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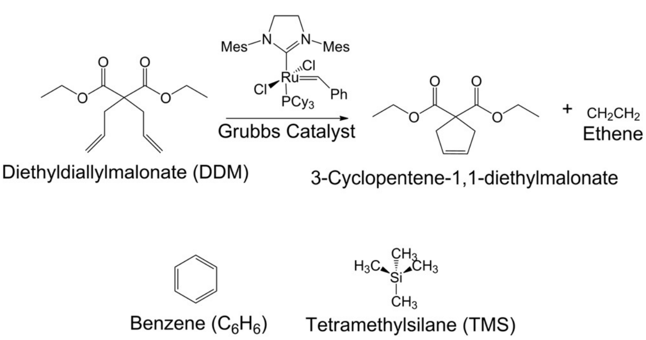
Dynamic Coupling at the Ångström Scale

Krishna Kanti Dey[+], *Frances Ying Pong*[+], *Jens Breffke, Ryan Pavlick, Emmanuel Hatzakis, Carlos Pacheco, and Ayusman Sen**

Abstract: *While momentum transfer from active particles to their immediate surroundings has been studied for both synthetic and biological micron-scale systems, a similar phenomenon was presumed unlikely to exist at smaller length scales due to the dominance of viscosity in the ultralow Reynolds number regime. Using diffusion NMR spectroscopy, we studied the motion of two passive tracers—tetramethylsilane and benzene—dissolved in an organic solution of active Grubbs catalyst. Significant enhancements in diffusion were observed for both the tracers and the catalyst as a function of reaction rate. A similar behavior was also observed for the enzyme urease in aqueous solution. Surprisingly, momentum transfer at the molecular scale closely resembles that reported for microscale systems and appears to be independent of swimming mechanism. Our work provides new insight into the role of active particles on advection and mixing at the Ångström scale.*

Research on active, self-powered systems has undergone tremendous growth in the past decade.[1–4] These systems usually involve microscale active particles that autonomously move and interact with each other, forming reversible assemblies in the presence of localized physicochemical triggers.[5–8] An important aspect of the dynamics of such active assemblies is their effect on their immediate surroundings. Studies conducted with micron-scale organisms and catalytic particles show that such active assemblies exert considerable influence over the behavior of their surroundings.[9–16] Diffusion of inert tracer particles dispersed in a suspension of micron-scale swimmers is dependent upon the total activity of a system; the higher the total activity of the system, the greater the diffusion enhancement of the tracers.[10–12] Qualitatively, the enhancement was found to be independent of swimming patterns and mechanisms, signifying the generic role of hydrodynamic coupling among the swimmers and their surroundings, which facilitates the distribution of momentum.[11] A key question is whether these effects are also observable at the ultralow Reynolds number regime (i.e. molecular scale). A recent theoretical paper predicts that the advection effects induced by active molecular catalysts should also result in significant enhancement of diffusion of passive molecules present in solution.[17] Here we present experimental demonstration of diffusion enhancement of passive molecular tracers in the presence of active catalyst molecules.

We measured the diffusion of molecular tracers in a solution of Grubbs second generation catalysts noninvasively using diffusion NMR spectroscopy.[18–21] In order to investigate momentum transfer at the Ångström level, we elected to study the ring-closing metathesis (RCM) reaction of diethyl diallylmalonate (DDM) catalyzed by Grubbs second generation catalyst (hydrodynamic radius $R_H =$ 6 Å[22]). The reaction is well-understood, robust, and is easy to monitor by NMR spectroscopy over a reasonable time scale, making it an acceptable model system. Upon metathesis, DDM is converted into the cyclic compound, 3-cyclopentene-1,1-diethylmalonate, and one molecule of ethene (Scheme 1). We had earlier demonstrated that substrate turnover at room temperature can substantially enhance the motion of Grubbs catalyst molecules in solution.[22] This observation is consistent with the recent proposal that Ångström-scale chemically-powered motors are capable of moving in a self-generated concentration gradient.[23] Our previous observation, coupled with the recent theoretical suggestion,[17] prompted us to quantify the collective effect of these molecular swimmers on their surroundings during catalysis. In our experiments, tetramethylsilane (TMS) and benzene were used as passive tracer particles (Scheme 1) and their diffusion was measured in the presence and absence of substrate turnover.



Scheme 1. Ring closing metathesis reaction of DDM by Grubbs 2nd generation catalyst. Upon metathesis, DDM is converted into the cyclic compound, 3-cyclopentene-1,1-diethylmalonate, and one molecule of ethene. Momentum transfer from active catalytic sites upon substrate turnover was quantified by measuring the diffusion of TMS and benzene in a solution of Grubbs catalyst at different DDM concentrations.

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[*] Dr. K. K. Dey,[+] F. Y. Pong,[+] Dr. J. Breffke, Dr. R. Pavlick, Dr. E. Hatzakis, Dr. C. Pacheco, Dr. A. Sen
Department of Chemistry, The Pennsylvania State University
University Park, PA 16802 (USA)
E-mail: asen@psu.edu

[+] These authors contributed equally to this work.

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The principle of diffusion NMR spectroscopy has already been well-reviewed.[18–21] The details of NMR measurements and instrumentation are provided in the Supporting Information. The typical curve fit which is used to estimate the diffusion coefficient of tracers is shown in Figure S1 in the Supporting Information.

To analyze how substrate turnover by molecular catalysts influences the dynamics of their surroundings, the diffusion coefficients of TMS and benzene (estimated hydrodynamic radii: 2.46 and 1.33 Å, respectively (see the Supporting Information) were measured in a C_6D_6 solution of Grubbs catalyst. The diffusion coefficient of the tracers could be determined by tracking their peaks in the ^{1}H spectrum (TMS, 0 ppm; benzene, 7.16 ppm). Tracer and substrate concentrations and solution volume were kept consistent for all active and control samples.

To minimize the effect of convection due to possible solvent evaporation or escape of ethene, the experiments were performed in high-pressure, screw-capped NMR tubes. However, as shown in Figure S2, for the substrate concentration range used in the experiments, the diffusion coefficients were nearly the same in the closed and open systems. In addition, contrary to our observations, convection due to an ethene gradient should have resulted in similar enhancements in diffusion for both tracers and catalyst molecules.

Viscosity did not contribute to the changes in diffusion observed in the experimental samples in which catalytic turnover took place. To confirm our observation, we measured the viscosity of the Grubbs catalyst solution both as a function of substrate concentration and as function of time. The addition of 3 mM catalyst to the substrate solution did not change its viscosity significantly ($(8.68\pm0.27)\times10^{-4}$ Pa s without catalyst compared to $(8.39\pm0.28)\times10^{-4}$ Pa s with catalyst). Furthermore, when observed for a period of nearly 30 min, the viscosity of the reacted mixture was approximately the same as that of the unreacted solution, signifying that the conversion of reactant to product does not influence the solution viscosity at any point during the reaction (see the Supporting Information). Picosecond fluorescence anisotropy decay measurements were used to examine the rotational dynamics of a tracer fluorophore, allowing us to monitor changes in the local viscosity of a sample during the course of the reaction.[24] No significant changes in viscosity were observed in the measurements (see the Supporting Information for details).

The diffusion of both TMS and benzene measured in a solution containing 3 mM Grubbs catalyst and various concentrations of DDM is shown in Figure 1 A. DDM concentrations were calculated using 1D ^{1}H-NMR spectroscopy, while tracer diffusions were simultaneously measured using diffusion NMR spectroscopy. In the absence of reaction, the diffusion coefficients of the tracers remained constant over time ($D_{\mathrm{TMS}} = (2.46\pm0.01)\times10^{-9}\,\mathrm{m^2\,s^{-1}}$ and $D_{\mathrm{Benzene}} = (2.68\pm0.02)\times10^{-9}\,\mathrm{m^2\,s^{-1}}$) and were comparable with the values estimated using the Stokes-Einstein equation (see the Supporting Information for details). In contrast, in the presence of a reaction, the diffusion increased significantly. The reaction rate increases as a function of the substrate concentration, which in turn enhances tracer diffusion. Additionally, when an active sample containing catalyst and substrate was monitored for an extended period of time (> 5 h), the tracers gradually returned to their Brownian (or base) diffusion values as the substrate was exhausted (Figure 1 B). These results strongly suggest that substrate turnover is responsible for the observed enhancement in tracer diffusion in our systems.

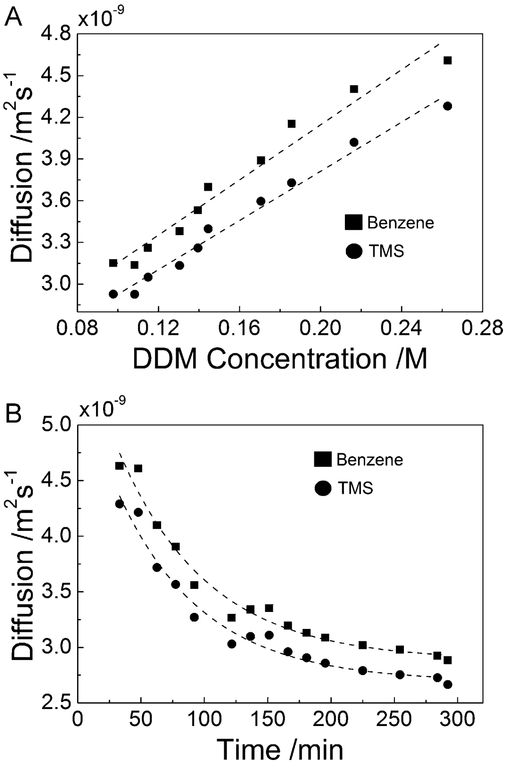

Figure 1. Measured diffusion of TMS and benzene as a function of substrate concentration and time. A) Diffusion coefficients of TMS and benzene measured in a solution containing 3 mM Grubbs catalyst plotted against changing DDM concentrations. At higher concentrations of DDM, both the reaction rate and tracer diffusion increase significantly. The data presented are the average of three independent measurements with a maximum standard deviation of $2.78\times10^{-10}\,\mathrm{m^2\,s^{-1}}$ and $4.08\times10^{-10}\,\mathrm{m^2\,s^{-1}}$, for TMS and benzene, respectively. B) Time dependent decrease in diffusion of TMS and benzene in a solution of 3 mM Grubbs catalyst and 1 M DDM, monitored over an extended period of time. Upon completion of reaction, the diffusion values returns to base values, which are close to those measured in the absence of any reaction. The data presented are the average of three independent measurements with a maximum standard deviation of $2.62\times10^{-10}\,\mathrm{m^2\,s^{-1}}$ and $3.78\times10^{-10}\,\mathrm{m^2\,s^{-1}}$, for TMS and benzene, respectively.

In addition to the passive tracers, we also measured the diffusion of the catalyst molecules under identical experimental conditions to quantify the diffusion enhancement of the swimmers themselves in the presence of reaction. In an active solution, the catalyst molecules also behave as tracers for each other, because the motion of each molecule is influenced by its active neighbors. Figure 2 A shows the diffusion of Grubbs catalysts measured at 3 mM catalyst and different DDM concentrations. Like the tracers, the diffusion of the catalysts at first increases significantly and then

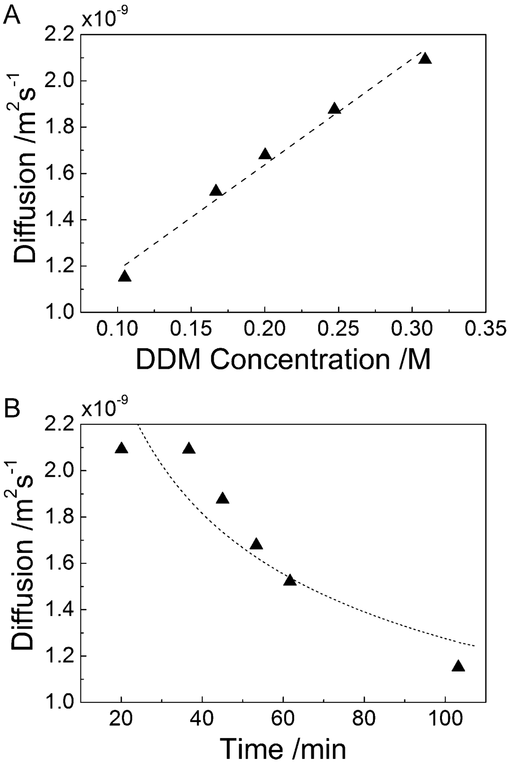

Figure 2. Measured diffusion of Grubbs catalyst as a function of substrate concentration and time. A) Diffusion of 3 mм Grubbs catalysts measured as a function of DDM concentration. The diffusion of the catalysts increases with increasing substrate concentration. The data presented are the average of three independent measurements with a maximum standard deviation of 3.03×10^{-10} m^2 s^{-1}. B) Decrease in catalyst diffusion over time as the reaction proceeds towards completion in which the starting substrate concentration was 1 м. The data presented are the average of three independent measurements with a maximum standard deviation of 2.39×10^{-10} m^2 s^{-1}.

approaches the base value as the reaction progresses toward completion (Figure 2B).

The diffusion values of both TMS and benzene increase monotonically with higher concentrations of substrate, a phenomenon that is consistent with previous observations on the advective displacement of particles by active microswimmers.[10–12] What makes the present system unique is that Grubbs catalyst is the smallest self-powered system to display dynamic coupling and control over tracer diffusion via catalytic turnover. Higher reaction rate resulted in an increased rate of net momentum transfer to the passive tracers thereby enhancing their overall diffusion. Miño et al. measured the tracer diffusion with increased number densities of microscopic swimmers (bacteria and self-propelled bimetallic rods) and found a linear dependence of the former on the total active flux of the system (defined as the product of number density and average ballistic speed of the swimmers).[11] Similarly, Kurtuldu et al. showed a linear relationship between the volume fraction of the active algal cells and diffusion of passive tracers suspended therein.[12] Both these systems show a direct dependence of tracer diffusivity on the total number of active events occurring in the system. Remarkably, even at the Ångström scale the diffusion of tracer molecules follows a similar trend, showing the generic influence of hydrodynamic coupling in transferring momentum around active swimmers and the scalability of this phenomenon down to the molecular level.

Our diffusion results can be used to draw a correlation between the behavior of active swimmers in a range of length scale and their effect on the surroundings. Following the definition proposed by Miño et al.,[11] we calculated the active flux (= number density of active molecules × ballistic speed) in our system for Grubbs molecular catalysts. The ballistic speed u of the catalyst molecules at different substrate concentrations was obtained from their net change in diffusion and value of rotational diffusion coefficient using the relation $\Delta D = u^2/6D_r$.[25] Here, ΔD is the change in diffusion of a swimmer and and D_r is its rotation diffusion coefficient that is related to its radius R, which can be obtained from: $D_r = kT/8\pi\eta R^3$. In this equation, k, T and η are Boltzmann's constant, temperature and viscosity of the system (for details, see the Supporting Information). As shown in Figure 3A, the diffusion coefficients of TMS, benzene and the Grubbs catalyst plotted against the active flux follow linear profiles. We also calculated the ballistic speed of the enzyme urease—another low Reynolds number swimmer—at different concentrations of its substrate urea, using previously published data.[26] As with the organometallic system, for active urease solution, each enzyme molecule is expected to behave as a tracer for the others around it; accordingly, we plotted the diffusion of active urease as a function of active flux calculated at various substrate concentrations. Like the Grubbs catalyst, a linear profile was observed, as shown in the Figure S3. The behavior in the nanoscale systems, are similar to that reported for systems containing active micron-scale swimmers, where the tracer diffusion (D_T) was found to vary linearly with the active flux (J_A).[11] The relation between D_T and J_A can be defined as $D_T = D_{B,T} + \beta \times J_A$, where $D_{B,T}$ corresponds to normal Brownian diffusion of the tracers and $\beta^{0.25}$ is defined as the interaction length scale, the physical significance of which remains to be established. We found that the interaction length scale decreases somewhat with increasing size of the swimmers (5.51×10^{-9} m^2 s^{-1} for benzene, 5.36×10^{-9} m^2 s^{-1} for TMS, and 4.74×10^{-9} m^2 s^{-1} for Grubbs catalyst as seen in the inset bar graph of Figure 3B).

The scalability in behavior of the active swimmers towards their surroundings can be assessed by comparing the $\beta^{0.25}$ values. The $\beta^{0.25}$ values of bacteria and catalytic rods have been reported by Miño et al. to be 1.5 μm and 1.9 μm, respectively. For Grubbs molecular catalyst, we can consider the average $\beta^{0.25}$ value (measured for three different tracers) to be 5.20 nm; that calculated for urease is 72 nm. Remarkably, the $\beta^{0.25}$ values vary linearly with the dimension of the active swimmers (Figure 3B), suggesting that they affect their surroundings similarly, irrespective of their mechanism of energy transduction and propulsion.

The experimental observations demonstrate transfer of momentum from the active catalyst molecules to the surrounding medium. As discussed previously,[22] the enthalpy change for the ring-closing metathesis of DDM is approximately +8 kcal mol^{-1} (endothermic) and therefore cannot

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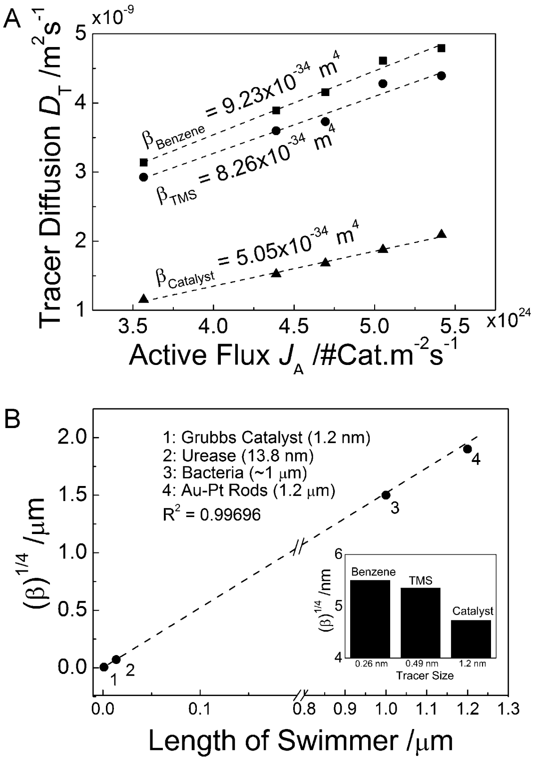

Figure 3. Generic behavior of active swimmers in transferring momentum to their surroundings. A) Change in tracer and catalyst diffusion as a function of total active flux of the system. The active flux was calculated using the number density of catalyst and ballistic speeds of swimmers at different substrate concentrations. For the Ångström-sized tracers, the diffusion changed linearly with the active flux, similar to what was observed in systems with micron-scale swimmers. B) Variation of interaction length scales calculated (and taken from literature) for swimmers of different sizes. The results show that the active swimmers transfer momentum to their surroundings similarly over a wide range of swimmer dimensions. The inset shows how the interaction length scales calculated for different molecular tracers change with their size under the influence of the same molecular swimmer (Grubbs catalyst).

contribute to the observed enhanced diffusion of the tracers. The most plausible mechanism involves reaction-generated advection caused by active force dipoles (catalyst molecules) "stirring" the solution.[17] Moreover, there are reports on the existence of nonlinear instabilities in fluids above some critical flow threshold, even when the system is expected to be linear and dominated by viscous drag.[27,28]

In conclusion, we have demonstrated transfer of momentum from active, Ångström-sized catalysts to their immediate surroundings by monitoring the change in diffusion of molecular tracers present in a system undergoing catalytic substrate turnover. The diffusion enhancement is correlated with the total activity of the system, which has been previously observed in systems containing micron-scale swimmers. Our observations are consistent with the recent prediction of long-range hydrodynamic effects due to active force dipoles "stirring" the medium.[17] This model also predicts a linear dependence of diffusion enhancement on substrate concentration as is observed in our system. The results described open up a new area of mechanochemistry: intrinsic force generation by molecular-scale catalysts. The catalysis-induced force generation may be sufficient for the recently reported stochastic motion of the cytoplasm and for the convective transport of fluid in cells.[29,30] Momentum transfer at the Ångström scale not only provides novel insights into the dynamics of low Reynolds number systems but offers opportunities for controlled mass and energy transfer, thereby contributing to the rapidly developing frontiers of small scale mixing, assembly and delivery.

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