## Universal Geometric Theory of Mesoscopic Stochastic Pumps and Reversible Ratchets

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We construct a unifying theory of geometric effects in mesoscopic stochastic kinetics. We demonstrate that the adiabatic pump and the reversible ratchet effects, as well as similar new phenomena in other domains, such as in epidemiology, all follow from very similar geometric phase contributions to the effective action in the stochastic path integral representation of the moment generating function. The theory provides the universal technique for identification, prediction, and calculation of pumplike phenomena in an arbitrary mesoscopic stochastic framework.

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Introduction. —A number of effects in classical statistical physics, such as the reversible ratchet [1-3] and the adiabatic pump [4,5], are known (or anticipated) to have a geometric origin. The distinct feature of these effects is that, under a slow perturbation, transport coefficients are not a simple average of those in the strict static case, but contain an extra component, which changes its sign under a time-reversal of the perturbation. Examples and applications can be found in various fields, such as metrology, motility at low Reynolds numbers, ion pumping through cell membrane, and dissipative chemical kinetics [6]. Although these effects have been well studied in their respective fields (cf. [7]), in our opinion, a general theory for stochastic kinetics that would clearly disambiguate the pump (or ratchet) currents from other nonequilibrium transport, provide a unified view of disparate pumplike phenomena, and suggests universal quantitative methods to calculate statistics of pump fluxes is still missing.

In this Letter, we address this problem using a recently introduced stochastic path integral representation of the moment generating functional (MGF) for fluxes in mesoscopic stochastic systems [8,9]. We demonstrate that the technique can be employed to calculate the moments of pump fluxes in a general stochastic system in a mesoscopic (many particles) and adiabatic (slowly varying external driving) regimes, and that it makes a clear distinction between the pump fluxes and other currents by relating the former to a geometric phase contribution to the flux MGF. To demonstrate the universality of the effect we derive the geometric phase in three distinct applications.

Pump current from particle exclusion.—Let two absorbing states *S* and *P* (substrate and product in a Michaelis-Menten enzymatic reaction [5], cellular compartments, cities), exchange particles (molecules, humans) via an intermediate system *B* (bin, enzyme, channel, transportation hub). Our goal is to find the  $S \rightarrow P$  flux *J* and its fluctuations in the mesoscopic regime (the number of particles in the bin  $N \gg 1$ ) and on time scales much longer than the fluctuation time in *B*.

Particles interact, and the in- and outgoing transition rates may depend on the number of particles in the bin, N(t). The simplest example of this kind is when the bin has a finite size, so that  $N \le N_B = \text{const} < \infty$ . Then the inrates are proportional to the number of empty spaces in the bin, while the per particle outrates are not affected by the occupancy. The full kinetic scheme is

(i)  $S \rightarrow B$ ; rate  $k_1(N, t) = q_1(t)(N_B - N)$ ;

- (ii)  $B \rightarrow S$ ; rate  $k_{-1}(N) = q_{-1}N$ ;
- (iii)  $P \rightarrow B$ ; rate  $k_{-2}(N, t) = q_{-2}(t)(N_B N)$ ;
- (iv)  $B \rightarrow P$ ; rate  $k_2(N) = q_2 N$ .

We allow  $q_1$  and  $q_{-2}$  to undergo a slow periodic modulation with a frequency  $\omega$ , which can be achieved in the biochemical context by coupling *S* and *P* to particle baths with modulated chemical potentials. In other transport problems, such as transportation systems, the same modulation may be produced by time-of-day variations. We note that, unlike in [8], our formulation has three time scales: fast instantaneous jumps among states, equilibration of the bin, and adiabatic changes of the rates.

Now the path integral technique of [8] can be applied. Since  $N \gg 1$ , there exists a time scale  $\delta t$ , over which many transitions into and out of *B* happen, but the fractional change in the bin occupancy remains small,  $1 \ll \delta N \ll$ *N*. Then the rate changes  $\delta k_i$ , i = -2, -1, 1, 2 are also small, and all transitions are uncorrelated and Poissonian. Thus the probability of the number of particle transitions for the *i*th reaction over time  $\delta t$ , denoted by  $\delta Q_i$ , is  $P(\delta Q_i, t) = \frac{1}{2\pi} \int_{-\pi}^{\pi} d\chi_i e^{-i\chi_i \delta Q_i + N_B H_i(\chi_i, t) \delta t}$ , where  $N_B H_i \delta t = k_i(N, t) [\exp(i\chi_i) - 1] \delta t \equiv k_i(N, t) e_{\chi_i} \delta t$  is the MGF of a Poisson distribution with the mean  $k_i \delta t$ . Note that we define  $e_x \equiv e^{ix} - 1$  for any *x*.

Now we turn to the MGF of the net particle number  $Q_P$  transferred into P over a long time interval (0, T). Closely following [8], we write it as an integral over fluxes at each moment of (discretized) time weighted by  $\prod_i P(\delta Q_i, t)$  and constrained by particle conservation laws

$$\langle e^{i\chi_{c}\mathcal{Q}_{P}} \rangle = \int \prod_{k=1}^{T/\delta t} dN(t_{k}) \prod_{i=\pm 2,\pm 1} d\delta \mathcal{Q}_{i}(t_{k}) P[\delta \mathcal{Q}_{i}(t_{k})]$$

$$\times e^{i\chi_{c}(\delta \mathcal{Q}_{2}(t_{k}) - \delta \mathcal{Q}_{-2}(t_{k}))} \delta[N(t_{k+1}) - N(t_{k})$$

$$- \delta \mathcal{Q}_{1}(t_{k}) - \delta \mathcal{Q}_{-2}(t_{k}) + \delta \mathcal{Q}_{-1}(t_{k}) + \delta \mathcal{Q}_{2}(t_{k})].$$
(1)

Here we used the identity  $Q_P = \sum_{k=1}^{T/\delta t} [\delta Q_2(t_k) - \delta Q_{-2}(t_k)]$ , and we introduced a variable  $\chi_C$ , which is conjugated to  $Q_P$  and "counts" particle transfers into or out of *P*. Now, using the Fourier representation of the  $\delta$ -function, we integrate over  $\delta Q_i(t_k)$  and  $\chi_i(t_k)$  and reduce (1) to a path integral over *N* and its conjugated  $\chi$ 

$$\langle e^{i\chi_C Q_P} \rangle = \int DN(t) D\chi(t) e^{\int_0^T dt (i\chi \dot{N} + N_B H(\chi, N, t))}, \qquad (2)$$

where all prefactors are absorbed into the measure, and

$$H(\chi, N, t) = [q_1(t)e_{-\chi} + q_{-2}(t)e_{-(\chi + \chi_C)}](1 - N/N_B) + [q_{-1}e_{\chi} + q_2e_{(\chi + \chi_C)}]N/N_B.$$
(3)

Equations (2) and (3) are a special case of the result in [8], and the explicit time dependence of *H* is due to the slow periodic changes in  $q_1(t)$  and  $q_{-2}(t)$ .

The exponent in (2) has a factor of  $N_B$  in it. Thus for  $N_B \rightarrow \infty$ , the path integral is dominated by the *saddle point* or *classical* values  $\chi_{cl}$  and  $N_{cl}$ ,

$$i\dot{\chi}_{\rm cl} = \frac{\partial H(\chi_{\rm cl}, N_{\rm cl}, t)}{\partial N_{\rm cl}}, \quad i\dot{N}_{\rm cl} = -\frac{\partial H(\chi_{\rm cl}, N_{\rm cl}, t)}{\partial \chi_{\rm cl}}.$$
 (4)

Since the Hamiltonian (3) is linear in N there are no higher order in 1/N corrections.

Assuming adiabatic and periodic variation of  $q_1$  and  $q_{-2}$ and setting the derivatives in (4) to zero, we get

$$e^{-i\chi_{\rm cl}} \approx \frac{K_- + K}{2(q_1 + q_{-2}e^{-i\chi_c})},$$
 (5)

$$N_{\rm cl} \approx \frac{N_B(q_1 + q_{-2}e^{-i\chi_C})}{q_1 + q_{-2}e^{-i\chi_C} + (q_{-1} + q_2e^{i\chi_C})e^{2i\chi_{\rm cl}}}, \quad (6)$$

where  $\approx$  denotes the accuracy of  $O(\omega/q_i)$ ,  $K_{\pm} \equiv q_1 + q_{-2} \pm (q_{-1} + q_2)$ , and  $K \equiv (K_+^2 + 4q_1q_2e_{\chi_c} + 4q_{-1}q_{-2}e_{-\chi_c})^{1/2}$ . Since the Hamiltonian is quadratic in its arguments near the saddle point, corrections of the order  $O(\omega/q_i)$  in (5) and (6) lead to  $O[(\omega/q_i)^2]$  contributions to the MGF, setting the accuracy of our results. We have

$$\langle e^{i\chi_{c}Q_{P}}\rangle \approx e^{N_{B}\left[\int_{c}\mathbf{A}\cdot d\mathbf{q} + \int_{0}^{T}H(\chi_{cl},N_{cl},t)dt\right]},$$
(7)

where the vector  $\mathbf{A}$ ,  $A_i = i\chi_{cl}(\partial_{q_i}N_{cl})/N_B$ , is defined in the space of parameters  $q_i$ , and the contour  $\mathbf{c}$  is given by  $q_i(t)$ . It generates a path-dependent phase, which makes the crucial difference from the steady state contribution and is the main object of our discussion in this work. For the periodic driving, as we consider here, with a period  $T_0 = 2\pi/\omega$  and with fixed  $q_{-1}$  and  $q_2$ , we rewrite the contour integral as the integral of  $F_{q_1,q_{-2}} = \partial_{q_1}A_{-2} - \partial_{q_{-2}}A_1$  over the surface  $\mathbf{S}_{\mathbf{c}}$  enclosed by  $\mathbf{c}$ . Then

$$Z \equiv \langle e^{i\chi_C Q_P} \rangle \approx e^{N_B S_{\text{geom}} + N_B S_{\text{cl}}},\tag{8}$$

$$S_{\text{geom}} = \frac{T}{T_0} \oint_{\mathbf{c}} \mathbf{A} \cdot d\mathbf{q} = \frac{T}{T_0} \int_{\mathbf{S}_{\mathbf{c}}} dq_1 dq_{-2} F_{q_1, q_{-2}}(\mathbf{q}), \quad (9)$$

$$F_{q_1,q_{-2}}(\mathbf{q}) = -e_{-\chi_C}(e^{i\chi_C}q_2 + q_{-1})K^{-3}, \qquad (10)$$

$$S_{\rm cl} = \frac{-T}{2T_0} \int_0^{T_0} dt (K_+ - K). \tag{11}$$

The two-form  $F_{q_1,q_{-2}}(\mathbf{q})$  is an analog of the Berry curvature in quantum mechanics. Nonzero Berry curvature, as follows from (9), is responsible for the reversible component in the particle fluxes. Its presence in our model is due to particle exclusion within the central bin. If  $k_1$  and  $k_{-2}$  were independent of N,  $F_{q_1,q_{-2}}$  would be zero.

Now all cumulants of the flux into the *P* absorbing state can be derived easily by differentiating (8) with respect to  $\chi_C$ . In particular, the average flux is

$$J = J_{\text{pump}} + J_{\text{cl}}$$
  
=  $N_B \bigg[ \iint_{S_C} dq_1 dq_{-2} \frac{q_2 + q_{-1}}{T_0 K_+^3} + \int_0^{T_0} dt \frac{q_1 q_2 - q_{-1} q_{-2}}{K_+ T_0} \bigg],$   
(12)

where the pump term is due to the particle interactions and the corresponding geometric contribution, while the classical flux would exist even in the stationary limit. Notice that J is  $N_B$  times its value for a single driven Michaelis-Menten enzyme [5]. The same holds for the entire MGF, and hence for all flux moments. Thus we refer the reader to [5] for further analysis of the model. Here we note that this scaling is not a coincidence since the current model is equivalent to  $N_B$  independent enzymes, with N being the number of enzyme-substrate complexes.

In [5], we used an analogy with the quantum mechanical Berry phase to derive the pump flux (12). While formally applicable to any stochastic system, this approach requires diagonalization of an effective evolution Hamiltonian, which is a complicated task for mesoscopic systems. In contrast, the classical mesoscopic stochastic treatment used now is simpler and more generally applicable, as we show below. Existence of these alternative approaches is not surprising because any discrete quantum mechanical system can be mapped onto a mathematically equivalent classical Hamiltonian system [10], and then the Berry phase transforms into a dynamic contribution to the classical action [11]. Thus the present derivation shows that one can derive the classical Hamiltonian for a discrete Markov chain by considering many identical independent copies of the system.

The reversible ratchet effect.—Now we show that the geometric contribution to MGF is responsible also for the ratchet effect in a periodic potential. Consider a system of noninteracting particles moving in a periodic potential V(x, t), which changes adiabatically with time so that  $V(x, t) = V(x, t + T_0)$  and V(x, t) = V(x + L, t). In the overdamped case, the average density of particles  $\rho$  satisfies the Fokker-Plank equation

$$\partial_t \rho(x,t) = -\partial_x [A(x,t)\rho(x,t)] + D\partial_x^2 \rho(x,t), \quad (13)$$

where *D* is the diffusion coefficient, and  $A(x, t) = -\partial_x V(x, t)$  is the force. The current in this model under an adiabatic deformation of the potential was previously studied in [2], and the similarity of the final expression and the quantum Berry phase was pointed out. The close connection between the classical ratchets and the Berry phase also has been anticipated in [1,3]. In our following rederivation, we explicitly show that the ratchet current has its origins in the geometric phase, emerging from the complex geometric phase of the particle flux MGF.

To study diffusion without the external field, A(x, t) = 0, Refs. [9] derived the path integral for the MGF by discretizing the space into small intervals of length  $a \ll L$ , indexed by *i*. Then Poisson transition rates among the neighboring intervals are prescribed in a way that the continuous limit  $a \rightarrow 0$  recovers the diffusion equation. This reduces the path integral derivation to a solved problem of stochastic transitions among a discrete set of states. To include the force A(x, t), we assume that it creates an asymmetry in the left and right transition rates. For example, (13) can be recovered if the transition rates are such that during a short time  $\delta t$  the average numbers of particles transferred left and right are  $\langle \delta Q_{i \rightarrow i-1} \rangle = D \rho_i \delta t / a$  and  $\langle \delta Q_{i \to i+1} \rangle = D \rho_i \delta t / a + A(x_i) \rho_i \delta t$ , respectively. We then repeat the same steps as in [9] to write the MGF of the current in discrete time, as in (1):

$$Z(\chi_{C}) = \langle e^{i\chi_{C}Q_{C}} \rangle$$

$$= \prod_{K=1}^{T/\delta t} \prod_{i=1}^{N} \int d\rho_{i}(t_{k}) d(\delta Q_{i \to i+1}) d(\delta Q_{i \to i-1})$$

$$\times P[\delta Q_{i \to i+1}(t_{k})] P[\delta Q_{i \to i-1}(t_{k})]$$

$$\times \delta[\text{conservation}] e^{i\chi_{C}(\delta Q_{N \to 1}(t_{k}) - \delta Q_{1 \to N}(t_{k}))}. \quad (14)$$

Here the net flux through the system is  $Q_C = \sum_k (\delta Q_{N \to 1}(t_k) - \delta Q_{1 \to N}(t_k))$ ,  $\chi_C$  is its conjugate,  $P[\cdot]$  are Poisson distributions, and  $\delta$ -functions enforce particle conservation on each site and at each moment of time. Performing the usual transitions to and from Fourier representations and taking a continuum limit, we find [12]:

$$Z = \int D\rho(x, t) D\chi(x, t) e^{\int_0^{T_0} dt \int_0^L dx [i\chi\dot{\rho} + H(\rho, \chi)]}, \quad (15)$$

$$H(\rho,\chi) = -iA\rho\partial_x\chi + iD\partial_x\rho\partial_x\chi - D\rho(\partial_x\chi)^2.$$
 (16)

The dependence on the counting field  $\chi_C$  in (16) is hidden in the boundary conditions on  $\chi$  [8], which, for a periodic system with the spatial period *L*, are  $\rho(L) = \rho(0)$ , and  $\chi(L) = \chi(0) - \chi_C$ . Now, solving the saddle point equations and substituting the result back into the action in the path integral, we write the MGF in a familiar form  $Z(\chi_C) = \exp[S_{\text{geom}}(\chi_C) + S_{\text{cl}}(\chi_C)]$ , where  $S_{\text{geom}}(\chi_C) = \int_0^{T_0} dt \int_0^L dx(i\chi_{\text{cl}}\dot{\rho}_{\text{cl}})$ , and  $S_{\text{cl}}(\chi_C) = \int_0^{T_0} dt \int_0^L dxH(\rho_{\text{cl}}(\chi_C), \chi_{\text{cl}}(\chi_C))$ .

The analysis simplifies if we are interested only in mean currents, rather than in their fluctuations. Then we consider  $\chi_C \ll 1$  and find the contribution to  $\log Z$ that is linear in it. In fact, only  $S_{geom}$  has this contribution in our case. To determine it, it is sufficient to find  $\rho_{cl}(x, t)$ to the zeroth order and  $\chi_{cl}(x, t)$  to the first order in  $\chi_C$ . This results in  $\rho_{cl}(x, t) \approx [Q_0/R_-(L, t)]e^{-V(x,t)/k_BT}$ ,  $\chi_{cl}(x, t) \approx -\chi_C R_+(x, t)/R_+(L, t)$ , where  $R_{\pm}(x, t) = \int_0^x e^{\pm V(x',t)/k_BT} dx'$ , and  $Q_0 = \int_0^L \rho_{cl}(x, t)|_{\chi_C=0} dx$  is the number of particles per unit cell. This leads to  $Z(\chi_C, T_0) =$  $\exp[i\chi_C JT_0 + O(\chi_C^2)]$ , where the terms in  $O(\chi_C^2)$  can reveal the higher order cumulants, and the average current  $J = -(i/T_0)(\partial_{\chi_C} \log Z)_{\chi_C=0}$  is

$$J = \frac{Q_0}{T_0} \int_0^{T_0} dt \int_0^L dx (\partial_t u_+ \partial_x u_-),$$
(17)

where we introduced  $u_{\pm}(x, t) = R_{\pm}(x, t)/R_{\pm}(L, t)$ .

For a uniformly shifting potential  $V(x, t) = V(x - tL/T_0)$ ,  $R_{\pm}(L, t)$  are time-independent, and  $J = Q_0/T_0 - (Q_0/T_0)L^2/[R_+(L)R_-(L)]$ . The first term in this expression is the quantized contribution, dominant in the limit of a large potential amplitude. In [3], this quantization of the classical ratchet current was connected to the Chern number of the Bloch band for the potential V(x). This reversible ratchet example points to the importance of the geometric phase to the general theory of molecular motors.

Pump current in the SIS epidemiological model.—In a final calculation, we show how the stochastic path integral allows derivation of a pumplike effect in novel mesoscopic scenarios, specifically where, unlike in our first example, the system cannot be factored into noninteracting identical stochastic subsystems, and where the technique of [5] is not feasible. We consider the standard susceptible-infected-susceptible (SIS) mechanism of an infection outbreak, which is a good model for influenza. State of the art epidemiological modeling uses deterministic dynamics [13]. However, it is understood that stochasticity may be essential. Thus here we discuss if stochasticity, and especially effects due to slow variability of the infectivity and the recovery rates, can effect disease outbreaks.

Let us denote infected individuals by I and their number by N. The disease spreads due to a permanent infection source and because it can be transmitted by the infected individuals. All infected people eventually recover. Thus the full kinetic scheme is

(i)  $\emptyset \rightarrow I$ ; rate  $k_1$  (permanent infection source);

(ii)  $I \rightarrow \emptyset$ ; rate per infected individual  $k_2$  (recovery);

(iii)  $I \rightarrow I + I$ ; rate per infected individual  $k_3$  (infection spread by contacts).

We assumed that outbreaks are small in comparison to the total population size, so that  $k_1$  and  $k_3$  are independent of N and most of the population is always in the susceptible state (still  $N \gg 1$ ). This requires  $k_2 > k_3$ , so that, if stochasticity is unimportant, the deterministic steady state solution is  $N_{st} = k_1/(k_2 - k_3)$ , and the stationary flux into and out of the infected state is  $J_{st} = k_2 N_{st} = k_1 k_2 / K_-$ , where now  $K_- = k_2 - k_3$ .

This and similar birth-death processes with timeindependent rates have been extensively studied previously, and here we are interested in estimating (possibly substantial) effects of rate time-dependence. The Hamiltonian in the path integral for this model is

$$H(\chi, N, t) = k_1(t)e_{-\chi} + k_2 N e_{(\chi + \chi_C)} + k_3(t) N e_{-\chi}, \quad (18)$$

where  $\chi$  is the conjugated variable to *N*, and  $\chi_C$  counts the flux out of *I*. For simplicity, we assume that only  $k_1$  and  $k_3$  vary, and the recovery rate  $k_2$  remains constant. With  $N \gg 1$ , we can use the saddle point analysis, which is exact since *H* is linear in *N*.

Now consider a periodic time dependence of the rates  $k_i$ , which may be due to the time-of-day or seasonal effects. As before, the MGF has both the classical and the geometric terms, i.e.,  $Z = \exp(S_{cl} + S_{geom})$ . The classical one is the average of the stationary MGF over the period of the rates variation,  $T_0$ , while the geometric one is again an integral over the surface  $S_c$  inside the contour enclosed by  $k_i(t)$ :

$$S_{\rm cl} + S_{\rm geom} = \frac{T}{T_0} \int_0^{T_0} dt H[\chi_{\rm cl}(t), N_{\rm cl}(t), t] + \frac{T}{T_0} \iint_{\mathbf{S}_{\rm c}} dk_1 dk_3 F_{k_1, k_3}(\mathbf{k}), \qquad (19)$$

$$F_{k_1,k_3}(\mathbf{k}) = \frac{k_2(K_- - 2k_3e_{\chi_C} - \kappa)}{2k_3^2\kappa^2},$$
 (20)

$$H(\chi_{\rm cl}, N_{\rm cl}, t) = \frac{k_1(K_- - \kappa)}{2k_3},$$
 (21)

where  $\kappa = \sqrt{K_-^2 - 4k_2k_3e_{\chi_c}}$ . This corresponds to the mean flux  $J = J_{\text{pump}} + J_{\text{cl}}$ , where  $J_{\text{pump}} = 1/T_0 \iint_{S_c} dk_1 dk_3 k_2 K^{-3}$  is the pump current due to the geometric contribution, and the classical flux is  $J_{\text{cl}} = 1/T_0 \int_0^T J_{\text{st}} dt$ . Notice, in particular, that  $J_{\text{pump}} \propto K_-^{-3}$ , and it can become very large near  $K_- = 0$ , potentially changing the system's phase diagram. Fluctuations are also easy to compute by further differentiating (19).

*Conclusion.*—Using the stochastic path integral technique, we built a universal theory of geometric fluxes in mesoscopic classical stochastic kinetics, and we proposed a general approach for identification and calculation of pumplike currents for such systems, unifying familiar stochastic pumps, reversible ratchets, and new phenomena. In the adiabatic limit, the MGF of pump fluxes is provided by the term that depends on the choice of the contour in the parameter space, but does not depend on the rate of the motion along this contour, and thus has a geometric origin. The solution of the stationary saddle point equations is sufficient for calculations of this geometric contribution in the case of a large number of particles; this description is complementary to the Berry phase approach in [5]. These results will provide means to study such poorly understood systems as ratchets with interacting diffusing particles, or time-dependent epidemiological models on complex social networks. Analysis in terms of stochastic path integrals and geometric effects is possible for these and other systems and will be reported elsewhere. Importantly, since the approach provides a unifying geometric viewpoint, it will open doors to a deeper understanding and crossfertilization among different subfields of physics.

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