The Berry Phase and the Pump Flux in Stochastic Chemical Kinetics

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Review

Presentation compiled on November 20, 2025

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Nice videos

Rachets A stochastic ratchet harnesses random thermal fluctuations and spatial or temporal asymmetry to produce directed motion without violating the second law of thermodynamics.

https://www.youtube.com/watch?v=DTvA_JuNEPE

Enzymes and Single molecular reaction

https://www.youtube.com/watch?v=N1J9P-mqcK4

Introduction: Motivation and Context

- Resurgence of interest in stochastic kinetics due to single-molecule experiments [1].
- Classical Michaelis-Menten (MM) kinetics are stochastic in reality.
- Focus on **"Stochastic Ratchets"** or **"Pump Effects"**:
  - A system with a periodic, zero-mean perturbation (e.g., oscillating concentrations) responds with a finite, directional flux [11-15].
- This phenomenon is well-known in *quantum* pumps, where it has a geometric **Berry Phase** interpretation [27-30].

The Central Question

Can a similar Berry Phase theory be constructed for **purely classical, stochastic Markov chains** (like an enzyme) to explain this pump flux?

Berry Phase: Basic Idea

Setup: A quantum system with Hamiltonian $\hat{H}(\mathbf{k})$, where $\mathbf{k} = \mathbf{k}(t)$ is a set of slowly varying control parameters.

Adiabatic theorem: If $\mathbf{k}(t)$ changes slowly, the system remains in the instantaneous eigenstate $\hat{H}(\mathbf{k}(t))\,|u(t)\rangle = E(t)\,|u(t)\rangle$.

If the parameters trace a closed loop in parameter space after time T, the physical state returns to itself up to a phase:

$$\phi = \phi_{\text{dyn}} + \phi_B.$$

Dynamical phase:

$$\phi_{\text{dyn}} = -\int_0^T E(t)\,dt.$$

Geometric (Berry) phase: A phase depending only on the *path* in parameter space.

Berry Phase: Geometry

The geometric phase acquired under a cyclic adiabatic evolution is:

$$\phi_B = i \oint_C \langle u(\mathbf{k}) \mid \nabla_{\mathbf{k}} u(\mathbf{k}) \rangle \cdot d\mathbf{k}.$$

Define the **Berry connection**:

$$\mathbf{A}(\mathbf{k}) = i \langle u(\mathbf{k}) \mid \nabla_{\mathbf{k}} u(\mathbf{k}) \rangle.$$

Then,

$$\phi_B = \oint_C \mathbf{A} \cdot d\mathbf{k}.$$

Key properties:

- Purely geometric — depends only on the closed path C.
- Independent of the rate of traversal (adiabatically).

The Model System (Fig. 1)

- A minimal model of a single Michaelis-Menten enzyme or a cell membrane channel.
- **L (Left):** Substrate (Absorbing State)
- **R (Right):** Product (Absorbing State)
- **"Bin":** The enzyme, which can be:
  - Empty (Unbound, P_e)
  - Filled (Bound, P_f)
- All transitions are stochastic.(Involves some rate/probability)

Figure: Fig. 1: Transition rates into and out of the absorbing states L (substrate) and R (product).

The Goal

Understand the $L \to R$ current (J) when rates (e.g., k_1, k_{-2}) are varied **periodically** and **slowly** (adiabatically).

Master Equation

System States

The evolution is described by two probabilities, P_{nE} and P_{nSE}:

- $\mathbf{P_{nE}}$: Probability of the system being in the **free enzyme** (E) state, having produced n product molecules.
- $\mathbf{P_{nSE}}$: Probability of the system being in the **bound (substrate-enzyme, SE)** state, having produced n product molecules.

The time evolution is given by the Master Equations (Eq. 30):

$$\frac{d}{dt}P_{nE} = -(k_1 + k_{-2})P_{nE} + k_{-1}P_{nSE} + k_2 P_{(n+1)SE}$$

$$\frac{d}{dt}P_{nSE} = -(k_{-1} + k_2)P_{nSE} + k_1 P_{nE} + k_{-2}P_{(n-1)E}$$

Derivations 2: The Full Counting Statistics (FCS)

Goal

Find the statistics of the net flux (total number of products n) over time T using the Probability Generating Function (PGF).

We introduce the Generating Functions $\mathbf{U}(\chi, t) = [U_E(\chi, t), U_{SE}(\chi, t)]^T$:

$$U_E(\chi, t) = \sum_{n=-\infty}^{\infty} P_{nE}(t) e^{in\chi}, \quad U_{SE}(\chi, t) = \sum_{n=-\infty}^{\infty} P_{nSE}(t) e^{in\chi}.$$

χ is the counting field. The total PGF is $Z(\chi, t) = U_E(\chi, t) + U_{SE}(\chi, t)$.

The Full Counting Statistics is $S(\chi, T) = \ln Z(\chi, T)$. All cumulants of the net flux $n(T)$ are obtained by differentiation:

$$\langle n(T) \rangle = -i \left. \frac{\partial S}{\partial \chi} \right|_{\chi=0},$$

$$\mathrm{var}(n(T)) = (-i)^2 \left. \frac{\partial^2 S}{\partial \chi^2} \right|_{\chi=0}.$$

Derivations 3: The χ-Hamiltonian Formalism

Tilted Master Equation

Multiplying the Master Equations by $e^{in\chi}$ and summing over n gives a 2x2 matrix equation:

$$\frac{d}{dt}\begin{pmatrix} U_E \\ U_{SE} \end{pmatrix} = -\hat{H}(\chi, t)\begin{pmatrix} U_E \\ U_{SE} \end{pmatrix}.$$

The evolution operator $\hat{H}(\chi, t)$ is the tilted or χ-Hamiltonian:

$$\hat{H}(\chi, t) = \begin{pmatrix} k_1 + k_{-2} & -k_{-1} - k_2 e^{i\chi} \\ -k_1 - k_{-2} e^{-i\chi} & k_{-1} + k_2 \end{pmatrix}.$$

Jumps increasing n (rate k_2) get a factor $e^{i\chi}$; jumps decreasing n (rate k_{-2}) get $e^{-i\chi}$.we assume the adiabatic approximation, i. e., the rates km oscillate with the frequency $min_m km$

Derivations 4: The Time-Ordered Solution

The formal solution for $\mathbf{U}(\chi, t)$ uses the time-ordering operator $\hat{T}$:

$$\mathbf{U}(\chi, t) = \hat{T}\left(e^{-\int_{t_0}^{t} \hat{H}(\chi, t')dt'}\right)|p(0)\rangle,$$

where $|p(0)\rangle = (P_E(0), P_{SE}(0))^T$.

The total PGF is

$$Z(\chi, t) = \langle 1|\hat{T}\left(e^{-\int_{t_0}^{t} \hat{H}(\chi, t')dt'}\right)|p(0)\rangle,$$

where $\langle 1| = (1, 1)$.

Adiabatic Approximation and Intermediate Time Scale

Introduce δt satisfying

$$\frac{1}{\omega} \gg \delta t \gg \max_m \frac{1}{k_m},$$

transitions occur during δt, rates k_m remain constant.

Define time slices $t_j = t_0 + j\,\delta t$

$$Z \approx e^{-\hat{H}(\chi,t_N)\delta t} e^{-\hat{H}(\chi,t_{N-1})\delta t} \ldots e^{-\hat{H}(\chi,t_0)\delta t}\, p(t_0).$$

$$\hat{1} = |u_0(t_i)\rangle\langle u_0(t_i)| + |u_1(t_i)\rangle\langle u_1(t_i)|,$$

where $|u_0(t_i)\rangle$ is the eigenstate of $\hat{H}(\chi, t_i)$ with eigenvalue λ_0 of smallest real part.

Since $\delta t \gg 1/k_i$, we have

$$|e^{-\lambda_0 \delta t}| \gg |e^{-\lambda_1 \delta t}|,$$

only the dominant eigenstate $|u_0(t)\rangle$ survives.

Derivations 4: Adiabatic Evolution

- **Assumption (Adiabatic):** The system evolves slowly, so it always remains in the "ground state" $|u_0\rangle$ of $\hat{H}(\chi, t)$.
- The pgf is approximated by discretizing time into steps δt (Eq. 14):

$$Z \approx \prod_i e^{-\lambda_0(\chi, t_i)\delta t} \langle u_0(t_i) \rangle u_0(t_{i-1})$$

Justification of the Overlap Approximation

$$\langle u_0(t_i) \mid u_0(t_{i-1})\rangle \approx \exp\big[-\delta t\,\langle u_0(t_i) \mid \partial_t u_0(t_{i-1})\rangle\big], \quad \delta t = t_i - t_{i-1}.$$

For a smooth, normalized state $|u_0(t)\rangle$:

$$|u_0(t+\delta t)\rangle = |u_0(t)\rangle + \delta t\,\partial_t|u_0(t)\rangle + O(\delta t^2),$$
$$\langle u_0(t+\delta t)| = \langle u_0(t)| + \delta t\,\langle \partial_t u_0(t)| + O(\delta t^2).$$

Thus,

$$\langle u_0(t+\delta t) \mid u_0(t)\rangle = 1 - \delta t\,\langle u_0(t) \mid \partial_t u_0(t)\rangle + O(\delta t^2).$$

Normalization $\partial_t\langle u_0|u_0\rangle = 0$ implies $\langle u_0|\partial_t u_0\rangle$ is purely imaginary. Hence,

$$1 - \delta t\,\langle u_0|\partial_t u_0\rangle = \exp\big[-\delta t\,\langle u_0|\partial_t u_0\rangle\big] + O(\delta t^2).$$

Counting Field

Start from the product form

$$Z \;\approx\; e^{-\lambda_{\min}(\chi,t_0)\,\delta t}\;\prod_{i=1}^{N} e^{-\lambda_0(\chi,t_i)\,\delta t}\,\langle u_0(t_i)\mid u_0(t_{i-1})\rangle.$$

First plug in the inner-product exponentiation for each slice:

$$\langle u_0(t_i)\mid u_0(t_{i-1})\rangle \approx \exp\big[-\delta t\,\langle u_0(t_i)\mid \partial_t u_0(t_{i-1})\rangle\big].$$

Thus every factor is an exponential and the whole product is

$$Z \approx \exp\left(-\lambda_{\min}(\chi,t_0)\,\delta t+\sum_{i=1}^{N}\big[-\lambda_0(\chi,t_i)\,\delta t-\delta t\,\langle u_0(t_i)\mid \partial_t u_0(t_{i-1})\rangle\big]\right).$$

Taking the logarithm directly yields $S(\chi)=\ln Z$ as the exponent. In the continuum limit ($\delta t\to 0$)

$$S(\chi)\approx-\int_{t_0}^{t} dt\,\big[\lambda_0(\chi,t)+\langle u_0(t)\mid \partial_t u_0(t)\rangle\big],$$

and for periodic driving (period T_0, total time T)

Derivations 5: The Final Result (Berry Phase!)

By approximating the overlap and integrating over one full period T_0, the FCS splits into two parts (Eq. 15):

$$S(\chi) \approx S_{geom} + S_{cl}$$

Classical Part (S_{cl})

Depends on the eigenvalue λ_0. This is the standard, expected contribution.

$$S_{cl} = -\frac{T}{T_0} \int_0^{T_0} dt\, \lambda_0(\chi, t)$$

Geometric Part (S_{geom})

Depends only on the path of the eigenstate $|u_0\rangle$. This is the **Berry Phase**!

$$S_{geom} = -\frac{T}{T_0} \int_0^{T_0} dt\, \langle u_0(t) \mid \partial_t u_0(t) \rangle]$$

Derivations 6: The Berry Curvature

The geometric term S_{geom} is a line integral in the parameter space (the **k-space**) along the contour c of the oscillating rates (Eq. 17):

$$S_{geom} = -\frac{T}{T_0} \oint_c \mathbf{A} \cdot d\mathbf{k} \quad \text{where} \quad A_m = \langle u_0 \rangle \, \partial_{k_m} u_0$$

Using Stokes' theorem, this line integral becomes a surface integral over the **Berry Curvature** F (Eq. 18):

$$\oint_c \mathbf{A} \cdot d\mathbf{k} = \iint_{s_c} dk_1 dk_{-2} \, F_{k_1, k_{-2}}$$

The Crucial Insight

- The Berry Curvature F is **ZERO** when $\chi = 0$.
- It is the **counting field** χ that introduces a "nontrivial topology" (p. 5) into the problem, making the geometric phase visible. This is why the effect was missed in standard analyses.

Results 1: The Mean Flux

The mean flux $J = \langle n \rangle / T$ is found by differentiating $S(\chi)$. The total flux J splits into two parts:

$$J = J_{cl} + J_{pump}$$

Classical Flux (J_{cl})

J_{cl} is simply the classical (deterministic) Michaelis-Menten current, averaged over one period .

Pump Flux (J_{pump})

J_{pump} is the new geometric current, derived from the Berry Curvature .

$$J_{pump} = \iint_{s_c} d^2k \, \frac{k_2 + k_{-1}}{T_0 K^3}$$

Key Property: J_{pump} is proportional to the *area* enclosed in parameter space and the *frequency* ω. It is a small effect: $J_{pump}/J_{cl} \sim \omega/k_m \ll 1$.

Results 2: Fluctuations (Noise)

A major contribution: This method provides the **first-ever analytical expression** for the *noise* (variance) of the current under periodic driving. The total noise $J^{(2)} = \langle \delta^2 n(T) \rangle / T$ also splits into two parts:

$$J^{(2)} = J^{(2)}_{cl} + J^{(2)}_{pump}$$

Classical Noise ($J^{(2)}_{cl}$)

$$J^{(2)}_{cl} = \frac{1}{T_0} \int_0^{T_0} dt \left[\frac{\kappa_+ + \kappa_-}{K} - \frac{(\kappa_+ - \kappa_-)^2}{K^3} \right]$$

Pump Noise ($J^{(2)}_{pump}$)

$$J^{(2)}_{pump} = \iint_{s_c} d^2k \left[\frac{k_2 - k_{-1}}{T_0 K^3} - \dots \right]$$

Numerical Verification (Fig. 2)

Findings:

- **(a) Mean Flux:** The plot of J_{pump} vs. ω shows a perfect **linear dependence**, exactly as the theory predicts.

Conclusion: The derivations are correct.

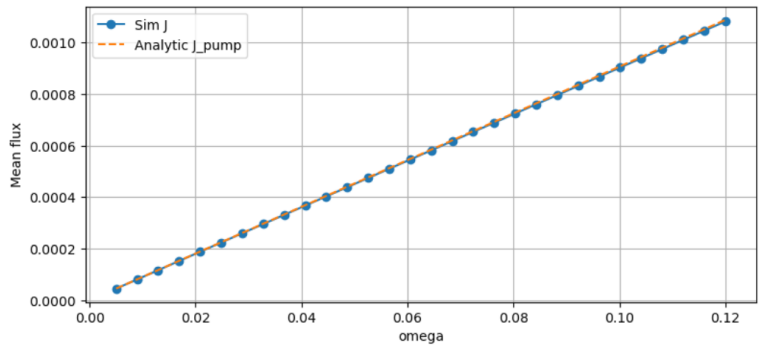

Figure: Fig. 2: Comparison of analytical predictions and numerical results.

Results 4: Intuition & Frequency Dependence

Adiabatic (Slow) Regime: $\omega \ll k_m$

- **Result:** $J_{pump} \sim \omega$
- **Intuition:** A particle binding "shields" the enzyme from the changing rates. This shielding is asymmetric with respect to the phase of k_1 and k_{-2}, creating a flux.

Fast (Non-Adiabatic) Regime: $\omega \gg k_m$

- **Result:** $J_{pump} \sim 1/\omega$
- **Intuition:** The system is too slow to follow the rapid oscillations. It only sees the time-averaged rates, and the pump effect vanishes.

Prediction

There must be a **maximum pump current** at an intermediate frequency $\omega \sim k_m$, where the system is fast enough to react but slow enough to "feel" the phase asymmetry.

Future Outlook: Is this Observable?

The Challenge

The pump flux J_{pump} is small, but the *classical noise* $J_{cl}^{(2)}$ is large. The main hurdle is observing the tiny J_{pump} signal in the sea of classical noise.

- With 10% rate oscillations, $J_{pump} \sim 10^{-2}$ particles/sec.
- But the classical noise $J_{cl}^{(2)} \sim 10$ particles/sec.

Experimental Prediction

- **Single Molecule Experiment:** Observing J_{pump} would require averaging for **days** to overcome the noise.
- **Ensemble Experiment ($\sim 10^6$ enzymes):** The effect becomes observable in **less than a minute**.

References I

1. Michaelis L. and Menten M. L., Biochem. Z., 49 (1913) 333.
2. Stochastic pump effect and geometric phases in dissipative and stochastic systems N.A. Sinitsyn(review)
3.

Questions?

Thank You