The Brownian ratchet for protein translocation

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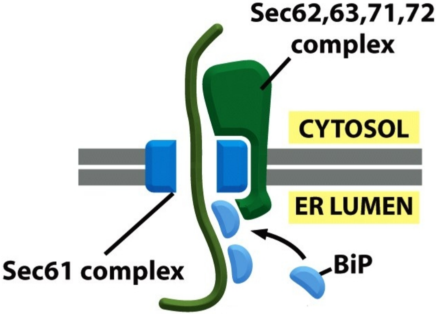
A. Depperschmidt and P. Pfaffelhuber, 2010. Asymptotics of a Brownian ratchet for Protein Translocation, Stoch. Proc. Appl., 120, 901-925

Protein translocation

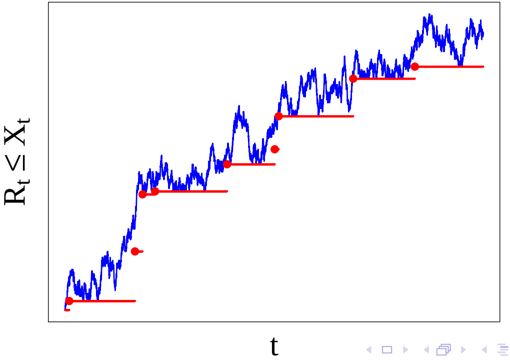
- Protein **diffuses** through a nanopore
- **Ratcheting molecules** bind to it



Molecular Biology of the Cell 5, Figure 12-44

The Brownian ratchet

- The dynamics of the γ-Brownian $(X_t, R_t)_{t\geq 0}$ is as follows:
- **X_t is Brownian motion**, reflected at R_t
- **R_t jumps** to $x \in [R_{t-}, X_t]$ at **rate $\gamma(X_t - R_{t-})dx$**



The law of large numbers

- **Theorem**

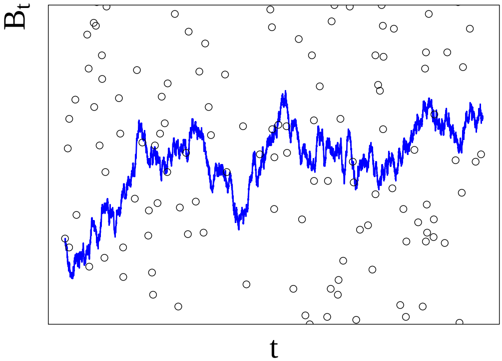
$$\frac{X_t}{t} \xrightarrow{t\to\infty} \frac{\Gamma(2/3)}{\Gamma(1/3)}\left(\frac{3\gamma}{4}\right)^{1/3} \text{ almost surely}$$

- **Interpretation**
  - Assume the protein is very long
  - γ proportional to concentration of ratcheting molecules
  - Speed of translocation into the ER lumen is $\sim \gamma^{1/3}$

  - **Double speed** requires **eight-fold increase** in number of ratcheting molecules

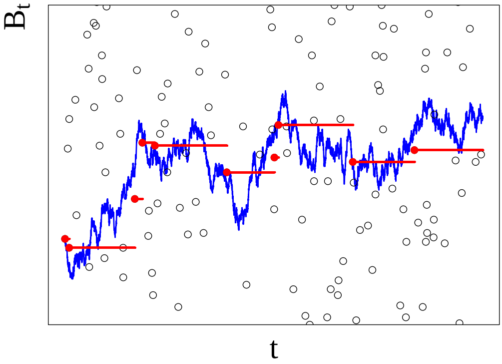
The graphical construction

- $(B_t)_{t\geq 0}$: **Brownian motion**
- Add rate-γ **Poisson process**



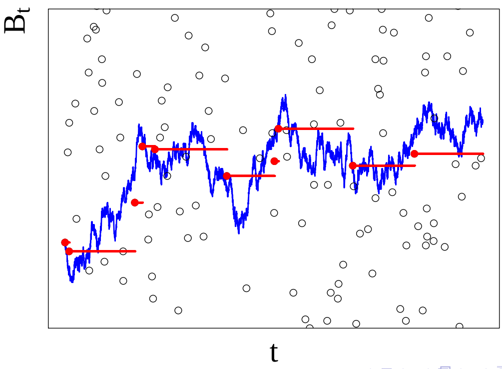
The graphical construction

- Some Poisson-points are **active** for some time
- **New** active Poisson-point is **between** B_t and **old** active point



The graphical construction

- A_t: **active** point at time t; Δ_t: **jump** in active point at time t
- $R_t \stackrel{d}{=} \sum_{s \leq t} |\Delta_s|$; $\mathbf{X_t \stackrel{d}{=} \sum_{s \leq t} |\Delta_s| + |B_t - A_t|}$



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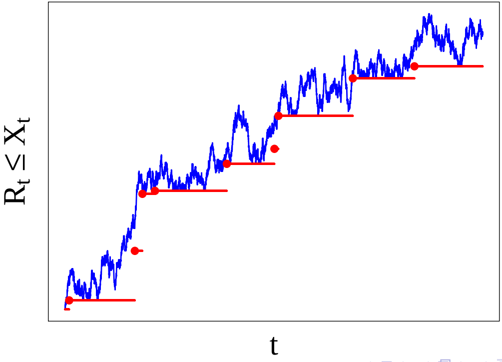
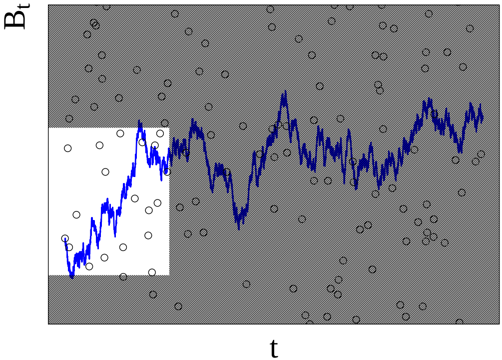


Why $\gamma^{1/3}$?

- in **rectangle** of size $\gamma^{-2/3} \times \gamma^{-1/3}$ expect **1 Poisson point**
- Brownian motion in **rectangle** is **again a Brownian motion**



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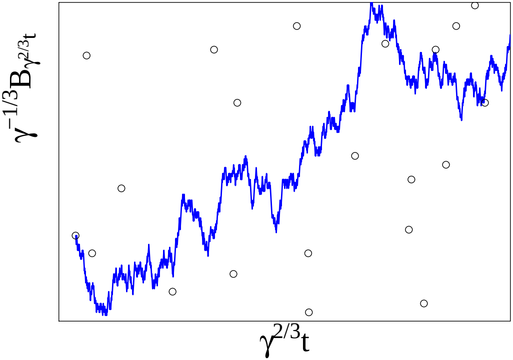

Why $\gamma^{1/3}$?

- We have **just shown** that

$$(X_t^1)_{t\geq 0} \text{ is } 1\text{−Brownian ratchet}$$

$$\Longrightarrow (\gamma^{-1/3} X^1_{\gamma^{2/3}t})_{t\geq 0} \text{ is } \gamma\text{-Brownian ratchet}$$

- So,

$$\frac{\mathbf{X_t^\gamma}}{\mathbf{t}} \stackrel{d}{=} \frac{\gamma^{-1/3} X^1_{\gamma^{2/3}t}}{t} = \gamma^{1/3} \frac{X^1_{\gamma^{2/3}t}}{\gamma^{2/3}t} \overset{\mathbf{t\to\infty}}{\approx} \gamma^{1/3} \frac{\mathbf{X_t^1}}{\mathbf{t}}$$

$\Longrightarrow$ Speed scales with $\gamma^{1/3}$.

A single jump of the Brownian ratchet

- B_x: **Brownian motion**, started in x, **killed** at rate $\frac{1}{2}|B_x|$, τ: killing time
- **Lemma:**

$$\mathbf{E}[B_x(\tau-)] = x + \frac{2\pi Ai(x)}{3^{1/6}\Gamma(2/3)},$$
$$\mathbf{E}[\tau] = 2\pi(Gi(x) + 3^{-1/2}Ai(x)).$$

- **Proof**: For B_x, **Green function**

$$G(x,y)dy := \text{average time spent in } dy \text{ before being killed}$$

satisfies

$$u''(x) - xu(x) = 0,$$

which is solved by **Airy functions**.

A single jump of the Brownian ratchet

- B_x: **Brownian motion**, started in x, **killed** at rate $\frac{1}{2}|B_x|$, τ: killing time, U: uniform on $[0,1]$
- **Proposition:** The random variable Y with

$$Y \stackrel{d}{=} UB_Y(\tau-). \qquad (*)$$

satisfies

$$\mathbf{P}(Y \in dy) = 3Ai(y)dy.$$

- Proof: use $(*)$ to derive

$$\mathbf{P}(Y \in dy) = \int_0^\infty \mathbf{P}(Y \in dx) \int_y^\infty G(x,u)dudy$$

and do some calculations.

Outlook

- Brownian ratchet can be seen as a **regenerative process**
- **Central limit theorem** shown as well

- Current project: **Brownian ratchet with negative drift**