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Active micromixer based on artificial cilia

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We propose a design for an active micromixer that is inspired by the motion of ciliated micro-organisms occurring in nature. The conceptual design consists of an array of individually addressable artificial cilia in the form of microactuators covering the channel wall. The microactuators can be set into motion by an external stimulus such as an electric or a magnetic field, inducing either a primary or secondary motion in the surrounding fluid. To validate the concept and to help design the precise mixer configuration, we developed a computational fluid-structure model. This model is based on a fictitious domain method that couples the microactuator motion to the concomitant fluid flow, fully capturing the mutual fluid-structure interactions. The simulated flow patterns resulting from the motion of single and multiple actuated elements (in a microchannel filled with a Newtonian fluid) under the action of a time-periodic forcing function are analyzed using dynamical systems theory to quantify the mixing efficiency. The results show that with a proper actuation scheme, two microactuators placed on the same wall of a microchannel can indeed induce effective mixing by chaotic advection; their distance should be small, but collisions should be avoided, and they can be actuated in a rather broad regime around 90° out of phase. Placing actuators on opposite walls also induces exponential stretching in the fluid, but if their length is relatively small, of the order of 20% of the channel height, mixing effectiveness is higher when they are arranged on the same wall. © 2007 American Institute of Physics. [DOI: 10.1063/1.2762206]

I. INTRODUCTION

“Lab-on-a-chip” devices or “micro total analysis systems” are miniaturized devices for chemical analysis and biological assays, with applications in medical diagnostics and molecular medicine development. Compared to conventional laboratory-scale techniques, these devices offer a variety of advantages, such as faster speed of analysis, less material consumption, high throughput, etc.1–6 A key aspect of the systems concerns the controlled manipulation of often complex fluids within microscopic channels and chambers, with typical sizes ranging from tens to hundreds of micrometers.7,8 One of the essential microfluidic operations required is rapid and complete mixing of two or more solute streams.9

For fluid flow in microchannels, the Reynolds number, $Re = \rho VL/\mu$, where $\rho$ is the density of fluid, $\mu$ is the viscosity of fluid, and $V$ and $L$ are the characteristic velocity and length scales, respectively, is typically on the order of unity, since $\rho$ is of order $10^3$ while $\mu$, $V$, and $L$ are all of the order $10^{-3}$. Turbulence, therefore, is uncommon, in fact almost impossible, and mixing between the adjacent laminar streams occurs only by molecular diffusion. In a straight, smooth-walled microchannel, the axial length required for complete mixing increases linearly with the Peclet number, $Pe = VL/D$, where $D$ is the molecular diffusivity, which signifies convective transport of a solute relative to its diffusional transport. Since $D$ is of the order of $10^{-11}$, the Peclet number is of the order $10^3$ and hence the characteristic mixing length is too long for portable systems. In order to decrease the mixing length and the mixing time, considerable research is done based on the idea of generating transverse flows to aid mixing.10

Transverse flows in microchannels can either be generated through the use of external forces (active mixers) or by an interaction of a driven flow with the fixed geometry of a microchannel (passive mixers). Examples of passive mixers are the staggered herringbone structures consisting of repeatedly mirrored asymmetric grooves in one wall of the channel,11,12 curved serpentine channels,13 and spiral channels that use Dean flows.14 The operational flexibility of passive mixers is limited since, once a chosen geometry is engraved in the channel, it performs the same function offering little or no control. On the contrary, active mixers are quite flexible since the external forces producing mixing can be switched on and off or can be tuned.

Active mixers reported in the literature use a variety of phenomena, such as electrokinetic instabilities,15 magnetic stirring,16–18 magnetohydrodynamic effects,19 and acoustic microstreaming actuation.20,21 In this paper, we present a design for an active mixer that is inspired by nature, specifically by the motion of ciliated or flagellated micro-organisms such as E. coli or Paramecium; see Fig. 1. Cilia and flagella are microscopic hairs attached to the surface of the micro-organisms, which are rotated (flagella) or exhibit beating cycles (cilia) induced by molecular motors embedded in the cell membrane. This movement results in the propulsion of the micro-organism through the surrounding fluid. Typical lengths of the flagella and cilia are on the order of tens of micrometers.22 One of the essential microfluidic operations required is rapid and complete mixing of two or more solutes streams.9

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micrometers, whereas the beating or rotation frequency ranges from 10 to 100 Hz. We plan to mimic the above principle, albeit now for mixing, by covering the microchannel walls with arrays of individually addressable artificial cilia in the form of microactuators that are responsive to an external stimulus such as an electric or a magnetic field. Such microactuators, with sizes similar to those of natural cilia, can be manufactured from polymer-based materials using microsystems technologies.

This concept is promising for microfluid manipulation, as suggested by theoretical analyses of the flow generated by ciliary propulsion and as experimentally observed giving enhanced diffusion in a motile bacterial bath. Darnton et al. attached flagellated bacteria on the surface of cover-slips forming active bacterial carpets, which could potentially move fluids. However, directly using bacteria has disadvantages, such as the necessity to ensure a well-bound motile bacterial carpet at all times and the need to create an environment to keep bacteria alive, while there exists little control over the fluid motion induced and the presence of bacteria may not be acceptable for some applications. The artificial cilia proposed alleviate these disadvantages.

We developed a computational fluid-structure model to explore the feasibility of the concept for mixing and to help design the optimal mixer configuration with respect to the mechanical and geometrical properties of the microactuators as well as the actuation scheme. This model is based on a fictitious domain method and simulates both the microactuator motion as well as the concomitant fluid flow, fully capturing the fluid-structure interaction. The simulated flow patterns resulting from the motion of single and multiple actuated elements under the action of a time-periodic forcing function are analyzed using dynamical systems theory to quantify the mixing efficiency. The paper is organized as follows. In Sec. II, we briefly describe the governing equations as well as the fluid-structure model. In Sec. III, the response of a single microactuator is studied as a function of material and geometrical properties viz. the fluid viscosity, the shear modulus of the actuator material, and the length of actuator. In Sec. IV, a double actuator micromixer design is presented, evaluated, and optimized. Finally, in Sec. V we draw conclusions.

II. METHODS

A. Governing equations

The microactuators are modeled as an incompressible solid. Neglecting inertia and gravity, the conservation of momentum and mass for the solid reads

\[ \nabla \cdot \tau_s - \nabla p_s + \rho_s f_s = 0, \]

\[ \text{det}(F) = 1; \quad \text{with} \quad F = (\nabla_0 x_s)^T, \]

where \( \tau_s \) is the extra stress tensor, \( \rho_s \) is the hydrostatic pressure in the solid, \( f_s \) is the density of the solid, \( f_s \) is the time-periodic forcing function, \( F \) is the deformation gradient tensor, \( x_s \) is the position vector of the solid, and \( \nabla_0 \) and \( \nabla \) are gradient operators with respect to the reference and current configuration, respectively. The microactuator material is considered to be a Neo-Hookean solid, hence the extra stress tensor reads

\[ \tau_s = G(B - I) \quad \text{with} \quad B = F \cdot F^T, \]

where \( G \) is the shear modulus of the material, \( B \) is the Finger strain tensor, and \( I \) is the unity tensor.

Assuming isothermal conditions and neglecting external body forces, the fluid motion is governed by the Navier-Stokes equations:

\[ \rho_f \left( \frac{\partial v_f}{\partial t} + v_f \cdot \nabla v_f \right) = -\nabla p_f + \nabla \cdot \tau_f, \]

\[ \tau_f = 2\eta D \quad \text{with} \quad D = \frac{1}{2} [ \nabla v_f + (\nabla v_f)^T ], \]

and the equation of continuity:
with $v_f$ the fluid velocity, $\rho_f$ the fluid density, $p_f$ the hydrostatic pressure in the fluid, $\tau_f$ the extra stress tensor, $\eta$ the fluid viscosity, and $D$ the rate of deformation tensor. The microchannel considered to be filled with an incompressible Newtonian fluid initially at rest is modeled as a cavity by specifying a no-slip boundary condition on all walls of the channel:

$$v_f = 0,$$

on all walls of the channel.

The Strouhal number $St = L\omega/V$ is of the order 1, since $V$, the characteristic actuator velocity, scales with $L$, the characteristic actuator length, and $\omega$, the frequency of the applied forcing function as $L/\omega$. The inertia terms in Eq. (4) are therefore retained even though the Re is small.

### B. Fluid-solid coupling

Clearly there exists a coupling between the response of the microactuator to the time-periodic forcing function applied and the resulting fluid motion. This fluid-solid interaction is captured by specifying a no-slip boundary condition at the interface between the microactuator and the surrounding fluid:

$$v_f - v_s = 0,$$  \hspace{1cm} (8)

where $v_s$ is the velocity of solid. The coupling constraint (8) is enforced weakly by introducing a distributed Lagrange multiplier $\lambda$ using a fictitious domain method.\textsuperscript{29,31,32} The method of van Loon et al.\textsuperscript{29} without adaptive remeshing is used here. Briefly, the fluid is described using a fixed mesh in an Eulerian setting while an updated Lagrangian formulation is used for the solid. The Lagrange multiplier $\lambda$ is defined along the fluid-solid interface to couple the fluid-solid responses and can be interpreted as a surface force exerted on the fluid by the solid. See van Loon et al.\textsuperscript{29} and van Loon et al.\textsuperscript{33} for details of the method.

### C. Solution process

The spatial discretization of the solid, i.e., the microactuator, is obtained by using Crouziex-Raviart elements that employ a biquadratic interpolation for the displacement and a linear discontinuous interpolation for the pressure. We deal with thin and small microactuators, therefore its thickness and mass are negligible as far as interaction with the fluid is concerned and, therefore, fluid and solid velocities are coupled at only one boundary between actuator and fluid.

The governing equations for the fluid [(4)–(6)] are solved using primitive variables, thus a velocity-pressure formulation is used. For spatial discretization again, Crouziex-Raviart elements, which employ a biquadratic interpolation now for the velocity and linear discontinuous interpolation for the pressure, are used. The nonlinear term $v_f \cdot \nabla v_f$ is linearized using Newton’s method. The time derivative in (4) is approximated by an implicit backward Euler scheme.

The discretization of the Lagrange multiplier is chosen to be linear discontinuous and spatially coinciding with the
element boundaries of the solid domain. The linearized version of the nonlinear set of equations is solved in a fully coupled way using a Newton-Raphson iterative scheme. At each iteration, the solution of the linearized set is obtained using a direct method based on a sparse multifrontal variant of Gaussian elimination. The entire solution process is implemented in the finite-element package SEPRAN.

D. Mixing quantification

To study mixing, we start with the analysis of the motion of fluid elements generated by the velocity field, thus we investigate the dynamical system,

\[ \frac{dx}{dt} = v_f(x,t), \]  

where \( v_f(x,t) \) is the generated velocity field. Integrating Eq. (9) with the initial condition \( x = X \) at \( t = 0 \) for a time length of \( T \) gives the position of a particle \( x \) at \( t = T \), since particles act as passive markers, without diffusion. Since this is purely kinematics, all complexity in solving the dynamical system (9) is associated with obtaining an accurate \( v_f(x,t) \).

To quantify mixing efficiency, the deformation of an initially rectangular fluid strip (colored black for convenience, otherwise having the same properties as the rest of fluid) placed horizontally in the microchannel, as shown in Fig. 10.
is followed by the adaptive front tracking technique presented in Galaktionov et al.\textsuperscript{45} In this technique, the boundary of the strip is tracked instead of designating the strip by a number of uniformly distributed material points. Initially, only a relatively small amount of markers are required to describe the boundary of the domain to be tracked in time. During the course of adaptive front tracking, nodes are inserted in between nodes where either the distance $d$ has grown beyond a certain limit, or when the angle $\alpha_i$ formed by two consecutive edges is smaller than a critical one $\alpha_c$, according to the following criteria:

\[ d < h_c \quad \text{if} \quad \alpha_i < \alpha_c \lor \alpha_{i-1} < \alpha_c, \quad (11) \]

with

\[ d = \|x_{i-1} - x_i\|, \quad (12) \]

\[ \alpha_i = \arccos \left( \frac{(x_{i+1} - x_i) \cdot (x_{i+1} - x_i)}{\|x_{i-1} - x_i\| \|x_{i+1} - x_i\|} \right), \quad (13) \]

where $h$ and $h_c$ are the maximum lengths in straight and curved regions of the boundary, respectively. In case Eqs. (10) and (11) are not satisfied, the edge between $x_{i-1}$ and $x_i$ is split into two parts and a new node is inserted at an earlier time level and tracked to the current time.

FIG. 5. $y$ component of the fluid velocity as a function of $x$ distance along the midheight of the microchannel at different time instants. The time instants reading from left to right and top to bottom correspond to $t=0$, 0.0625, 0.125, and 0.1875 s, respectively. The simulation parameters are as in Fig. 3.
The velocity field obtained from the numerical simulation is only known in a limited number of grid points, for a limited number of time steps, within a period. Hence, interpolation is necessary. The accuracy of interpolation is restricted by the accuracy of the discretized data. To ensure that the interpolation error is of the same order as the approximation error of the discretized data, a consistent interpolation scheme based on the same polynomial basis functions as used in the spatial numerical discretization is applied while a linear interpolation is applied between time levels. The system (9) is numerically integrated using an adaptive Runge-Kutta scheme (see Press et al.\textsuperscript{42}). The error tolerances imposed during the solution of system (9) are such that the errors in the trajectories of particles are mainly due to discretization errors of the numerical velocity field. In previous works, these effects have been systematically studied Souvaliotis et al.\textsuperscript{43} and Galaktionov et al.\textsuperscript{44,45}

As we impose incompressibility of the fluid in our mixer,
the velocity field has to obey the continuity equation (6) and any material volume has to preserve its area during motion. During the adaptive front tracking procedure used to follow material volumes, the enclosed area was kept within 0.5% variation even for the largest deformations. The enclosed area is computed along the curve by \((\mathbf{fx} \cdot \mathbf{n}) ds/2\), with the outward normal vector \(\mathbf{n}\) along the curve. Considering the huge increase of interfacial length during mixing, which is shown further on to be exponential, we can safely conclude that the solution is area-preserving.

### III. SINGLE MICROACTUATOR FLOW RESPONSE

First, we investigate how a single, one-dimensional microactuator, attached onto a wall of a two-dimensional microchannel and schematically shown in Fig. 2, responds to an applied, time-periodic body force. The channel height \(H\) is chosen 100 \(\mu\)m, the length of the fluid domain \(L\) is 600 \(\mu\)m, the microactuator thickness \(h\) is 1 \(\mu\)m, the solid density is 800 \(\text{kg/m}^3\), and the fluid density is 1000 \(\text{kg/m}^3\). The microactuator length \(l\) is varied between 20 and 40 \(\mu\)m, the shear modulus of the actuator, and its length \(G\) on the forcing function. The microactuator motion depends on the material and geometrical parameters, such as the fluid viscosity \(\eta\), the shear modulus \(G\) of the actuator, and its length \(l\) as well as on the forcing function.

#### A. Effect of viscosity of the surrounding fluid

Figure 6 shows the effect of fluid viscosity on the microactuator motion, monitored as its tip displacement in the \(x\) direction against time, for two microactuator lengths viz. 20 and 40 \(\mu\)m. For both cases it is clear that as the viscosity of the surrounding fluid increases from water like \((\eta=10^{-3} \text{ Pa s})\) to more like that of a polymeric system \((\eta=1 \text{ Pa s})\), not only does the amplitude of the displacement decrease, but also the microactuator displacement becomes progressively more out of phase with the forcing function applied. The tip displacement for \(l=40 \mu\text{m}\) displays a “flattening” behavior as opposed to a sine behavior for \(l=20 \mu\text{m}\). This is because the microactuator with \(l=40 \mu\text{m}\) deforms readily and aligns parallel to the \(x\) direction—the
direction in which the external force is applied—arresting a further deformation. However, it is interesting to note that for the range of viscosities expected to be encountered in microfluidic applications, typically about $10^{-3}$ Pa s, the microactuator response is almost independent of the fluid viscosity at these length scales.

**B. Effect of shear modulus of the microactuator material**

The effect of shear modulus on the microactuator motion, plotted as its tip displacement in the $x$ direction versus time, is displayed in Fig. 7. Clearly, the modulus of the material has a considerable influence on the motion. For the shorter actuators of 20 μm, the effect is more pronounced with the tip displacement increasing by a factor of about 8 as compared to a factor of about 2 for the actuator of 40 μm length, as the modulus decreases an order of magnitude from 2 to 0.2 MPa. This modulus range can in practice be obtained by using elastomers or polymer gels, such as reported in Lotters et al. and Unger et al., to fabricate the microactuators.

**C. Effect of the microactuator length**

The length of the microactuator is one of the parameters that can be tailored perhaps more easily than its thickness, to suit the required level of displacement and three different values, viz. 20, 30, and 40 μm are chosen. By keeping the force density constant at $f_0 = 41.25$ kN/kg, we necessarily (linearly) change the magnitude of the total force acting at any time instant on the microactuator. We opted to keep the force density constant since its value was based on the strength of magnetic fields that are practically realizable. The results in Fig. 8 show that, as expected, both the magnitude of displacement and the rate of displacement (slopes in Fig. 8) increase with an increase in the length. The flattened tip
displacement behavior, especially for $l=40\, \mu m$, is again due to the parallel alignment of the microactuator with respect to the force applied.

IV. DOUBLE-ACTUATOR MICROMIXER

Now we try to validate the concept of employing artificial cilia as micromixers by introducing a second actuator, see Fig. 9. The flow field of the surrounding fluid depends in this configuration on the responses of both actuator, see Figs. 4 and 5. Mixing can be expected to depend on, e.g., their position, on the same wall or on opposite walls, their spacing, on the actuation scheme, and on the geometrical and material properties of the individual actuators. For simplicity, only identical microactuators are considered.

A. Microactuators on the same side of the microchannel

1. Actuation scheme: Phase lag

We start with both actuators on the same wall of the microchannel, see Fig. 9. The microactuators are 1 $\mu m$ thick with a shear modulus $G=0.2$ MPa, their spacing $d$ is 26 $\mu m$, which is roughly equal to their length $l$, and they are actuated by a time-periodic scheme with a phase lag $\phi$, see Eq. (14). For $\phi=0$, both microactuators move in tandem in the same direction, while for $\phi=\pi$ their motion is in opposite directions. The fluid velocity field generated (during a period) depends on the actuation scheme and spacing.

Figure 10 shows the time evolution of a strip, with the original position of $210\leq x\leq 390\, \mu m$ and $45\leq y\leq 65\, \mu m$ for two actuation schemes, viz., $\phi=\pi/2$ and $\pi$. The deformation using a single microactuator is shown as a reference. Clearly, the stretching and folding process of fluid elements is much more pronounced for $\phi=\pi/2$ than for $\phi=\pi$. Differences observed can be understood by a careful inspection of the corresponding flow fields also shown in Fig. 10. For both $\phi=\pi/2$ and $\phi=\pi$, the flow patterns show two vortices, but for $\phi=\pi$ they are equally dominant during a period while for $\phi=\pi/2$ their dominance alternates during a period, leading to the formation of a so-called blinking vortex system, which has been shown by Aref\textsuperscript{38} to yield chaotic mixing. This demonstrates the influence of the actuation scheme on mixing. To quantify mixing, the time evolution of the interfacial area (perimeter in the present 2D case) of the black strip is cal-
culated and plotted in Fig. 11. For $\phi = \pi/2$, the fluid strip is stretched exponentially in time—an indication of chaotic mixing. This demonstrates that the multiple microactuator configuration can indeed be used to perform efficient mixing. In order to identify the optimal $\phi$ for the present configuration, the whole $\phi$ space from 0 to $\pi$ was explored; $\phi = 3\pi/2$ gave approximately the same length stretch evolution as $\phi = \pi/2$, so $\phi$ space is assumed to be symmetric about $\phi = \pi$. The time at which the strip starts experiencing exponential stretching is roughly estimated from the length stretch versus time curve by drawing a tangent that follows the long-time stretch behavior and reading its intersection with the time axis. A phase map is constructed by plotting the time for exponential stretching estimated for 10 different values of $\phi$; see Fig. 12. From the phase map, it is apparent that the strip starts experiencing exponential stretching in a short time of about 25 s for a broad range of $\phi$’s from $\pi/3$ to $2\pi/3$ around $\phi = \pi/2$, which is the optimal value. For $\phi$ values close to 0 and $\pi$, only linear stretching is observed.

2. Spacing between the microactuators

In the preceding section, the spacing between the two microactuators was fixed at 26 $\mu$m, roughly equal to the length of individual microactuator. This was done with the aim of delineating the role of actuation scheme, i.e., the phase lag on mixing. Now the influence of the spacing on mixing is studied at the identified optimal value of $\phi = \pi/2$. Figure 13 presents the results obtained for three different spacing values, viz., 26, 40, and 60 $\mu$m, where it can be seen that with increasing spacing, the stretching becomes progressively weaker. This result is due to the (combined) manner in which the two actuators affect the fluid velocity field. At a certain larger value of $d$, the fluid velocity, especially in the region between the two actuators, is predominantly affected by the motion of either of the two actuators, thus basically reverting to a single actuator. On the other hand, if the spacing between the two actuators is smaller than their length, or twice the maximum deflection of an actuator, the actuators collide. From the results, it appears that the actuators should be placed as close to each other as possible, but sufficiently distant to avoid collision.

B. Microactuators on the opposite side of the microchannel

The investigation of mixing performance using an opposite wall arrangement of the two actuators is initiated with
microactuators of \( l = 20 \, \mu m \) separated with a horizontal spacing of \( 26 \, \mu m \). Two phase lags, viz., \( \phi = \pi/2 \) and \( \pi \), are considered keeping all other parameters the same. The time evolution of the fluid strip, which has the same dimensions as previously but is now centered at \( y = 50 \, \mu m \), is shown in Fig. 14. Stretching of the strip in the present configuration, even for \( \phi = \pi/2 \), is obviously less compared to the results with the actuators on the same wall, see Fig. 10. This may be due to too large tip-to-tip distances leading to an insufficient combined influence on the fluid velocity field. Therefore, the length \( l \) of the actuators was increased from 20 to 40 \( \mu m \). In view of this change, the horizontal spacing between the actuators was also increased to 40 \( \mu m \) to keep the ratio of tip-to-tip separation distance to the actuator length equal. Also, the shear modulus \( G \) of the actuator material was increased by an order of magnitude to 2 MPa to have approximately the same displacement as with an actuator of \( l = 20 \, \mu m \), \( d = 26 \, \mu m \), and \( G = 0.2 \) MPa. The time evolution of the fluid strip, now having dimensions of \( 210 \leq x \leq 390 \, \mu m \) and \( 45 \leq y \leq 55 \, \mu m \) for \( \phi = \pi/2 \) and \( \pi \), is shown in Fig. 15. For \( \phi = \pi/2 \), the stretching of the strip is exponential and comparable with that seen for the one-wall arrangement with \( l = 20 \, \mu m \), \( d = 26 \, \mu m \), and \( G = 0.2 \) MPa, see Fig. 16. In fact, the stretching distribution, i.e., the stretching

FIG. 15. Comparison of the deformation of an initially rectangular strip obtained by two different actuation schemes viz. phase lags of \( \pi/2 \) (left column) and \( \pi \) (right column) for an opposite wall arrangement of the two microactuators separated by a horizontal spacing of 40 \( \mu m \). The individual microactuators are 40 \( \mu m \) in length, have a shear modulus of 2 MPa, and are operated at a frequency of 4 Hz. The instantaneous flow streamlines (normal lines) as well as the positions of two microactuators (thick lines) are also shown.

FIG. 16. Quantification of the increase in interfacial length shown in Figs. 14 and 15.
experienced by the material elements locally, a relevant quantity to understand global mixing, is seen to be better than that observed for a one-wall arrangement of microactuators; this can be seen by comparing the striation thickness, i.e., the thickness of the black strip in Fig. 10 with those in Fig. 15.

V. CONCLUSION

To assess the feasibility of the proposed artificial cilia based active micromixer, a fluid-structure interaction model based on the fictitious domain method was applied. From the results of a single microactuator motion, we conclude that the response of the microactuator is independent of the viscosity of the fluids expected to be encountered in microfluidic applications and is predominantly dependent on the modulus of the microactuator material. We have shown that effective mixing by chaotic advection can be obtained with cilia-like microactuators integrated in a microfluidic channel. The results show that with a well-chosen geometrical arrangement and actuation scheme, exponential mixing can be obtained even with only two microactuators.

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