

## Single-particle survival in parallel gated trapping

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Any chemical reaction  $A^* + B \rightarrow C$  whose progress is modulated by another reaction of the form  $A^* \rightleftharpoons A$  is said to be gated. The gating reaction  $A^* \rightleftharpoons A$  represents a reversible fluctuation from a reactive state  $A^*$  to an unreactive state  $A$  not reacting with  $B$ . Reversibly blocked chemical reactions, conformational fluctuations in proteins, and reactions occurring within biomembranes or involving biological molecules have all been studied recently in contexts related to gating. This article calculates certain trapping rates and mean survival times in the presence of a single gated trap. Unlike previous methods, the formalism in this paper is based directly on trapping rates and not on Green's functions. The trapping rate formalism leads quite naturally to explicit solutions for some recently developed ("parallel") gating models, solutions that might be quite difficult to derive within a Green's-function formalism. These solutions give time-dependent rate coefficients for parallel gated chemical reactions. [S1063-651X(96)05512-2]

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### I. INTRODUCTION

Any chemical reaction  $A^* + B \rightarrow C$  whose progress is modulated by another reaction of the form  $A^* \rightleftharpoons A$  is said to be gated. The gating reaction  $A^* \rightleftharpoons A$  represents a reversible fluctuation from a reactive state  $A^*$  to an unreactive state  $A$  not reacting with  $B$ . In some situations, a fourth species  $D$  may be responsible for the interconversion  $A^* + D \rightleftharpoons A$ . When other effects due to the blocker  $D$  can be neglected, reversible chemical blocking is completely equivalent to gating.

Several recent articles have investigated gating [1,2], dynamic trapping [3,4], or other related problems [5]. Early studies of gating [6,7] derived the Smoluchowski mean-field rate constant [8–10] for a single ligand binding to a single gated protein. Gating has also been studied in other biological contexts, e.g., reactions occurring within biomembranes [4] or small molecules migrating through heme proteins [5]. Medical therapies can also involve blocking chemical reactions. Gating and blocking have practical implications, particularly as medical therapies, just by changing effective reaction rate constants [11].

Green's-function methods can solve some gating problems explicitly [3,4], e.g., the following "multiple Poisson gating" model for a ligand binding to a protein [2]. Assume a protein has  $J$  structural components, each of which fluctuates between two states, one active (+) and permissive for binding, the other blocked (-). The fluctuations  $(-)\frac{\alpha_j}{\beta_j}(+)$  for the  $j=1, \dots, J$  components are assumed to be independent Poisson processes with rate constants  $\alpha_j$  and  $\beta_j$ . In this model, the ligand can bind only when all the  $J$  protein components are active (+).

Perhaps not literally, but as a metaphor, the gates in this model are arranged "in series": all the gates  $(-)\frac{\alpha_j}{\beta_j}(+)$  in the series  $j=1, \dots, J$  must be open to permit passage (i.e.,

ligand binding). The series metaphor suggests the examination of contrasting "parallel" gating models, where just a single open gate  $(-)\frac{\alpha_j}{\beta_j}(+)$  suffices to permit passage. Because the Green's functions for parallel gating are quite complicated, they only furnish formal solutions [2]. On the other hand, because this article shows that the trapping rates for parallel gating have a simple form, it can exploit them to determine explicit mean survival times, trapping rates, and Smoluchowski rate constants [8–10] for a single particle moving in the presence of a single, parallel gated, static trap.

Throughout, gating is assumed independent of particle movement, which simplifies the analysis when particle movement and gating are combined into a single process. The states of this combined process [1–4,12,13] are ordered pairs indicating both the particle position and the gating state at time  $t$ . The concept of "failed first trapping opportunities" [11] then solves parallel gating problems by relating the gated and ungated trapping rates.

The plan of this article follows. Section II gives general results relating gated and ungated trapping. Section III then gives some parallel gating trapping rates, which are used to derive mean survival times, trapping rates, and rate constants for the corresponding parallel gating models. Section IV describes some further implications and elaborations of these results.

### II. GENERAL RESULTS FOR TRAPPING RATES

The two pivotal results in this section are an auxiliary result in Eq. (4), which relates the stationary density of particle movement and the reactivity of a single, ungated trap directly to the time-dependent Smoluchowski rate coefficient; and the main result in Eq. (7), which relates the gated and ungated trapping rates using the concept of failed first trapping opportunities.

Consider a single particle moving in some spatial continuum  $\Omega$  without any traps, e.g., a three-dimensional volume. If the particle movement is homogeneous in time, the Green's function  $G(\mathbf{x}, t | \mathbf{x}_0)$  is by definition the probability

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density that a particle initially at position  $\mathbf{x}_0$  will be at position  $\mathbf{x}$  at time  $t$  later.

Often, the particle movement has a stationary density  $\rho(\mathbf{x})$  that it leaves unchanged. Usually, the stationary density of physical interest is a ( $t \rightarrow \infty$ ) equilibrium density. By definition, any stationary density  $\rho$  satisfies  $\rho(\mathbf{x}) \equiv \int_{\Omega} G(\mathbf{x}, t | \mathbf{x}_0) \rho(\mathbf{x}_0) d\mathbf{x}_0$  at all times  $t$ . (This article uses  $\equiv$  to imply equality for all values of a variable. Here, e.g., the equation holds for all  $t \geq 0$ .)

When traps are present, let  $S(t | \mathbf{x}_0)$  be the probability that a particle initially at position  $\mathbf{x}_0$  remains untrapped at time  $t$  later. The character of the traps can remain unspecified for the time being: they may be single or multiple and they may be discrete or continuous (Refs. [2, 14] contain examples). By definition, the trapping rate  $\sigma(t | \mathbf{x}_0)$  satisfies  $\int_0^t \sigma(\tau | \mathbf{x}_0) d\tau = 1 - S(t | \mathbf{x}_0)$  ( $:=$  denotes a definition). In this article,  $\sigma(t | \mathbf{x}_0)$  is a convenient fundamental quantity;  $S(t | \mathbf{x}_0)$  can be derived from  $\sigma(t | \mathbf{x}_0)$  if necessary.

The time-dependent Smoluchowski rate coefficient

$$k(t) := \int_{\Omega} \sigma(t | \mathbf{x}_0) \rho(\mathbf{x}_0) d\mathbf{x}_0 \quad (1)$$

is the trapping rate starting from the distribution  $\rho$ . Since equations will generally be more useful to us after Laplace transformation

$$\hat{k}(s) = \int_{\Omega} \hat{\sigma}(s | \mathbf{x}_0) \rho(\mathbf{x}_0) d\mathbf{x}_0, \quad (2)$$

where the carets denote Laplace transforms, i.e.,  $\hat{f}(s) := \int_0^{\infty} e^{-st} f(t) dt$ .

In general, there are two cases: (i)  $\int_{\Omega} \rho(\mathbf{x}) d\mathbf{x} = \infty$  (typified by free Brownian motion in three dimensions) and (ii)  $0 < \int_{\Omega} \rho(\mathbf{x}) d\mathbf{x} < \infty$  (typified by Brownian motion in a finite volume with reflecting boundaries). The following assumes that  $\int_{\Omega} \rho(\mathbf{x}) d\mathbf{x} = \infty$  and defers the case  $0 < \int_{\Omega} \rho(\mathbf{x}) d\mathbf{x} < \infty$  to Sec. IV.

The asymptotic rate of trapping  $k_{\infty} := \lim_{t \rightarrow \infty} k(t)$ , if it exists, provides the Smoluchowski rate constant for mean-field approximations to chemical kinetics [8–10]. Standard theorems [15] show  $k_{\infty} = \lim_{t \rightarrow \infty} k(t) = \lim_{s \rightarrow 0} s \hat{k}(s)$ . Since many gating results are more easily phrased in terms of characteristic times  $k_{\infty}^{-1}$  than rates  $k_{\infty}$ , it is useful [2] to define

$$\hat{\lambda}(s) := [s \hat{k}(s)]^{-1} = \left\{ s \int_{\Omega} \hat{\sigma}(s | \mathbf{x}_0) \rho(\mathbf{x}_0) d\mathbf{x}_0 \right\}^{-1}, \quad (3)$$

so that  $k_{\infty}^{-1} = \hat{\lambda}(0)$ .

From now on, assume a single ungated point trap at position  $\mathbf{r} = \mathbf{a}$ . For clarity, equations that pertain only to single ungated point traps will be flagged as follows: the usual state variable  $\mathbf{x}$  will be replaced by  $\mathbf{r}$  and the state space  $\Omega$  will be replaced by (a volume)  $V$ . Single point traps are important because when symmetries reduce trapping problems on a continuum (e.g., three-dimensional Brownian motion in the presence of a partially absorbing sphere) to trapping problems on a line, trapping surfaces reduce to trapping points. Although the volume  $V$  is then reduced to a subset of a line, Sec. IV examines lattice applications, where  $V$  retains a di-

mension  $d > 1$ . The lattice applications justify the continued use of boldface vector notation below.

Define the reactivity  $\kappa$  of a point trap  $\mathbf{r} = \mathbf{a}$  to be the probability per unit time that a particle at  $\mathbf{r} = \mathbf{a}$  becomes trapped. Perfect absorption at  $\mathbf{r} = \mathbf{a}$  is included in the following analysis as a limiting case  $\kappa \rightarrow \infty$  of partial absorption.

Physical interpretation justifies the following identity for all times  $t$ :

$$\kappa \rho(\mathbf{a}) \equiv \int_V \sigma(t | \mathbf{r}_0) \rho(\mathbf{r}_0) d\mathbf{r}_0 + \kappa \rho(\mathbf{a}) \int_0^t \sigma(\tau | \mathbf{a}) d\tau. \quad (4)$$

Start from the stationary density  $\rho$ . When particles are trapped at  $\mathbf{r} = \mathbf{a}$ , replace them so that the density  $\rho(\mathbf{a})$  is maintained at  $\mathbf{r} = \mathbf{a}$ . Since there is effectively no trapping now, the stationary density  $\rho(\mathbf{r})$  is also maintained at every position  $\mathbf{r}$ . At any time  $t$ , the left-hand side of Eq. (4) is the rate at which particles are trapped and replaced to maintain the density  $\rho(\mathbf{a})$  at  $\mathbf{r} = \mathbf{a}$ . The right-hand side displays two contributions to this particle turnover: (i) particles that are being trapped and replaced for the first time [ $\int_V \sigma(t | \mathbf{r}_0) \rho(\mathbf{r}_0) d\mathbf{r}_0$ ] and (ii) particles that were trapped in the time interval  $(t - \tau, t - \tau + d\tau)$  and replaced [ $\kappa \rho(\mathbf{a}) d\tau$ ], and then trapped again at time  $t$  [ $\sigma(\tau | \mathbf{a})$ ].

Equation (4) transforms to

$$\int_V \hat{\sigma}(s | \mathbf{r}_0) \rho(\mathbf{r}_0) d\mathbf{r}_0 = \kappa \rho(\mathbf{a}) s^{-1} [1 - \hat{\sigma}(s | \mathbf{a})]. \quad (5)$$

Thus, for a single partially absorbing point trap  $\mathbf{r} = \mathbf{a}$ , Eqs. (3) and (5) show

$$s \hat{k}(s) = [\hat{\lambda}(s)]^{-1} = \kappa \rho(\mathbf{a}) [1 - \hat{\sigma}(s | \mathbf{a})]. \quad (6)$$

(Equation (6) can be derived without Eq. (4), using Eqs. (8) and (10) in Ref. [2], the equation  $\hat{S}(s | \mathbf{x}_0) = s^{-1} [1 - \hat{\sigma}(s | \mathbf{x}_0)]$ , and Eqs. (2) and (3) in this paper.)

We now superimpose gating on the point trap at  $\mathbf{r} = \mathbf{a}$ . The following gives the bare essentials of single-trap gating, since a more general discussion of multiple-trap gating is given elsewhere [2].

Briefly, a gated system has, in addition to the above particle-trap structure, a gating state  $\mathbf{q}$  that evolves in a gating state space  $\Omega_Q = \{\mathbf{q}_1, \mathbf{q}_2, \dots, \mathbf{q}_N\}$ , where  $N$  is finite. Above, the ungated trap at  $\mathbf{r} = \mathbf{a}$  traps with a constant reactivity  $\kappa$ , but with gating its reactivity  $\kappa$  depends on the gating state  $\mathbf{q}_i$ . Thus, when the gating state becomes  $\mathbf{q}_i$ , the reactivity at  $\mathbf{r} = \mathbf{a}$  becomes  $\kappa(\mathbf{q}_i)$ ,  $i = 1, 2, \dots, N$ . The ‘‘gated state’’  $\mathbf{x} = (\mathbf{q}, \mathbf{r})$  completely specifies the particle-trap system and is the ordered pair specifying both the gating state and particle position. The gated state  $\mathbf{x}$  evolves in a ‘‘gated state space’’  $\Omega = \Omega_Q \times V$ .

Note that the terms ‘‘gating state’’ and ‘‘gated state’’ are used to distinguish between  $\mathbf{q}$  and  $\mathbf{x} = (\mathbf{q}, \mathbf{r})$ . Note also that integrals  $\int_{\Omega} d\mathbf{x}$  over  $\Omega = \Omega_Q \times V$  are an implicit combination of a gating sum  $\sum_{\mathbf{q} \in \Omega_Q}$  and a continuum integral  $\int_V d\mathbf{r}$ .

We now restrict the discourse to parallel gating, as described in the Introduction. In parallel gating,  $\kappa(\mathbf{q}_i) \equiv \kappa$  for  $i = 1, \dots, N - 1$  and  $\kappa(\mathbf{q}_N) = 0$ . Thus a parallel gated trap has a constant reactivity  $\kappa$ , except for the gating state  $\mathbf{q}_N = (-)$ , corresponding to the unreactive state  $A$  of the Introduction.

Parallel gating can be solved by regarding the unreactive state  $\mathbf{q}_N=(-)$  as a perturbation on the ungated trap. Assume that  $\sigma(t|\mathbf{r}_0)$  would be the trapping rate if the reactivity at  $\mathbf{r}=\mathbf{a}$  were always the constant  $\kappa$ . The trapping rate  $\sigma(t|\mathbf{r}_0)$  corresponds to ‘‘first trapping opportunities’’ [11], which may fail occasionally because of the  $(-)$  gating state: with gating, not all trapping opportunities actually lead to trapping. Let  $\sigma_-(t|\mathbf{q}_0, \mathbf{r}_0)$  denote the rate at which first trapping opportunities fail [ $\sigma$  for trapping,  $-$  for failure because of the  $(-)$  gating state].

If a first trapping opportunity fails, the particle is at  $\mathbf{r}=\mathbf{a}$  and the trap is unreactive  $(-)$ . Thus the gated state is  $(-, \mathbf{a})$ . Assume that  $(-, \mathbf{a})$  is a regenerative state for the system, i.e., when the state  $(-, \mathbf{a})$  occurs, the system’s past and its future are independent. By conditioning on the first trapping opportunity, the actual gated trapping rate  $\sigma_g(t|\mathbf{q}_0, \mathbf{r}_0)$  can be divided into two contributions

$$\begin{aligned} \sigma_g(t|\mathbf{q}_0, \mathbf{r}_0) &= \sigma(t|\mathbf{r}_0) - \sigma_-(t|\mathbf{q}_0, \mathbf{r}_0) \\ &+ \int_0^t \sigma_-(\tau|\mathbf{q}_0, \mathbf{r}_0) \sigma_g(t-\tau|-, \mathbf{a}) d\tau. \end{aligned} \quad (7)$$

The first contribution [ $\sigma(t|\mathbf{r}_0) - \sigma_-(t|\mathbf{q}_0, \mathbf{r}_0)$ ] represents first trapping opportunities that succeeded; the second contribution (the integral) represents first trapping opportunities that failed, but where the particle was trapped later anyway. The transform of Eq. (7) is

$$\begin{aligned} \hat{\sigma}_g(s|\mathbf{q}_0, \mathbf{r}_0) &= \hat{\sigma}(s|\mathbf{r}_0) - \hat{\sigma}_-(s|\mathbf{q}_0, \mathbf{r}_0) \\ &+ \hat{\sigma}_-(s|\mathbf{q}_0, \mathbf{r}_0) \hat{\sigma}_g(s|-, \mathbf{a}). \end{aligned} \quad (8)$$

Substitute  $(\mathbf{q}_0, \mathbf{r}_0)=(-, \mathbf{a})$  into Eq. (8), solve for  $\hat{\sigma}_g(s|-, \mathbf{a})$ , and substitute back into Eq. (8) to get

$$\hat{\sigma}_g(s|\mathbf{q}_0, \mathbf{r}_0) = \hat{\sigma}(s|\mathbf{r}_0) - \hat{\sigma}_-(s|\mathbf{q}_0, \mathbf{r}_0) \frac{1 - \hat{\sigma}(s|\mathbf{a})}{1 - \hat{\sigma}_-(s|-, \mathbf{a})}. \quad (9)$$

To derive an equation for  $\hat{\lambda}_g(s)$  for the gated trap from Eq. (3), Eq. (9) must be multiplied by  $\rho(\mathbf{x}_0)=\rho(\mathbf{q}_0, \mathbf{r}_0)$ , summed with respect to  $\mathbf{q}_0$ , integrated with respect to  $\mathbf{r}_0$ , and multiplied by  $s$ , all this being followed by taking reciprocals. We now prepare some preliminary simplifications for the task.

If the density  $\rho(\mathbf{q}_0, \mathbf{r}_0)$  of gated states is stationary, so are the marginal probabilities  $\rho(\mathbf{q}_0):=\int_V \rho(\mathbf{q}_0, \mathbf{r}_0) d\mathbf{r}_0$  and marginal probability densities  $\rho(\mathbf{r}_0):=\sum_{\mathbf{q}_0 \in \Omega_Q} \rho(\mathbf{q}_0, \mathbf{r}_0)$ . Assume the independence of the gating state and particle position, so that  $\rho(\mathbf{q}_0, \mathbf{r}_0)=\rho(\mathbf{q}_0)\rho(\mathbf{r}_0)$ .

[As an aside, in the case  $\int_V \rho(\mathbf{r}) d\mathbf{r}=\infty$  the stationary density  $\rho$  is often normalized so that  $\rho(\mathbf{r}) \rightarrow 1$  at infinity. The independence condition  $\rho(\mathbf{q}, \mathbf{r})=\rho(\mathbf{q})\rho(\mathbf{r})$  conveniently distributes the density  $\rho(\mathbf{r})$  among the gating states  $\mathbf{q}$ , thereby retaining the usual normalization  $\sum_{\mathbf{q} \in \Omega_Q} \rho(\mathbf{q}, \mathbf{r})=\rho(\mathbf{r}) \rightarrow 1$  at infinity.]

Now, if the initial gating probability  $\rho(\mathbf{q}_0)$  is stationary, it is also stationary at the first trapping opportunity. Thus a fraction  $\rho(-)$  of first trapping opportunities fail. In mathematics, this says that for all initial particle positions  $\mathbf{r}_0$ ,

$$\sum_{\mathbf{q}_0 \in \Omega_Q} \hat{\sigma}_-(s|\mathbf{q}_0, \mathbf{r}_0) \rho(\mathbf{q}_0) = \rho(-) \hat{\sigma}(s|\mathbf{r}_0). \quad (10)$$

Multiply Eq. (9) by  $\rho(\mathbf{q}_0, \mathbf{r}_0)$  and integrate over  $\Omega=\Omega_Q \times V$  to get

$$\begin{aligned} &\int_{\Omega} \hat{\sigma}_g(s|\mathbf{q}_0, \mathbf{r}_0) \rho(\mathbf{q}_0, \mathbf{r}_0) d\mathbf{q}_0 d\mathbf{r}_0 \\ &= \int_V \hat{\sigma}(s|\mathbf{r}_0) \rho(\mathbf{r}_0) d\mathbf{r}_0 \\ &\times \left[ 1 - \rho(-) \frac{1 - \hat{\sigma}(s|\mathbf{a})}{1 - \hat{\sigma}_-(s|-, \mathbf{a})} \right], \end{aligned} \quad (11)$$

because  $\rho(\mathbf{q}_0, \mathbf{r}_0)=\rho(\mathbf{q}_0)\rho(\mathbf{r}_0)$  and  $\sum_{\mathbf{q}_0 \in \Omega_Q} \rho(\mathbf{q}_0)=1$ , and because of Eq. (10). Multiply by  $s$ , take reciprocals, and note Eqs. (5) and (6). The result, in a form most useful to present purposes, is

$$\hat{\lambda}_g(s) = \hat{\lambda}(s) + \left\{ \kappa \rho(\mathbf{a}) \frac{1 - \hat{\sigma}_-(s|-, \mathbf{a})}{\rho(-)} - [\hat{\lambda}(s)]^{-1} \right\}^{-1}. \quad (12)$$

To determine  $\hat{\sigma}_-(s|-, \mathbf{a})$  in Eq. (12), let  $Q(-, t|-, \mathbf{a})$  be the gating Green’s function, which gives the probability that a trap starting in the  $(-)$  state will be in the  $(-)$  state at time  $t$  later. Since particle movement and gating are independent, the rate at which failed first trapping opportunities occur for a particle presently at  $(-, \mathbf{a})$  is  $\sigma_-(t|-, \mathbf{a})=\sigma(t|\mathbf{a})Q(-, t|-, \mathbf{a})$ , since a failed first trapping opportunity means that the particle returned to  $\mathbf{r}=\mathbf{a}$  and would have been trapped, except that the gating state also returned to  $(-)$ . As a transformed equation, this gives

$$\hat{\sigma}_-(s|-, \mathbf{a}) = \int_0^{\infty} e^{-st} \sigma(s|\mathbf{a}) Q(-, t|-, \mathbf{a}) dt. \quad (13)$$

### III. SURVIVAL RESULTS FOR PARALLEL GATED TRAPPING

This section gives solutions for three specific models of parallel gating. The first model, Poisson gating, has been solved before [2,7], but, nevertheless, provides a simple prototype for parallel gating. Poisson gating provides a basis for solving the second model, double parallel Poisson gating, explicitly. This model is the special case  $J=2$  of the third model, multiple parallel Poisson gating, which is solved implicitly as a generalization of the  $J=2$  case.

#### A. Poisson gating

In Poisson gating, there are only two gating states, one reactive and the other unreactive. The reactive state  $\mathbf{q}_1=(+)$  permits trapping, whereas the unreactive state  $\mathbf{q}_2=(-)$  inhibits it completely. The interconversions  $(-) \xrightleftharpoons[\beta_0]{\alpha_0} (+)$  are Poisson processes with rate constants  $\alpha_0$  and  $\beta_0$ .

For Poisson gating [2], the probabilities  $\rho_{pg}(-)=\beta_0(\alpha_0+\beta_0)^{-1}$  and  $\rho_{pg}(+)=\alpha_0(\alpha_0+\beta_0)^{-1}$  are sta-

tionary, while the gating Green's function relevant to Eq. (13) is

$$Q_{pg}(-, t|-) = \rho_{pg}(-) + \rho_{pg}(+)e^{-(\alpha_0 + \beta_0)t}. \quad (14)$$

Equations (13) and (14) and the shift property of Laplace transforms  $\hat{f}(s + \alpha) = \int_0^\infty e^{-st} [e^{-\alpha t} f(t)] dt$  give

$$\hat{\sigma}_{pg-}(s|-, \mathbf{a}) = \rho_{pg}(-)\hat{\sigma}(s|\mathbf{a}) + \rho_{pg}(+)\hat{\sigma}(s + \alpha_0 + \beta_0|\mathbf{a}). \quad (15)$$

Recall Eq. (6), which gives  $\hat{\sigma}(s)$  in terms of  $\hat{\lambda}(s)$ . Since  $\rho_{pg}(-)/\rho_{pg}(+) = \beta_0/\alpha_0$ , Eq. (15) substituted in Eq. (12) yields

$$\hat{\lambda}_{pg}(s) = \hat{\lambda}(s) + \frac{\beta_0}{\alpha_0} \hat{\lambda}(s + \alpha_0 + \beta_0), \quad (16)$$

in agreement with previous results [2,7].

### B. Double parallel Poisson gating

In double parallel Poisson gating, two components (e.g., possibly the particle *and* the trap) undergo Poisson gating and trapping is unreactive only if both components are blocked (-). With subscripts 1 and 2 referring to the components, Eq. (14) and its notation are easily extended to give

$$Q_{dp}(-, t|-) = [\rho_1(-) + \rho_1(+)e^{-(\alpha_1 + \beta_1)t}] \times [\rho_2(-) + \rho_2(+)e^{-(\alpha_2 + \beta_2)t}]. \quad (17)$$

Equations (13) and (17) yield

$$\begin{aligned} \hat{\sigma}_{dp-}(s|-, \mathbf{a}) &= \rho_1(-)\rho_2(-)\hat{\sigma}(s|\mathbf{a}) + \rho_1(-)\rho_2(+) \\ &\times \hat{\sigma}(s + \alpha_2 + \beta_2|\mathbf{a}) + \rho_1(+)\rho_2(-) \\ &\times \hat{\sigma}(s + \alpha_1 + \beta_1|\mathbf{a}) + \rho_1(+)\rho_2(+) \\ &\times \hat{\sigma}(s + \alpha_1 + \beta_1 + \alpha_2 + \beta_2|\mathbf{a}). \end{aligned} \quad (18)$$

When substituted in Eq. (12), Eq. (18) gives

$$\begin{aligned} \hat{\lambda}_{dp}(s) &= \hat{\lambda}(s) + \left\{ \left[ \frac{\beta_1}{\alpha_1} \hat{\lambda}(s + \alpha_1 + \beta_1) \right]^{-1} \right. \\ &+ \left[ \frac{\beta_2}{\alpha_2} \hat{\lambda}(s + \alpha_2 + \beta_2) \right]^{-1} \\ &\left. + \left[ \frac{\beta_1\beta_2}{\alpha_1\alpha_2} \hat{\lambda}(s + \alpha_1 + \beta_1 + \alpha_2 + \beta_2) \right]^{-1} \right\}^{-1}, \end{aligned} \quad (19)$$

derived much like Eq. (16). Through Eq. (3), Eq. (19) implicitly relates the transformed rates  $\hat{k}_{dp}(s)$  and  $\hat{k}(s)$  for the double gated and ungated problems. Also, since the characteristic time  $k_{dp\infty}^{-1} = \hat{\lambda}_{dp}(0)$  and the ungated characteristic time  $k_\infty^{-1} = \hat{\lambda}(0)$ , setting  $s=0$  in Eq. (19) gives

$$\begin{aligned} k_{dp\infty}^{-1} &= k_\infty^{-1} + \left\{ \left[ \frac{\beta_1}{\alpha_1} \hat{\lambda}(\alpha_1 + \beta_1) \right]^{-1} + \left[ \frac{\beta_2}{\alpha_2} \hat{\lambda}(\alpha_2 + \beta_2) \right]^{-1} \right. \\ &\left. + \left[ \frac{\beta_1\beta_2}{\alpha_1\alpha_2} \hat{\lambda}(\alpha_1 + \beta_1 + \alpha_2 + \beta_2) \right]^{-1} \right\}^{-1}. \end{aligned} \quad (20)$$

### C. Multiple parallel Poisson gating

In multiple parallel Poisson gating, the unreactive state requires  $J$  Poisson components to be blocked (-):

$$Q_{mp}(-, t|-) = \prod_{j=1}^J [\rho_j(-) + \rho_j(+)e^{-(\alpha_j + \beta_j)t}]. \quad (21)$$

Just as in Poisson gating or double parallel Poisson gating, Eq. (13) permits  $\hat{\sigma}_{mp-}(s|-, \mathbf{a})$  to be written down explicitly from Eq. (21).

Equation (19) generalizes to

$$\begin{aligned} \hat{\lambda}_{mp}(s) &= \hat{\lambda}(s) + \left\{ \sum_{j=1}^J \left[ \frac{\beta_j}{\alpha_j} \hat{\lambda}(s + \alpha_j + \beta_j) \right]^{-1} \right. \\ &+ \sum_{\substack{j,k=1 \\ j \neq k}}^J \left[ \frac{\beta_j\beta_k}{\alpha_j\alpha_k} \hat{\lambda}(s + \alpha_j + \beta_j + \alpha_k + \beta_k) \right]^{-1} + \dots \\ &\left. + \left[ \left( \prod_{j=1}^J \frac{\beta_j}{\alpha_j} \right) \hat{\lambda} \left( s + \sum_{j=1}^J (\alpha_j + \beta_j) \right) \right]^{-1} \right\}^{-1}. \end{aligned} \quad (22)$$

By analogy with Eq. (19), Eq. (22) implicitly determines the transformed rate  $\hat{k}_{mp}(s)$  and characteristic time  $k_{mp\infty}^{-1} = \hat{\lambda}_{mp}(0)$  for multiple parallel Poisson gating.

## IV. DISCUSSION

This article has provided a trapping rate formalism for solving problems with a single moving particle in the presence of a single, parallel gated, static trap when gating is independent of the particle movement. The solution for the multiple parallel Poisson gating model Eq. (22) can be represented schematically as  $\hat{\lambda}_{mp} = \hat{\lambda} + \{\Sigma[(\beta/\alpha)\hat{\lambda}]^{-1}\}^{-1}$ . As a contrast, the Introduction described the multiple *serial* Poisson gating model, which has the schematic solution  $\hat{\lambda}_{mg} = \hat{\lambda} + \{\Sigma(\beta/\alpha)\hat{\lambda}\}$  [see [2], Eq. (34)]. The solutions for multiple serial and parallel Poisson gating bear an imperfect but striking resemblance to serial and parallel electrical resistances:  $R = \Sigma R_i$  and  $\{\Sigma R_i^{-1}\}^{-1}$ . Thus our gating nomenclature is apt, since it suggests both the modeling metaphors and the solution forms.

The trapping rate formalism developed here, like Green's function formalisms [2-4], can be extended to lattice problems if continuum integrals  $\int_\Omega d\mathbf{x}$  are replaced by lattice sums  $\Sigma_{\mathbf{x} \in \Omega}$ . Also, Sec. III of Ref. [2] shows how to use  $\hat{\lambda}(s)$  in its Eq. (20) to relate gated and ungated mean survival times in the case  $0 < \int_\Omega \rho(\mathbf{x}) d\mathbf{x} < \infty$ .

Zhou and Szabo [1] have extended Smoluchowski theory to include gating effects for a single trap surrounded by multiple particles. In their theory, a gated trap gives different results from independently gated particles. Their solutions all require  $k(t)$  in Eq. (1) from the corresponding gated single-particle, single-trap problem, however. The formalisms in this paper and Ref. [2] are therefore particularly well adapted to the Zhou-Szabo theory because they relate  $\hat{k}(s) = [s\hat{\lambda}(s)]^{-1}$  for the gated and ungated problems.

This article clarifies some points in gating theory by emphasizing trapping rates instead of Green's functions [2–4]. For example, Eq. (7) requires that the system regenerate only when the particle is at a trap. Regeneration at other positions (e.g., as in a fully Markovian particle movement) is un-

necessary. The physical interpretation of Eq. (7) also naturally emphasized trapping opportunities, a concept already found useful for analyzing the blocking of viral attachment [11]. These observations may further simplify the theories of blocking and gating.

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