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Influence of molecular rebinding on the reaction rate of complex formation

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S1 Validation of simulation routine

To validate the simulation routine, we tested the simplest model of diffusion-limited reaction proposed by von Smoluchowski. We designed a 3D toy model consisting of a spherical target - a mesh located at the center of the simulation box. The diameter of the target $2R_\mathrm{T}$ was no longer than one-tenth of the size of the simulation box to avoid the effect of the boundaries. Simultaneously $2R_\mathrm{T}$ was at least ten times bigger than mean radial displacement to be sure that during a single simulation step, the particles do not jump over the target without interaction. At the boundaries of the simulation box, we keep a constant concentration of molecules, which creates an infinite reservoir of molecules. The molecules are uniformly distributed across the simulation box. After the molecules reach the boundaries of the target, they are absorbed and removed from the pool. After that, another molecule is created at the boundary of the box. This approach allowed to keep the concentration of molecules in the box unchanged. We count an event whenever the target's boundary absorbs the molecule. For analyzed systems, we performed 15 simulation runs. Each of the 15 data sets was analyzed separately. For each data set, we calculated a cumulative number of reaction acts occurring in time.

According to the von Smoluchowski theory, Equation (S1) provides the number of times the particles P will hit the target T within a given time t,[1,2]

$$N(t) = 4\pi R_\mathrm{T} D c N_\mathrm{A}\left(t + \frac{2R_\mathrm{T}\sqrt{t}}{\sqrt{\pi D}}\right), \tag{S1}$$

where N_A stands for Avogadro's constant. In the limit of $t \to \infty$ Equation (S1) simplifies to the form:

$$N(t) = k_\mathrm{D} c t. \tag{S2}$$

We tested relation (S2) for data obtained within the diffusion limited model where no rebindings are expected. We analyze the cumulative number of particles that hit the target and get annihilated as a function of time. We fit the data with Equation (S2) with k_D as a free parameter. As expected, the average number of observed reaction acts increases linearly with time, and the average k_D agrees with its theoretical value. Figure S1 depicts representative results for $N(t)$.

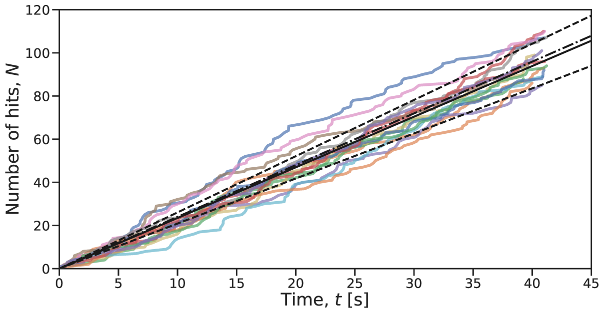

Fig. S1 The figure shows the cumulative number of times, N, the particles hit the target. The data were gathered for simulations with the absorbing target (model depicted in Figure 1**a** from the main text). The plot was acquired for the system containing 10 pM of particles whose diffusion coefficient equals to 320 $\mu\mathrm{m}^2/s$. The plot represents 15 simulation runs plotted together. For each simulation run we fitted the cumulative curve separately using Equation (4) (main text) with k_D as a free parameter. The solid lines correspond to Equations (4) from main text with mean value of k_D obtained from fitting. Dashed lines correspond to the mean value of k_D plus/minus standard deviations from the average. The dashed-dotted line corresponds to the prediction made based on Equation (4) with k_D calculated as $k_\mathrm{D} = 4\pi R_\mathrm{T} D N_\mathrm{A}$.

S2 Distribution of residence time in a spherical domain

We performed an analysis of the distribution of the particles' residence time within the target. The simulations were performed according to the scheme depicted in Figure 1**a** from the main text, with only one searching molecule starting its Brownian journey exactly at the boundary of the target. An attempt to determine the Brownian particle's residence probability inside the spherical target (in three dimensions) was also studied by Agmon.[3] He proposed the probability distribution of residence times under the assumption of uniform distribution of particles inside the sphere. His approach, however, does not apply to our simulations. In our system, we have exactly one particle with the initial position located at the boundary of the sphere. In the first step, the particle can jump either inside or outside the sphere.

We performed simulations covering six decades of Δt (from 1 ps to 0.1 μs). The distribution of residence times obtained for all Δt are shown in Figure S2. The data represented in Figure S2 follow the slope characterised by the $t^{-3/2}$ dependence resulting from the Brownian excursions in a half-space,[4] where the curvature of the sphere can be approximated as plane.

S3 Number of rebindings calculated for reaction-diffusion model

We compared $\langle N_\mathrm{reb}\rangle$ calculated from Equations (7) and (9) from the main text, with the $\langle N_\mathrm{reb}\rangle$ calculated as $\langle N_\mathrm{reb}\rangle = 1/p(r)$, with

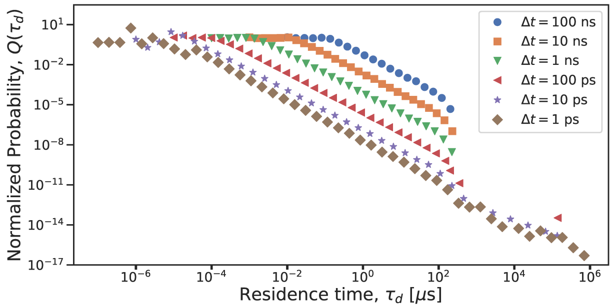

Fig. S2 Plot shows the normalized probability of residence $Q(\tau_{\mathrm{d}})$ of the particle inside the transparent target (model depicted in Figure 1**c**, main text). The data were gathered for the system characterized by $D = 20$ $\mu\mathrm{m}^2/s$, $R = 100$ nm, and Δt varying from 1 ps to 100 ns. The probability data were normalized to the maximal value and plotted every two data points.

$p(r)$ given by Equation (10) from the main text.[5,6] We found that for all studied systems, $\langle N_{\mathrm{reb}} \rangle$ calculated from Equation (10) is lower than the one calculated from Equation (7). The values calculated from Equation (10) were equal to $\langle N_{\mathrm{reb}} \rangle = 1/p(r) = 2$, while Equation (7) leads to the value of $\langle N_{\mathrm{reb}} \rangle = 3$ for all studied systems. This, one could say, an insignificant difference was remarkably visible when we plotted the $N(t)$ dependence; cf. Figure S3,

S4 Estimation of the HPTS's R_{T} on the basis of the van der Waals radii.

To estimate the R_{T} for the photodissociation of HPTS, we assumed that the proton, after dissociation, is immediately captured by the surrounding water molecules and form the hydronium ion. Therefore R_{T} should be given as a sum of radii of the HPTS and hydronium ion. We estimated the van der Waals radii using the following procedure. The SMILES codes of HPTS and hydronium ion were imported into the Avogadro software and represented as van der Waals spheres. The same was done for the carbon atom. Next, all models were exported as *.wrl* files and imported to the CellBlender software. From the HPTS molecule model, we removed one of the spheres that corresponded to the dissociating proton. Next, all spheres forming a given model (HPTS or hydronium ion) were joined together, to form a single mesh, utilizing the boolean unite modifier. Finally, we used a Mesh Analysis tool in the CellBlender to calculate the volume occupied by each model. Knowing the van der Waals radius of the carbon atom, 0.17 nm, we calculated its volume. We use it as a reference value to calculate the van der Waals volumes of the HPTS and hydronium ion. Finally, approximating both molecules with spheres, we calculated the corresponding van der Waals radii.

Notes and references

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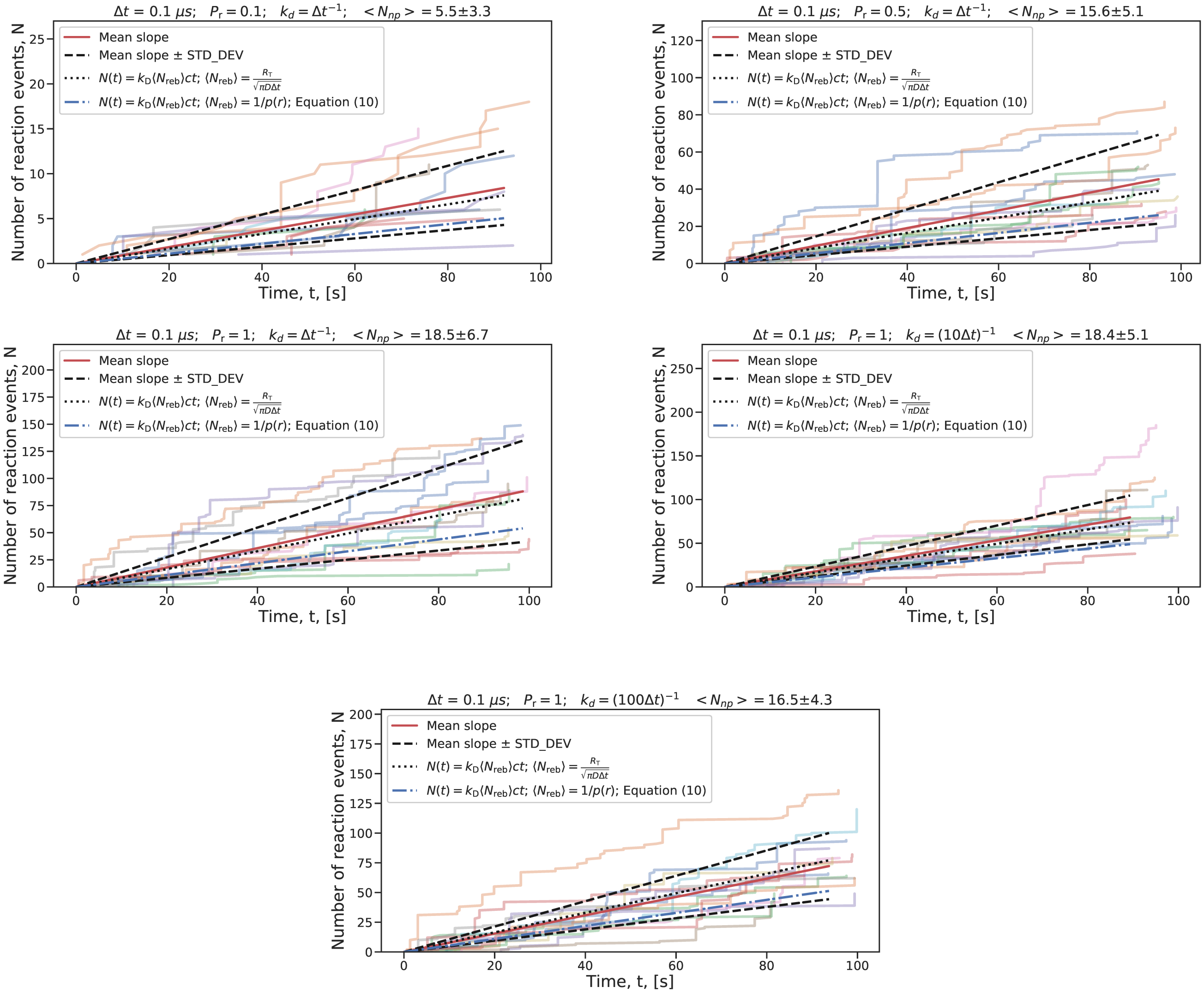

Fig. S3 The cumulative number of reaction events N occurred in time t for fifteen simulation runs (solid color lines). Data for each simulation run was fitted separately using the $N(t) = act$ dependence, where a was used as a free parameter, and c stands for concentration. The values of a were further averaged. The solid red line corresponds to $N(t)$ with the mean value of a, and the black dashed line corresponds to the mean value of a plus/minus standard deviation. The black dotted and the red solid lines represent $N(t)$ calculated according to Equation (9) from the main text. The blue dashed dotted line corresponds to the $N(t)$ dependence calculated using $\langle N_{\mathrm{reb}} \rangle \equiv 1/p(r)$ from Equation (10) from the main text. Simulation parameters, including P_{r} and k_{d}, are given in the title of the plot. N_{np} denotes the number of new particles (or particles whose excursion took longer than $\tau_{\mathrm{c}} = L^2/6D$) that reacted with the target molecule T. L stands for the mean interparticle distance.