R, the peak is essentially a Gaussian centered in $x = -\mu E_2 T_2^R$. During the next application of the sawtooth potential during T_1^R, the tail of the distribution for $x > x_1$ will reconcentrate in the maximum $x = x_1 + x_2$, whereas the tail for $x < -x_2$ will reconcentrate in the maximum $x = -(x_1 + x_2)$.

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Consequently, the nonreactive species A_{nr} will have a vanishing velocity if

$$E_2 = \frac{x_2 - x_1}{2\mu T_2^R} \qquad (26)$$

Expression of the Effective B Concentration. The assumption of uniform concentration in **B** is not valid. In fact, **B** experiences the field during T_1^R and relaxes during T_2^R: its concentration profile periodically breathes as a function of time. Here, one of the difficulties of the analytical treatment comes from the nonlinearity induced by the variation of $B(x,t)$ (see eqs 5−7 in the Numerical Analysis Section). We introduce a model valid for the resonant couple $\{A^R, C^R\}$ that takes into account the consumption and the movement of **B** in an effective manner. We suppose that $\{A^R, C^R\}$ at chemical equilibrium is initially deposited at an abscissa corresponding to a maximum of the sawtooth potential in a medium with a uniform concentration of species **B**. The sawtooth potential is applied during T_1^R and the ramp potential during T_2^R. The concentration profiles after $T_1^R + T_2^R$ are eventually used to calculate B_{eff} defined as the apparent uniform **B** concentration seen by A^R.

Before the application of the sawtooth potential, the medium is supposed to contain **B** at a uniform concentration B_0. We choose the origin of the abscissa in a hole of the potential. The resonant couple $\{A^R, C^R\}$ is deposited in the closest maximum of the potential at abscissa $x = x_2$. After time T_1^R, where the sawtooth potential is applied, A^R and **B** are essentially at chemical and electrical equilibrium. Species **B** is located in the holes of the potential; its distribution can be approximated by a sum of δ peaks $\sum_n = B_0(x_1 + x_2)\delta(x - n(x_1 + x_2))$ where n is an integer. Species A^R essentially remains at its initial place: its distribution is given by $(4D \ln(2)/x_2^2)(N/\mu\Delta\psi/x_1^2 + 4D \ln(2)/x_2^2)\delta(x - x_2)$. Considering the widening of these profiles by pure diffusion and their translation due to the uniform field E_2 during time T_2^R, we obtain the initial conditions for the determination of B_{eff} defined as

$$B_{eff} = \frac{1}{T_1^R \int_{-\infty}^{+\infty} A^R(x, t)\, dx} \int_0^{T_1^R} dt \int_{-\infty}^{+\infty} A^R(x,t)B(x, t)\, dx \qquad (27)$$

During the next application of the sawtooth potential during time T_1^R and under the effect of the largest constant field $-\Delta\psi/x_2$, the two profiles evolve according to

$$A^R(x,t) = \frac{\dfrac{4D \ln 2}{x_2^2}N}{\left(\dfrac{\mu\Delta\psi}{x_1^2} + \dfrac{4D \ln 2}{x_2^2}\right)2\sqrt{\pi DT_2^R}}$$
$$\exp\left[-\frac{(x - x_2 + \mu E_2 T_2^R - \mu\Delta\psi t/x_2)^2}{4DT_2^R}\right] \qquad (28)$$

$$B(x,t) = \frac{B_0(x_1 + x_2)}{2\sqrt{\pi DT_2^R}}\exp\left[-\frac{(x - \mu E_2 T_2^R + \mu\Delta\psi t/x_2)^2}{4DT_2^R}\right] \qquad (29)$$

Introducing these expressions in the definition of B_{eff} given in eq 27, we finally find

$$B_{eff} = \frac{B_0(x_1 + x_2)x_2}{4\mu\Delta\psi\left(\dfrac{x_1^2}{\mu\Delta\psi} + \dfrac{x_2^2}{4D \ln 2}\right)}\left[1 - \operatorname{erf}\left(-\frac{\mu E_2 x_2}{2D\sqrt{2 \ln 2}} + \sqrt{\frac{\ln 2}{2}}\right)\right] \qquad (30)$$

where erf is the error function. The values of the initial concentration B_0, the effective concentration B_{eff}, and the profile of species **B** deduced from the numerical integration of eqs 5−7 after an entire number of field periods $(T_1^R + T_2^R)$ are compared in Figure 2. Note that the effective concentration B_{eff} is about 100 times smaller than the initial concentration B_0 for the typical parameter values chosen in Figure 2.

Numerical Results. We numerically integrate the evolution eqs 8−10 given in the Numerical Analysis Section to directly obtain the velocity v of a mixture component $\{A, C\}$ submitted to the periodic potential sequence: $\psi^1(x)$ during T_1, $\psi^2(x)$ during T_2.

Evaluation of the Approximate Analytical Approach. In this subsection, we evaluate the relevance of the preceding approximate analytical approach for a given set of parameters $(\Delta\psi, x_1, x_2, B_0, E_2)$. We study the velocity v as a function of the rate constants k_1 and k_2 for optimized values of times $T_1 = T_1^R$ and $T_2 = T_2^R$, respectively, defined by eqs 21 and 25. Figure 3 shows that v exhibits a maximum v^R: the periodic stop of
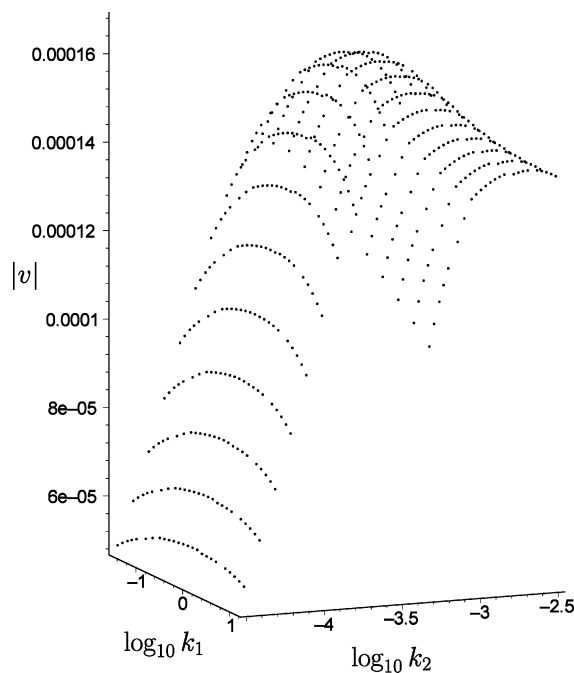

Figure 3. Absolute value of velocity $|v|$ as a function of $\log_{10} k_1$ and $\log_{10} k_2$. Same parameters as in Figure 2 with $E_2 = 6.25 \times 10^{-4}$. The results were obtained from numerical integration of the partial differential equations (eqs 8−10).

the sawtooth potential does not cancel the resonance phenomenon that we observed for a permanent sawtooth potential.[6] The value of the maximum velocity v^R is 20% lower than in the case of a permanent sawtooth potential. The decrease of the velocity is due to the ramp applied during T_2^R and not to the stop of the sawtooth potential (see Supporting Information). Note that the selectivity of the procedure does not depend on the value of the velocity. The maximum velocity v^R is reached for values of the rate constants that only differ by a factor 3 from the analytical values k_1^R and k_2^R given in eqs 13 and 14. This

TABLE 1: Dependence of the Normalized Velocity v/v^R on the Rate Constants k_1 and k_2 for a Given Set of Parameters ($\Delta\psi = 1$, $x_1 = 32$, $x_2 = 16$, $B_0 = 1$, $D = 0.01$, $T_1^R = 11000$, $T_2^R = 9000$) in the Case of Sequences of Sawtooth Potential and Ramp Potential ($E_2 = 6.25 \times 10^{-4}$) at the Period $T_1^R + T_2^R$ or of a Permanent Sawtooth Potential with $B(x,t) = B_0$

k_1, k_2	K/K^R	$T_1^R + T_2^R$	permanent sawtooth potential
k_1^R, k_2^R	1	1.00	1.00
$k_1^R, 10k_2^R$	0.1	0.81	0.05
$10k_1^R, k_2^R$	10	0.92	0.31
$k_1^R, 0.1k_2^R$	10	0.36	0.03
$0.1k_1^R, k_2^R$	0.1	0.95	0.51
$0.01k_1^R, k_2^R$	0.01	0.80	0.30
$10k_1^R, 10k_2^R$	1	0.45	0.19
$0.1k_1^R, 0.1k_2^R$	1	0.33	0.30
$0.1k_1^R, 10k_2^R$	0.01	0.25	0.01
$10k_1^R, 0.1k_2^R$	100	0.31	0.03
A_{nr}	0	0	0.00

reasonable agreement supports our analytical derivation of the effective concentration B_{eff} given in eq 30. Actually eqs 2 and 3 also give only a rough estimation of the resonant rate constants for a permanent sawtooth potential; in this case, their predictions already differ by a factor of 3 from the values deduced from a numerical integration of the evolution equations. Eventually, the value of E_2 deduced from the numerical solutions of eqs 8–10 differs by only 30% from the analytical prediction in eq 26.

Selectivity of the Separation Process. We now examine the selectivity of the separation method. Figure 3 displays the dependence of the velocity v on the rate constants k_1 and k_2, and Table 1 extracts some particular results. The resonance is not symmetric in the $\{k_1, k_2\}$ space (Figure 4a,b): it is less pronounced along the k_1 direction. Table 1 shows that the selectivity of the separation protocol is lower than for a permanent sawtooth potential but is still satisfactory. In particular, the selectivity is good when the two rate constants both differ from the resonant values k_1^R and k_2^R. It is additionally possible to separate species exhibiting identical equilibrium constants K^R but different rate constants (k_1, k_2): as an example, the velocity is divided by more than a factor of 2 by decreasing k_1 and k_2 by 1 order of magnitude (Figure 5).

Kinetic Control over Oriented Motion in a Mixture. We are now able to define a favorable extraction procedure of a reactant **A** with given rate constants (k_1, k_2) from a mixture of analogous components. Applying an alternating asymmetric sawtooth to ramp potential, we selectively confer an oriented motion to the chosen reactant.

We first address the geometry of the sawtooth potential ψ^1-(x). The values of k_2 and D impose the smallest length of the sawtooth potential. Following eq 13, we derive

$$x_2 = 2\sqrt{\frac{\ln(2)D}{k_2}} \tag{31}$$

Then, eqs 14 and 30 impose a relation between x_1, $\Delta\psi$, and the initial concentration B_0 of species **B**. Fixing for example x_1 and $\Delta\psi$, we have to fix

$$B_0 = \frac{4\mu\Delta\psi\left(1 + \dfrac{\mu\Delta\psi}{x_1^2 k_2}\right)}{(x_1 + x_2)x_2 k_1\left\{1 - \mathrm{erf}\left[\dfrac{(x_1 - x_2)}{2}\sqrt{\dfrac{k_2}{2D}} + \sqrt{\dfrac{\ln 2}{2}}\right]\right\}} \tag{32}$$
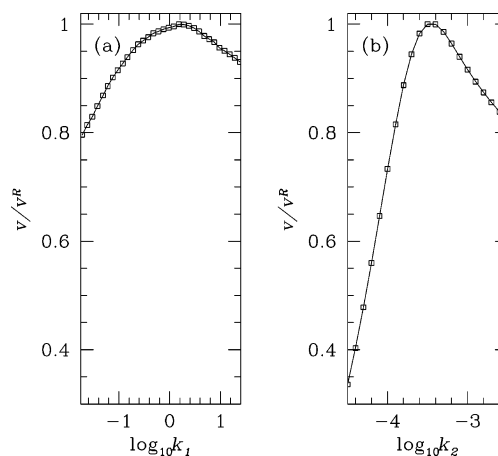
with x_2 given by eq 31.

Figure 4. Normalized velocity v/v^R as a function of of $\log_{10} k_1$ for $k_2 = k_2^R$ (a) or $\log_{10} k_2$ for $k_1 = k_1^R$ (b). Same parameters as in Figure 2 with $E_2 = 6.25 \times 10^{-4}$. The results were obtained from numerical integration of the partial differential equations (eqs 8–10).
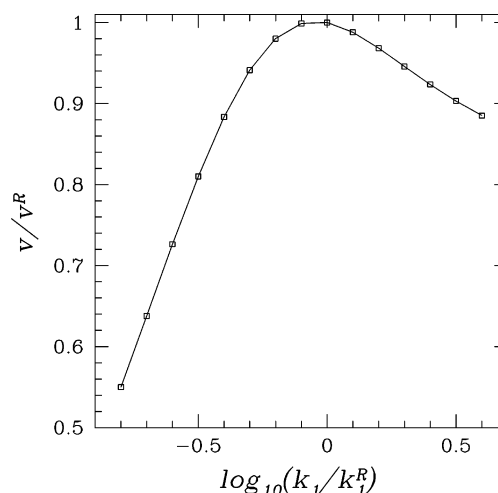

Figure 5. Separation of species with identical equilibrium constants $K^R = 5937.5$. Normalized velocity v/v^R as a function of $\log_{10} (k_1/k_1^R)$ for $k_2 = k_1/K^R$. Same parameters as in Figure 2 with $E_2 = 6.25 \times 10^{-4}$.

A possible extraction protocol could then be as follows. Introduce the mixture in the conditioned medium at B_0 and periodically apply the sequence: sawtooth potential during T_1, field E_2 obeying eq 26 during T_2, where T_1 and T_2 are obtained from eqs 21 and 25.

As an experimental illustration, we consider the selective extraction of a reactant **A** characterized by typical orders of magnitude for reactivity, diffusion coefficient, and electrophoretic mobility: $k_1 = 10^3$ M^{-1} s^{-1}, $k_2 = 1$ s^{-1}, $D = 10^{-9}$ m^2 s^{-1}, and $\mu = 4 \, 10^{-8}$ m^2 s^{-1} V^{-1}. We first get $x_2 = 50$ μm. Choosing $x_1 = 100$ μm and $\Delta\psi = 1$ V, we then obtain: $T_1 \approx T_2 = 1$ s, $B_0 = 1.025$ M, and $E_2 = 625$ V m^{-1}. Such values are compatible with the implementation of the present separation protocol in microsystems, for instance by using interdigitated microelectrodes to generate electric potentials.

The present protocol is thus appropriate to selectively extract from a mixture a charged reactant with given rate constants. With regard to the alternative approaches that we previously introduced,[8–11] the absence of an exact analytical solution here restricts the accuracy of the sorting criteria: instead of being precisely defined, the values of the rate constants exhibited by the fastest species will be only located in a narrow range (less than 1 order of magnitude) that should be nevertheless satisfac-

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tory for most applications. In contrast, it is important to notice that the design of the present separation protocol is not especially constraining from an experimental point of view. First, two parameters can be chosen at will in the set $\{x_1, \Delta\psi, B_0\}$. In addition, no drastic condition exists on rate constants nor on the minimal value of the electric field, contrary to the separation method based on the enhancement of the apparent diffusion coefficient.[8−10]

Conclusion

In this paper, we have designed a simple separation procedure on the basis of the model of Brownian motors. We solved the point raised by the difficulty in maintaining the chemical reaction out of equilibrium. We successfully demonstrated that a possible answer is to periodically switch off the sawtooth potential to maintain the system in a transient, nonequilibrium state. An appropriate temporal modulation of the electric potential preserves the oriented motion on macroscopic distances. The desired reactant is systematically located in front of the elution profile: this procedure allows us to extract any charged reactant that exhibits given rate constants toward a selected target. Easily adaptable to different sorting reactions, the present protocol essentially retains the attractive velocity and selectivity introduced in the original model. Eventually, the orders of magnitude derived in this paper show that the present approach can be easily implemented in microsystems where it could find applications in separation and analysis.

Supporting Information Available: Results and discussion in the absence of a ramp during T_2^R ($E_2 = 0$). Table S-1: sensitivity of the normalized velocity to variation of times T_1 and T_2 for a given set of parameters ($\Delta\psi$, x_1, x_2, B_0) with $E_2 = 0$. Table S-2: dependence of the normalized velocity (v/v^R) on the rate constants k_1 and k_2 for a given set of parameters ($\Delta\psi$, x_1, x_2, B_0, T_1^R, T_2^R) in the case of an alternating asymmetric sawtooth to flat potential at the period $T_1^R + T_2^R$ or of a permanent asymmetric sawtooth potential. Table S-3: dependence of the normalized apparent diffusion coefficient (D_{app}/D) on the rate constants k_1 and k_2 for a given set of parameters ($\Delta\psi$, x_1, x_2, B_0, T_1^R, T_2^R) in the case of an alternating sawtooth to zero potential at the period $T_1^R + T_2^R$ ($E_2 = 0$). Figure S-1: velocity v as a function of $\log_{10} T_1$ for the resonant couple (k_1^R, k_2^R) and for the negatively charged nonreactive species A_{nr} in the absence ($E_2 = 0$) of a potential ramp during T_2^R. Figure S-2: velocity v as a function of $\log_{10} k_2$ for $k_1 = k_1^R$ or of $\log_{10} k_1$ for $k_2 = k_2^R$. This material is available free of charge via the Internet at http://pubs.acs.org.

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