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Theory of diffusion-influenced reactions in complex geometries

by M. Galanti, D. Fanelli, Sergey D. Traytak & F. Piazza

Supplementary information

Contents

I. DERIVATION OF THE SYSTEM OF EQUATIONS (6).

We describe here the analytical procedure that enables one to solve the steady-state diffusion equation (i.e. the Laplace equation) for diffusion-influenced reactions with any finite number of spherical reactive boundaries. Having in mind applications of boundary problems both in bounded (e.g. reactive boundaries within some kind of nanoreactor) and unbounded domains, we consider the general case of N active spheres Ω_α of (encounter) radius σ_α located within some larger spherical domain Ω_0 of radius R_0, whose (inner) boundary represents the wall of this confining domain. The N spheres within Ω_0 are located at position $\boldsymbol{X}_\alpha$ with respect to a Cartesian reference frame with origin at the center of Ω_0. The problem in $\Omega = \Omega_0 \setminus \sum_{\alpha=1}^{N} \Omega_\alpha$ for the normalized density of ligands $u = \rho/\rho_B$ (ρ_B being the bulk ligand density) can be cast in the following form

$$\bigtriangledown^2 u = 0 \tag{1a}$$

$$\left(\frac{\partial u}{\partial \xi_\alpha} - h_\alpha u\right)\Big|_{\partial\Omega_\alpha} = 0 \qquad \forall\, \alpha = 1, 2, \ldots N \tag{1b}$$

$$\left(\frac{\partial u}{\partial \xi_{\mathbf{0}}} - h_0(1-u)\right)\Big|_{\partial\Omega_0} = 0 \tag{1c}$$

for any choice of the intrinsic reactivity of each sphere. Here $\xi_\alpha = r_\alpha/\sigma_\alpha$ and we take into account the $(N+1)$ spherical coordinate systems corresponding to each boundary: $\mathbf{r}_0 = (r_0, \theta_0, \phi_0)$, $\mathbf{r}_\alpha = (r_\alpha, \theta_\alpha, \phi_\alpha), \forall\, \alpha = 1, 2, \ldots N$, where θ and ϕ identify respectively the polar angle and the azimuthal angle. The parameter h_0 is the intrinsic reactivity of the inner surface of the spherical domain Ω_0 that contains all the N spheres Ω_α. The physical meaning of h_0 is to provide an *effective* representation for the existence of an *outside world* for the ligand molecules B, even if the boundary problem is *stricto sensu* solved in the bounded domain Ω. More precisely, for an isolated sink ($N = 1$) lying at the origin of the reference frame with the origin at the center of Ω_0, one can prove that

$$h_0 = \frac{D_{\mathrm{out}}}{D_{\mathrm{in}}}$$

where D_{out} and D_{in} are the values of the ligand diffusion coefficient outside and inside, respectively, an imaginary penetrable surface that coincides with the boundary of Ω_0. Of course, the actual value of h_0 is utterly irrelevant in the limit of a reaction occurring in the unbounded domain, i.e. for $R_0 \to \infty$.

The boundary problem (1a), (1b), (1c) can be solved by looking for solutions as combinations of regular and irregular harmonics, since the solution inside a single sphere can be written as a linear combination of regular harmonics,

$$u_0^+ = \sum_{n=0}^{\infty}\sum_{m=-n}^{n} A_{mn} u_{mn}^+(\mathbf{r_0}) = \sum_{n=0}^{\infty}\sum_{m=-n}^{n} A_{mn}\xi_0^n Y_{mn}(\mathbf{r_0}) = \sum_{n=0}^{\infty}\sum_{m=-n}^{n} A_{mn}\left(\frac{r_0}{R_0}\right)^n P_n^m(\mu_0)e^{im\phi_0} \tag{2}$$

where $\mu_0 = \cos\theta_0$, while the basis of irregular harmonics should be used outside spherical domains (regular harmonics diverge at infinity):

$$u_\alpha^- = \sum_{n=0}^{\infty}\sum_{m=-n}^{n} B_{mn}^\alpha u_{mn}^-(\boldsymbol{r}_\alpha) = \sum_{n=0}^{\infty}\sum_{m=-n}^{n} B_{mn}^\alpha \xi_i^{-n-1} Y_{mn}(\boldsymbol{r}_\alpha) = \sum_{n=0}^{\infty}\sum_{m=-n}^{n} B_{mn}^\alpha \left(\frac{r_\alpha}{\sigma_\alpha}\right)^{-n-1} P_n^m(\mu_\alpha)e^{im\phi_\alpha}. \tag{3}$$

where $\mu_\alpha = \cos\theta_\alpha$. Using the superposition principle for the Laplace equation, we can write the solution in Ω as a sum of linear combinations of regular (for Ω_0) and irregular (for each Ω_α) harmonics, namely

$$u = u_0^+ + \sum_{\alpha=1}^{N} u_\alpha^- = \sum_{n=0}^{\infty}\sum_{m=-n}^{n} A_{mn}\xi_0^n Y_{mn}(\mathbf{r_0}) + \sum_{\alpha=1}^{N}\sum_{n=0}^{\infty}\sum_{m=-n}^{n} B_{mn}^{\alpha}\xi_\alpha^{-n-1}Y_{mn}(\boldsymbol{r}_\alpha). \tag{4}$$

If one wishes to investigate a problem in an open domain, which is the case considered in this work, it is sufficient to let $R_0 \to \infty$ and to take into account only combinations of irregular harmonics. In this case, all coefficients A_{mn} vanish but for the constant A_{00}, so that the general expression appropriate to the unbounded domain reads

$$u = 1 + \sum_{\alpha=1}^{N} u_\alpha^- = 1 + \sum_{\alpha=1}^{N}\sum_{n=0}^{\infty}\sum_{m=-n}^{n} B_{mn}^{\alpha}\xi_\alpha^{-n-1}Y_{mn}(\boldsymbol{r}_\alpha). \tag{5}$$

In general, the coefficients of the expansion are determined by imposing the boundary conditions: in a neighbourhood of each boundary one has to express all the bases as functions of the local coordinates. More precisely, to determine the values of A_{mn} and B_{mn}^{α} in a neighbourhood of each $\partial\Omega_\alpha (\alpha = 1, 2, \ldots, N)$, one has to express u_0^+ and u_β^-, $\beta \neq \alpha$, as functions of the $\boldsymbol{r}_\alpha$ coordinates. Similarly, in a neighbourhood of $\partial\Omega_0$, one has to write every u_α^- as a function of $\boldsymbol{r}_0$. For this purpose, one can make use of the addition theorems for spherical harmonics [1].

More precisely, while imposing the condition on $\partial\Omega_0$ one needs to pick the re-expansion formula for irregular-irregular harmonics, that is,

$$r_\alpha^{-n-1}Y_{mn}(\boldsymbol{r}_\alpha) = \sum_{l=0}^{\infty}\sum_{s=-n}^{n} \frac{(-1)^{l+s}(n+l-m+s)!}{(n-m)!(l+s)!} L_{0\alpha}^{l} Y_{sl}(-\boldsymbol{L}_{0\alpha}) r_0^{-(n+l)-1} Y_{m-s,n+l}(\boldsymbol{r}_0) \tag{6}$$

where $\boldsymbol{L}_{0\alpha} = \boldsymbol{X}_\alpha$ is the constant vector connecting the center of $\partial\Omega_0$ to the center of $\partial\Omega_\alpha$, so that $\boldsymbol{r}_\alpha = \boldsymbol{r}_0 - \boldsymbol{L}_{0\alpha}$. The addition theorem together with the uniqueness of decomposition lead to the first family of equations: $\forall\, q = 0, 1, 2, \ldots, \infty, \forall g = -q - q + 1, ..q - 1, q$

$$A_{gq} + \frac{-h_0 - q - 1}{(q - h_0)} \sum_{\alpha=1}^{N}\sum_{n=0}^{q}\sum_{m=-n}^{n} B_{mn}^{\alpha} V_{g,q}^{\alpha,m,n} \mathbf{1}_{\{g-(q-n)\leq m\leq g+(q-n)\}} = 1, \tag{7}$$

where $\mathbf{1}_{\{m\in\mathcal{I}\}} = 1$ if $m \in \mathcal{I}$ and zero otherwise, and

$$V_{g,q}^{\alpha,m,n} = \frac{(-1)^{q-n+m-g}(q-g)!}{(n-m)!(q-n+m-g)!} \left(\frac{L_{0\alpha}}{R_0}\right)^{q-n} \left(\frac{R_0}{\sigma_\alpha}\right)^{-n-1} Y_{m-g,q-n}(-\boldsymbol{L}_{0\alpha}) \tag{8}$$

Writing the boundary conditions on each internal sphere $\partial\Omega_\alpha$ requires to express u_0^+ and u_β^-, $\beta \neq \alpha$, in $\boldsymbol{r}_\alpha$ coordinates. This calculation implies considering, respectively, the re-expansion formula for regular-regular harmonics, namely

$$r_0^n Y_{mn}(\mathbf{r_0}) = \sum_{q=0}^{n}\sum_{g=-q}^{q} \frac{(n+m)!}{(n-q+m-g)!(q+g)!} L_{0\alpha}^{n-q} Y_{m-g,n-q}(\boldsymbol{L}_{0\alpha}) r_\alpha^q Y_{gq}(\boldsymbol{r}_\alpha) \tag{9}$$

and the theorem for irregular-regular harmonics, *i.e.*

$$r_\beta^{-n-1}Y_{mn}(\boldsymbol{r_\beta}) = \sum_{q=0}^{\infty}\sum_{g=-q}^{q} (-1)^{q+g} \frac{(n-m+q+g)!}{(n-m)!(q+g)!} L_{\beta\alpha}^{-(n+q)-1} Y_{m-g,n+q}(\boldsymbol{L}_{\beta\alpha}) r_\alpha^q Y_{gq}(\boldsymbol{r}_\alpha), \tag{10}$$

where $\boldsymbol{L}_{\beta\alpha} = -\boldsymbol{L}_{\alpha\beta} = \boldsymbol{X}_\alpha - \boldsymbol{X}_\beta$ is the constant vector connecting the center of $\partial\Omega_\beta$ to the center of $\partial\Omega_\alpha$, so that $\boldsymbol{r}_\alpha = \boldsymbol{r}_\beta - \boldsymbol{L}_{\beta\alpha}$. After some algebra, the previous formulae, together with the use of the properties of harmonics decomposition, give $\forall\, \alpha = 1, 2, \ldots, N$, $\forall q = 0, 1, 2, \ldots, \infty, \forall g = -q, -q+1, , \ldots, ..., q-1, q$, the following family of equations

$$-B_{gq}^{\alpha} + \frac{q - h_\alpha}{h_\alpha + q + 1} \sum_{n=0}^{\infty} \sum_{m=-n}^{n} \left(A_{mn} H_{m,n}^{\alpha g q} \mathbf{1}_{q \le n} + \sum_{\beta=1, \beta\neq\alpha}^{N} B_{mn}^{\beta} W_{m,n}^{\alpha\beta g q} \right) = 0 \tag{11}$$

where

$$H_{m,n}^{\alpha g q} = \binom{n+m}{q+g} \left(\frac{\sigma_\alpha}{R_0}\right)^q \left(\frac{L_{0\alpha}}{R_0}\right)^{n-q} Y_{m-g,n-q}(\boldsymbol{L}_{0\alpha}) \tag{12a}$$

$$W_{m,n}^{\alpha\beta g q} = (-1)^{q+g} \frac{(n-m+q+g)!}{(n-m)!(q+g)!} \left(\frac{L_{\beta\alpha}}{R_0}\right)^{-(n+q)-1} \left(\frac{\sigma_\alpha}{R_0}\right)^q \left(\frac{R_\beta}{R_0}\right)^{n+1} Y_{m-g,n+q}(\boldsymbol{L}_{\beta\alpha}) \tag{12b}$$

Thus, we reduced the original boundary problem (1a), (1b), (1c) to an infinite-dimensional set of equations, whose variables are the coefficients A_{mn} and B_{mn}^{α} of the expansion in spherical harmonics

$$\begin{cases} -B_{gq}^{\alpha} + \dfrac{q - h_\alpha}{h_\alpha + q + 1} \displaystyle\sum_{n=0}^{\infty} \sum_{m=-n}^{n} \left(A_{mn} H_{m,n}^{\alpha g q} \mathbf{1}_{q \le n} + \sum_{\beta=1, \beta\neq\alpha}^{N} B_{mn}^{\beta} W_{m,n}^{\alpha\beta g q} \right) = 0 \\ A_{gq} - \dfrac{h_0 + q + 1}{(q - h_0)} \displaystyle\sum_{\alpha=1}^{N} \sum_{n=0}^{q} \sum_{m=-n}^{n} B_{mn}^{\alpha} V_{g,q}^{\alpha,m,n} \mathbf{1}_{\{g-(q-n) \le m \le g+(q-n)\}} = \delta_{g0}\delta_{q0} \end{cases} \tag{13}$$

with the matrices V, W, H containing the parameters which characterize the configuration and distributed reactivity of the spheres. The general block-matrix structure of system (13) is illustrated in Fig. 1 for a number of multipoles N_M. The block matrices $\widetilde{V}, \widetilde{H}, \widetilde{W}$ appearing in Fig. 1 are defined as follows

$$\begin{aligned} \widetilde{V}_{g,q}^{\alpha,m,n} &= -\frac{h_0 + q + 1}{q - h_0} V_{g,q}^{\alpha,m,n} \mathbf{1}_{\{g-(q-n) \le m \le g+(q-n)\}} \\ \widetilde{H}_{m,n}^{\alpha g q} &= \frac{q - h_\alpha}{h_\alpha + q + 1} H_{m,n}^{\alpha g q} \mathbf{1}_{q \le n} \\ \widetilde{W}_{m,n}^{\alpha\beta g q} &= \frac{q - h_\alpha}{h_\alpha + q + 1} W_{m,n}^{\alpha\beta g q} \end{aligned} \tag{14}$$

If we denote with U the coefficient matrix illustrated in Fig. 1 and with Y the vector of unknown coefficients, the linear system one has to solve can be written as

$$\sum_{j=1}^{\mathcal{N}} U_{ij} Y_j = \delta_{i1} \tag{15}$$

where $\mathcal{N} = (N+1)(N_M+1)^2$ is the dimension of matrix U. The row and column indexes of U can be obtained through a simple unfolding procedure as follows. Let $i_b = 1, 2, \ldots, N+1$ denote the i_b-th block. If the number of multipoles included in the calculation is N_M, each block has dimensions $(N_M+1)^2 \times (N_M+1)^2$. This can be seen easily, as

$$\sum_{\ell_{i_b}=0}^{N_M} (2\ell_{i_b} + 1) = (N_M + 1)^2$$

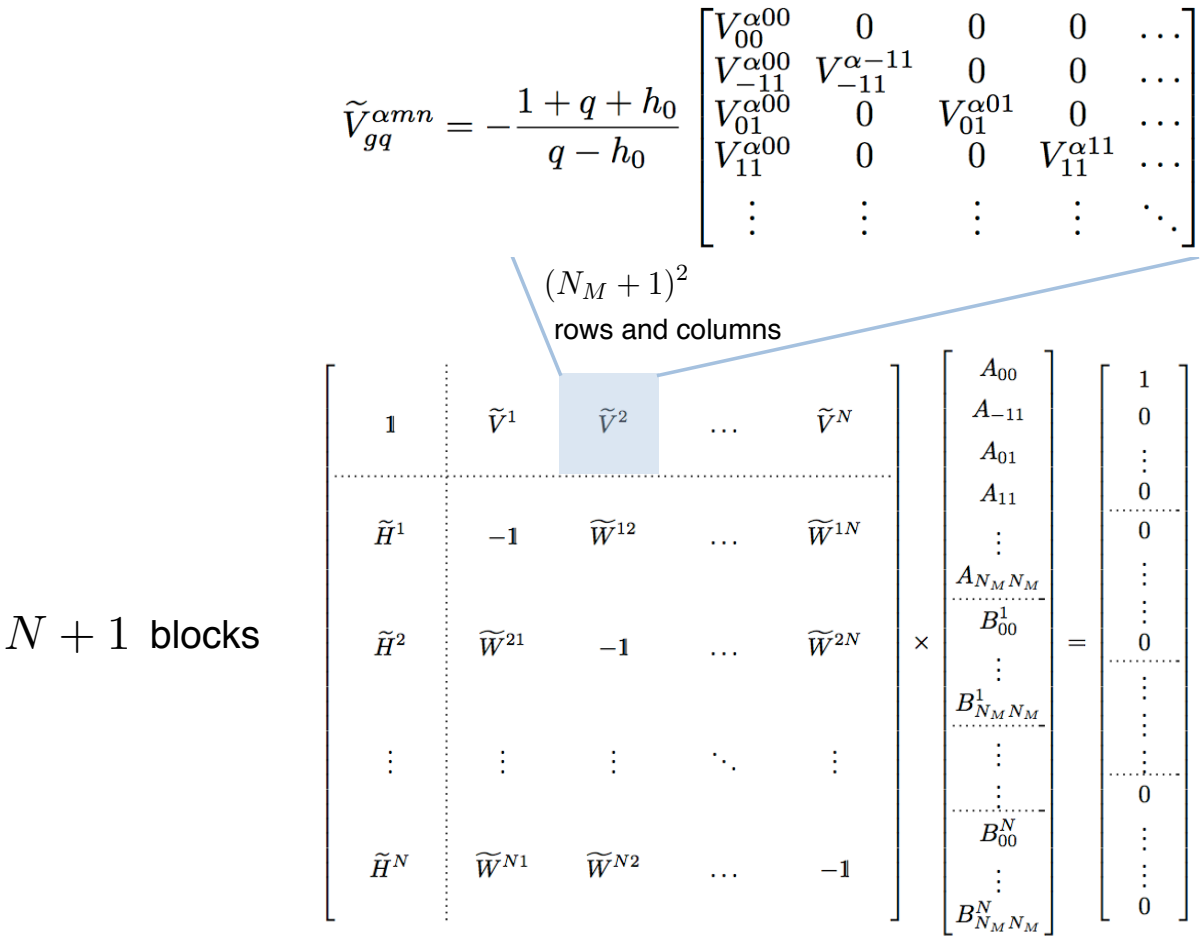

Figure 1: **Scheme of the matrix structure** (15) **of the linear system** (13). The matrix of unknown coefficients U has $N+1$ blocks if there are N spherical boundaries within Ω_0. If the maximum number of multipoles included in the calculation is N_M, each block has dimension $(N_M+1)^2$. Eq. (16) illustrates the unfolding rule that can be used to compute the indexes of the coefficient matrix U_{ij}. The block matrices $\widetilde{V}, \widetilde{H}, \widetilde{W}$ are defined by equations (14).

where ℓ_{i_b} is the index that specifies the multipole within the i_b-th block. Thus, the general unfolding rule for, e.g., the row index of U can be written as

$$i(i_b, \ell_{i_b}, m_{i_b}) = (N_M+1)^2(i_b-1) + \sum_{k=0}^{\ell_{i_b}-1}(2k+1) + \ell_{i_b} + 1 + m_{i_b} \tag{16}$$

It easy to check that the unfolding rule (16) prescribes $i = (N_M+1)^2(i_{i_b}-1)+1, 2, \ldots, (N_M+1)^2$ as $m_{i_b} = -\ell_{i_b}, -\ell_{i_b}+1, \ldots, \ell_{i_b}-1, \ell_{i_b}$ for $\ell_{i_b} = 0, 1, \ldots, N_M$.

The reaction rate corresponding to a given reactive boundary $\partial\Omega_\alpha$ is nothing but the flux of ligands to its surface (number of ligands per unit time)

$$k = -\int_{\partial\Omega_\alpha} J_\alpha|_{\partial\Omega_\alpha} dS$$

where

$$J_\alpha = -D\frac{\partial\rho}{\partial r_\alpha} = -\frac{D\rho_B}{\sigma_\alpha}\frac{\partial u}{\partial\xi_\alpha}$$

Using the expression of the solution in local coordinates and taking into account the properties of Legendre Polynomials, we have

$$\begin{aligned}\frac{k_\alpha}{k_{S_\alpha}} =&\frac{1}{2}\sum_{q=0}^{\infty}\sum_{g=-q}^{q}\Bigg[(-q-1)B_{gq}^{\alpha}+q\Bigg(\sum_{\beta=1,\beta\neq\alpha}^{N}\sum_{n=0}^{\infty}\sum_{m=-n}^{n}B_{mn}^{\beta}W_{m,n}^{\alpha\beta gq}\\ &+\sum_{n=0}^{\infty}\sum_{m=-n}^{n}A_{mn}H_{m,n}^{\alpha gq}\mathbf{1}_{q\leq n}\Bigg)\Bigg]\int_0^{2\pi}e^{ig\phi_\alpha}d\phi_\alpha\int_{-1}^{1}P_{gq}(\mu_\alpha)d\mu_\alpha\\ =&-\frac{1}{2}\sum_{q=0}^{\infty}\Bigg[(q+1)B_{0q}^{\alpha}-q\Bigg(\sum_{\beta=1,\beta\neq\alpha}^{N}\sum_{n=0}^{\infty}\sum_{m=-n}^{n}B_{mn}^{\beta}W_{m,n}^{(\alpha,\beta,0,q)}\\ &+\sum_{n=0}^{\infty}\sum_{m=-n}^{n}A_{mn}H_{m,n}^{\alpha 0q}\mathbf{1}_{q\leq n}\Bigg)\Bigg]\int_{-1}^{1}P_{0q}(\mu_\alpha)d\mu_\alpha=-B_{00}^{\alpha}\end{aligned} \tag{17}$$

where we recall that $\mu_\alpha = \cos\theta_\alpha$ and we have introduced the Smoluchowsky rate constant $k_{S_\alpha} = 4\pi D\sigma_\alpha$, which is the rate constant for an isolated sink of (encounter) radius σ_α in the unbounded domain.

To solve the system (17) one needs to truncate the expansion to include a finite number of multipoles, N_t. Thus, the resulting truncated system for N internal boundaries comprises $(N+1)(N_t+1)^2$ equations. The value of N_t that one should consider is dictated by the requested accuracy. Operatively, we have implemented a simple iterative scheme, which compares the solutions computed for N_t and N_t+1 until the necessary accuracy is attained. The accuracy considered in this paper corresponded to relative variations of the rate from one iterations to the following equal or smaller than 10^{-4}. We note that the number of multipoles to retain for a given value of the accuracy strongly depends on the specific geometry and reactivity of the considered boundaries.

II. OUTLINE OF THE PROCEDURE LEADING TO THE PERTURBATIVE EXPANSIONS (9) AND (10)

As an example of the procedure that we followed to obtain eqs. (9) and (10) in the main text, we will describe here in some detail the steps that led us to compute the first two non trivial terms. The extension to higher orders involves longer but straightforward calculations along similar lines. Let us rewrite the linear system obtained for the case of N reflecting spheres, and let us single out the coefficients of the central sink B_{gq}^0 from the B_{gq}^α that characterize the reflecting boundaries,

$$\begin{cases}-B_{gq}^{0}-\left(\delta_{g0}\delta_{q0}+\displaystyle\sum_{n=1}^{\infty}\sum_{m=-n}^{n}\sum_{\beta=1}^{N}B_{mn}^{\beta}W_{m,n}^{0\beta gq}\right)=0\\ -B_{gq}^{\alpha}+\dfrac{q}{1+q}\left(\displaystyle\sum_{n=0}^{\infty}\sum_{m=-n}^{n}B_{mn}^{0}W_{m,n}^{\alpha 0gq}+\sum_{n=1}^{\infty}\sum_{m=-n}^{n}\sum_{\beta=1,\beta\neq\alpha}^{N}B_{mn}^{\beta}W_{m,n}^{\alpha\beta gq}\right)=0\end{cases} \tag{18}$$

where

$$W_{m,n}^{\alpha\beta gq}=(-1)^{q+g}\frac{(n-m+q+g)!}{(n-m)!(q+g)!}\left(\frac{\sigma_\alpha^q\sigma_\beta^{n+1}}{{L_{\beta\alpha}}^{n+q+1}}\right)Y_{m-g,n+q}(\boldsymbol{L}_{\beta\alpha}) \tag{19}$$

Our goal is to obtain an expansion of the rate to the central sink, $k/k_S = -B^0_{00}$ in powers of the parameter $\varepsilon = \sigma/d$. For this purpose, we have to consider the following expressions for all the coefficients of the linear system:

$$\begin{aligned} B^0_{m,n} &= \sum_{j=0}^{\infty} \varepsilon^j Q^{0,j}_{m,n} \\ B^\alpha_{m,n} &= \sum_{j=0}^{\infty} \varepsilon^j Q^{\alpha,j}_{m,n} \end{aligned} \tag{20}$$

We have to take into account the number of multipoles which is necessary to obtain the desired order of approximation. The fourth order of the expansion in powers of ε requires only the terms for $n = 0$ and $n = 1$, namely

$$\begin{cases} B^0_{00} = -1 - \lambda^2\varepsilon^2 \sum_{\beta=1}^{N} \left(-\frac{1}{2}\sin\theta_{\beta 0} e^{-i\phi_{\beta 0}} B^\beta_{-11} + \cos\theta_{\beta 0} B^\beta_{01} + \sin\theta_{\beta 0} e^{i\phi_{\beta 0}} B^\beta_{11} \right) + o(\varepsilon^2) \\ B^\alpha_{-11} = \frac{\lambda}{2}\varepsilon^2 \sin\theta_{0\alpha} e^{i\phi_{0\alpha}} B^0_{00} + o(\varepsilon^2) \\ B^\alpha_{01} = -\frac{\lambda}{2}\varepsilon^2 \cos\theta_{0\alpha} B^0_{00} + o(\varepsilon^2) \\ B^\alpha_{11} = -\frac{\lambda}{4}\varepsilon^2 \sin\theta_{0\alpha} e^{-i\phi_{0\alpha}} B^0_{00} + o(\varepsilon^2) \end{cases} . \tag{21}$$

Substituting the expressions (20) in the above equations, the unknown coefficients $Q^{\alpha,j}_{m,n}$ are determined by equating the coefficients of equal powers of ε. With the use of basic trigonometric identities, including $\theta_{0\beta} = \pi - \theta_{\beta 0}$ and $\phi_{0\beta} = \pi + \phi_{\beta_0}$, we get the first coefficients of the expansion:

$$\begin{cases} Q^{0,0}_{00} = -1 \\ Q^{0,1}_{00} = Q^{0,2}_{00} = Q^{0,3}_{00} = 0 \\ Q^{0,4}_{00} = -\lambda^2 \sum_{\alpha=1}^{N} \left(-\frac{1}{2}\sin\theta_{\beta_0} e^{-i\phi_{\beta 0}} Q^{\beta,2}_{-11} + \cos\theta_{\beta_0} Q^{\beta,2}_{01} + \sin\theta_{\beta_0} e^{i\phi_{\beta 0}} Q^{\beta,2}_{11} \right) = \lambda^3 \frac{N}{2} \end{cases} \tag{22}$$

The corresponding expression for a collection of N reactive boundaries can be obtained with the same procedure, the only additional difficulty being the contribution of the pairwise distance between the neighbouring boundaries $L_{\alpha\beta}$, which enter the expansion already in the first-order terms. To carry out the approximation, it is necessary to express $L_{\alpha\beta}$ as a function of the perturbative parameter by using basic trigonometry, *i.e.*

$$\frac{\sigma}{L_{\alpha\beta}} = \frac{\varepsilon}{2\sin(\omega_{\alpha\beta}/2)}$$

where $\omega_{\alpha\beta}$ is the angle formed by the sinks α and β with respect to the central sink. As a consequence, the perturbative approximation (10) will depend on the configuration of the surrounding boundaries.

A. Evaluating the order of the expansion coefficients

The perturbative expansion of the rate to a central sink of radius σ in the case of N absorbing boundaries of radius $\sigma_1 = \lambda\sigma$ reads

$$\frac{k}{k_s} = 1 - \lambda N\varepsilon + \left[\lambda N + \lambda^2 \sum_{\substack{\alpha,\beta=1 \\ \beta\neq\alpha}}^{N} \frac{1}{\Gamma_{\alpha\beta}}\right]\varepsilon^2 - \left[\lambda^2 N^2 + \lambda^2 \sum_{\substack{\alpha,\beta=1 \\ \beta\neq\alpha}}^{N} \frac{1}{\Gamma_{\alpha\beta}} + \lambda^3 \sum_{\substack{\alpha,\beta,\delta=1 \\ \beta,\delta\neq\alpha}}^{N} \frac{1}{\Gamma_{\alpha\beta}\Gamma_{\alpha\delta}}\right]\varepsilon^3 + \dots \tag{23}$$

The expansion coefficients in the previous expression are not linear in the number of neighbouring boundaries, unlike the corresponding formula for the reflecting spheres (eq. (9) in the main text). To justify this claim, we can estimate explicitly the leading power in N of the second-order coefficient. For the sake of clarity, we will confine ourselves to a planar configuration with the N centres of the spheres lying at the vertices of a regular polygon and also take $\lambda = 1$. In this case, the pairwise distances for each pair $\Omega_\alpha, \Omega_\beta$ can be written explicitly, so that

$$\begin{aligned} \frac{k}{k_s} &= 1 - N\varepsilon + \left(N + \sum_{\alpha=1}^{N}\sum_{\beta\neq\alpha=1}^{N} \frac{1}{\Gamma(\alpha,\beta)}\right)\varepsilon^2 + o\left(\varepsilon^2\right) \\ &= 1 - N\varepsilon + \left(N + \underbrace{N\sum_{k=1}^{N-1} \frac{1}{2\sin(\pi k/N)}}_{a(N)}\right)\varepsilon^2 + o\left(\varepsilon^2\right). \end{aligned} \tag{24}$$

It can immediately be concluded that the order in N of $Q_{00}^{0,2} = N + a(N)$ is higher than two. One has

$$\lim_{N\to\infty} \frac{a(N)}{N^2} = \lim_{N\to\infty} \frac{1}{N}\sum_{k=1}^{N-1} \frac{1}{2\sin(\pi k/N)} = \int_0^1 \frac{dx}{2\sin(\pi x)} = \int_0^{\frac{\pi}{2}} \frac{dx}{\sin(x)} \geq \int_0^{\frac{\pi}{2}} \frac{dx}{x} \to \infty$$

A more precise estimate can be obtained using the approximation

$$\frac{1}{\sin(\pi k/N)} = \frac{N}{\pi k} + r(k,N)$$

where $r(k,N)$ is the rest. Assuming N odd and using the properties of the harmonic series (for large values of N one has $\sum_{k=1}^{N} k^{-1} \sim \ln N$), we get

$$N\sum_{k=1}^{N-1} \frac{1}{2\sin(\pi k/N)} = N\sum_{k=1}^{\frac{N-1}{2}} \frac{1}{\sin(\pi k/N)} \sim \frac{N^2}{\pi}\sum_{k=1}^{(N-1)/2} \frac{1}{k} \sim \frac{N^2}{\pi}\ln\left(\frac{N-1}{2}\right)$$

Since it is possible to show that $N\sum_{k=1}^{(N-1)/2} r(k,N)$ has order N^2, we conclude that, at least in the planar ordered configurations considered here, the second coefficient of the expansion has order $N^2 \ln N$. In fact, we have

$$\sum_{k=1}^{(N-1)/2} r(k,N) = \sum_{k=1}^{(N-1)/2} \left(\frac{1}{\sin(\pi k/N)} - \frac{N}{\pi k}\right)$$

and

$$\lim_{N\to\infty} \frac{1}{2N}\sum_{k=1}^{N} \left(\frac{1}{\sin(\pi k/2N)} - \frac{2N}{\pi k}\right) = \frac{1}{\pi}\int_0^{\frac{\pi}{2}} \left(\frac{1}{\sin(y)} - \frac{1}{y}\right) dy < \infty$$

because

$$\lim_{y\to 0} \frac{y - \sin y}{y\sin y} = 0$$

III. THE MONOPOLE APPROXIMATION

Let us write explicitly the linear system (6) for a configuration of N sinks randomly placed at a distance d from the central sink in the monopole approximation, that is, $\ell = q = 0$. We get $\forall\, i = 1, 2, \ldots, N$

$$B_{00}^{0} = -1 - \sum_{i=1}^{N} B_{00}^{i} W_{00}^{0i00} \tag{25a}$$

$$B_{00}^{i} = -1 - B_{00}^{0} W_{00}^{0i00} - \sum_{\beta\neq i=1}^{N} B_{00}^{\beta} W_{00}^{i\beta 00} \tag{25b}$$

We recall that in general the rate to the α-th sink is simply

$$\frac{k_\alpha}{k_{S_\alpha}} = -B_{00}^{\alpha}$$

where $k_{S_\alpha} = 4\pi D\sigma_\alpha$ is the (Smoluchowski) rate constant for an isolated sink of radius σ_α (in this special case we either have $\sigma_\alpha = \sigma$ or $\sigma_\alpha = \sigma_1$). After summing equation (25b) over i, and letting $x = B_{00}^{0}$, $y = \sum_{i=1}^{N} B_{00}^{i}$, we obtain

$$x + 1 + \lambda\varepsilon\, y = 0 \tag{26a}$$

$$y + N + N\varepsilon\, x + \lambda\varepsilon \sum_{i=1}^{N} \sum_{\beta\neq i=1}^{N} \frac{B_{00}^{\beta}}{\Gamma_{\alpha\beta}} = 0 \tag{26b}$$

Physically, the variable x is the negative of the rate constant to the central sink, $k/k_S = -x$, while the variable y stands for the total rate constant for the ensemble of N screening spheres, namely

$$\sum_{\alpha=1}^{N} \frac{k_\alpha}{k_{S_\alpha}} = -y$$

Obviously the solution to eqs. (26a) and (26b) will depend on the configuration of the spherical boundaries, which is embodied in the functions $\Gamma_{\alpha\beta}$. We can give an estimate of the *mean* rate to the central sink by averaging both equations over the multi-variate totally uncorrelated probability density of the angles between each pair of spherical sinks, $\mathcal{P}(\overrightarrow{w}) \equiv \prod_{\alpha\neq\beta} P(\omega_{\alpha\beta})$, with $P(\omega_{\alpha\beta}) = \sin\omega_{\alpha\beta}/2$, normalized such that $\int_0^\pi d\omega_1 \int_0^\pi d\omega_2 \ldots \int_0^\pi d\omega_{N(N-1)/2} \mathcal{P}(\overrightarrow{w}) = 1$. The excluded-volume constraint between screening sinks requires two given particles to lie at a distance greater than or equal to their diameter. This means that $2\arcsin(\lambda\varepsilon) \leq \omega_{\alpha\beta} \leq \pi\ \forall\alpha, \beta$, with $\lambda = \sigma_1/\sigma$ and $\varepsilon = \sigma/d$. The average of the configuration-dependent terms gives

$$\left\langle \frac{1}{\Gamma_{\alpha\beta}} \right\rangle = \int_{2\arcsin\lambda\varepsilon}^{\pi} \frac{P(\omega)\, d\omega}{2\sin(\omega/2)} = 1 - \lambda\varepsilon.$$

Noting that

$$\sum_{i=1}^{N} \sum_{\beta\neq i=1}^{N} B_{00}^{\beta} = (N-1) \sum_{i=1}^{N} B_{00}^{i} = (N-1)y$$

we finally get

$$\left\langle \frac{k}{k_S} \right\rangle = -\langle x \rangle = \frac{1-\lambda\varepsilon[N-(N-1)(1-\lambda\varepsilon)]}{1-\lambda\varepsilon[N\varepsilon-(N-1)(1-\lambda\varepsilon)]} \tag{27}$$

We note that for $N = 1$ eq. (27) reduces to the well-known formula for a system of two identical sinks [2], $k/k_S = 1/(1+\varepsilon)$. It is straightforward to prove that this function displays a minimum as a function of the distance d for certain choices of the parameters N and λ. Since $\varepsilon \propto d^{-1}$, the condition for the existence of a stationary point as the distance d is changed reads

$$\frac{d}{d\varepsilon}\left\langle \frac{k}{k_S} \right\rangle = -\frac{\lambda N[\varepsilon(\lambda\varepsilon(\lambda(N-1)+1)-2)+1]}{[\lambda\varepsilon(\lambda(N-1)\varepsilon+N(\varepsilon-1)+1)-1]^2} = 0 \tag{28}$$

From eq. (28) it follows that a minimum exists for

$$\lambda^2(N-1)+\lambda-1 \leq 0 \tag{29}$$

In this case, the distance d^* at which a minimum is found is

$$d^* = \sigma\left[\sqrt{1-\lambda[1+\lambda(N-1)]}+1\right] \tag{30}$$

If a minimum exists, it has to occur at a distance greater than or equal to the contact distance between the central sink and the screening particles. Thus, one should enforce the condition $d^* \geq \sigma + \sigma_1$. Therefore, in view of expression (30), it follows that one has to complement eq. (29) with the additional requirement

$$\sqrt{1-\lambda[1+\lambda(N-1)]}+1 \geq 1+\lambda \tag{31}$$

As quoted in the main text, the solution to the system of inequalities (29) and (31) reads

$$\begin{cases} \lambda \leq \lambda^*(N) \equiv (\sqrt{4N+1}-1)/(2N) < 1 & \text{for fixed } N \\ N \leq N^*(\lambda) \equiv (1-\lambda)/\lambda^2 & \text{for fixed } \lambda \end{cases} \tag{32}$$

IV. SCREENING BY REFLECTING OBSTACLES: THE CONFIGURATION ENTERS HIGHER POWERS OF $\varepsilon = \sigma/d$

Our perturbative procedure has shown that, in case of N reflecting boundaries, the rate constant is linear in N and depends only on the distance between the obstacles and the sink, d (eq. (9) in the main text). The configuration does not appear explicitly. However, this is only the case at large enough separations, as the specific $3D$ arrangement of obstacles indeed enters the perturbative expansion at the 7-th order in $\varepsilon = \sigma/d$. In order to prove this statement, let us consider two distinct planar configurations of the reflecting spheres, lying at the vertices of an equilateral triangle (configuration $\mathcal{C}_3$) and of a square (configuration $\mathcal{C}_4$). The seventh-order

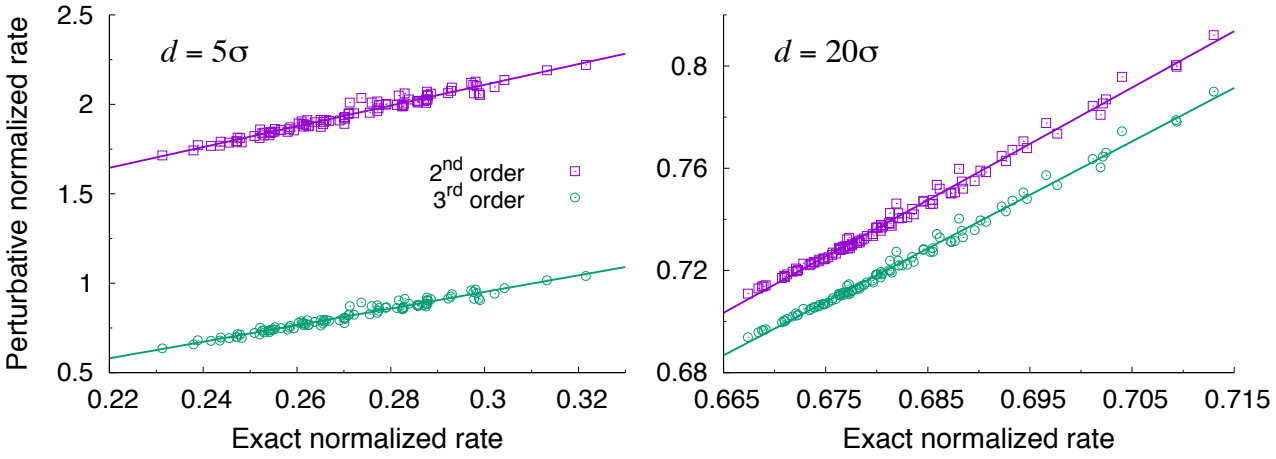

Figure 2: **Perturbative rate constants are to an excellent extent proportional to the exact values.** Perturbative (eq. (23)) vs exact rates to a sink of radius σ screened by $N = 50$ sinks of radius $\sigma_1 = \sigma/10$ arranged randomly at a fixed distance d from it. Each set comprises 100 independent configurations. The values of the rate are normalized to the Smoluchowski rate for the central sink, $k_S = 4\pi D\sigma$.

correction for a collection of spheres lying in the $z = 0$ plane, $\theta = \pi/2$, reads

$$\begin{aligned} Q_{00}^{0,7} &= -\frac{1}{16}\sum_{\beta=1}^{N}\sum_{\beta=1,\beta\neq\gamma}^{N}\frac{1}{\Gamma(\beta,\gamma)^3}\Big[\Big(e^{i(\phi_{0\beta}-\phi_{0\gamma})}+e^{-i(\phi_{0\beta}-\phi_{0\gamma})}\Big) \\ &\qquad +3\Big(e^{i(\phi_{0\beta}+\phi_{0\gamma}-2\phi_{\gamma\beta})}+e^{-i(\phi_{0\beta}+\phi_{0\gamma}-2\phi_{\gamma\beta})}\Big)\Big] \\ &= -\frac{1}{8}\sum_{\beta=1}^{N}\sum_{\beta=1,\beta\neq\gamma}^{N}\frac{1}{\Gamma(\beta,\gamma)^3}\Big[\cos(\phi_{0\beta}-\phi_{0\gamma})+3\cos(\phi_{0\beta}+\phi_{0\gamma}-2\phi_{\gamma\beta})\Big] \end{aligned} \tag{33}$$

One immediately recognizes from eq. (33) that the configuration enters the picture through the parameter $\Gamma(\beta,\gamma)$ and through the azimuthal angles $\phi_{\alpha\beta}$. Evaluating the corrections for the two regular polygons, $Q_{00}^{0,7}(\mathcal{C}_3)$ and $Q_{00}^{0,7}(\mathcal{C}_4)$, we find

$$\frac{Q_{00}^{0,7}(\mathcal{C}_3)}{N} = \frac{7}{24\sqrt{3}} \neq \frac{Q_{00}^{0,7}(\mathcal{C}_4)}{N} = \frac{3}{2\sqrt{2}} + \frac{1}{4}$$

This proves that for orders higher than six in ε, the perturbative expansion of the rate constant to the sink is no longer independent of the specific arrangement of reflecting obstacles.

V. COMPARING PERTURBATIVE EXPANSIONS OF THE RATE CONSTANT WITH THE EXACT VALUES

In Fig. 2 we plot the rate constant for a sink surrounded by competitive perfectly absorbing spheres, computed through eq. (23) (eq. (10) in the main text), as a function of the exact results, obtained by solving the linear system (6) in the main text. The purpose of these graphs is to show that the perturbative formula, even if it generally overestimates the exact results unless $N\varepsilon \propto N/d \ll 1$, nonetheless yields a result which is to an excellent extent *proportional* to it. Thus, eq. (23) provides an effective figure of merit to compare the effect of

different conformations, *e.g.* with the aim of *designing* configurations influencing the rate in some prescribed manner.

VI. SOFTWARE IMPLEMENTATION

The present calculations have been implemented in a computer code written in Fortran 77. The authors are planning to prepare a free version of the code to be distributed freely. The interested reader is invited to write to the corresponding author (`Francesco.Piazza@gmail.com`) for more information or to visit his group's homepage at `http://dirac.cnrs-orleans.fr/PB/`.

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[1] Morse, P. M. & Feshbach, H. *Methods of theoretical physics*, vol. 2 (McGraw-Hill Science/Engineering/Math, 1953).

[2] Traytak, S. D. The diffusive interaction in diffusion-limited reactions: the steady-state case. *Chemical Physics Letters* **197**, 247–254 (1992).