# Pink Noise and Sensory Adaptation

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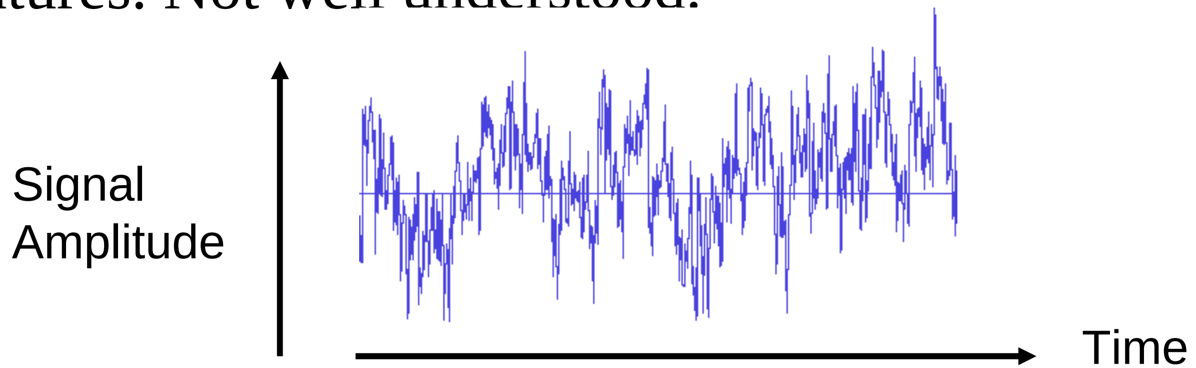
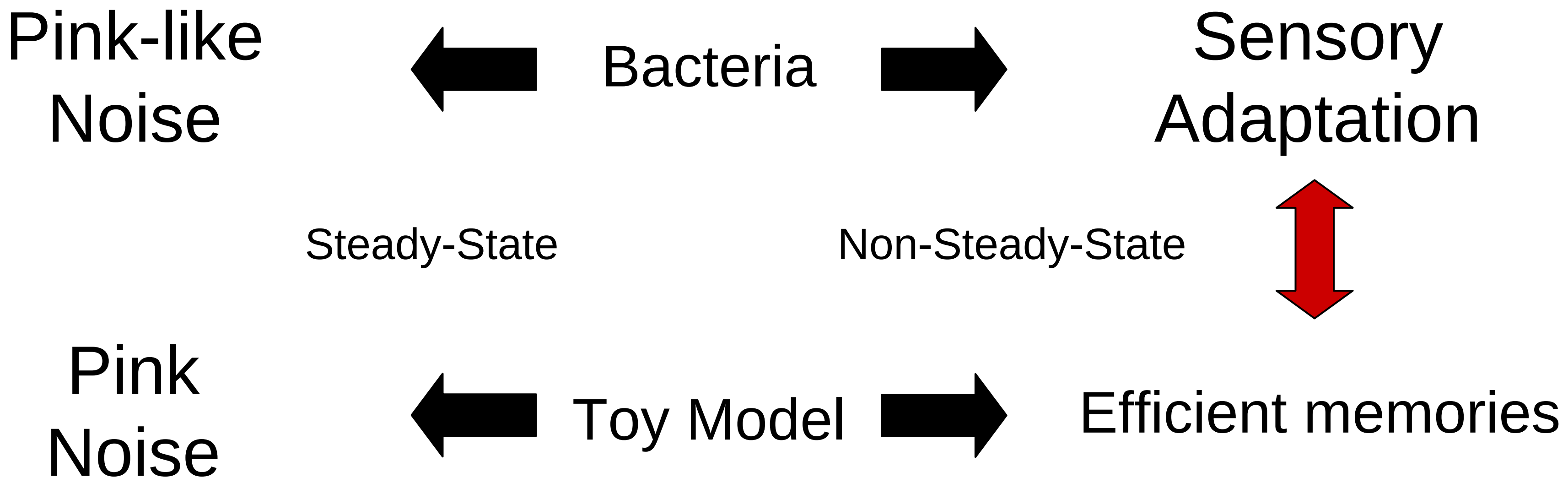
# What is Pink Noise?

- Pink Noise: a widespread kind of temporal fluctuation shown by systems named after its power spectral features. Not well understood.




- I will suggest that one source of Pink Noise in Nature might be Sensory Adaptation because adaptation can require efficient memories.

# In a diagram:



Pink-like Noise
Bacteria
Sensory Adaptation
Steady-State
Non-Steady-State
Pink Noise
Toy Model
Efficient memories

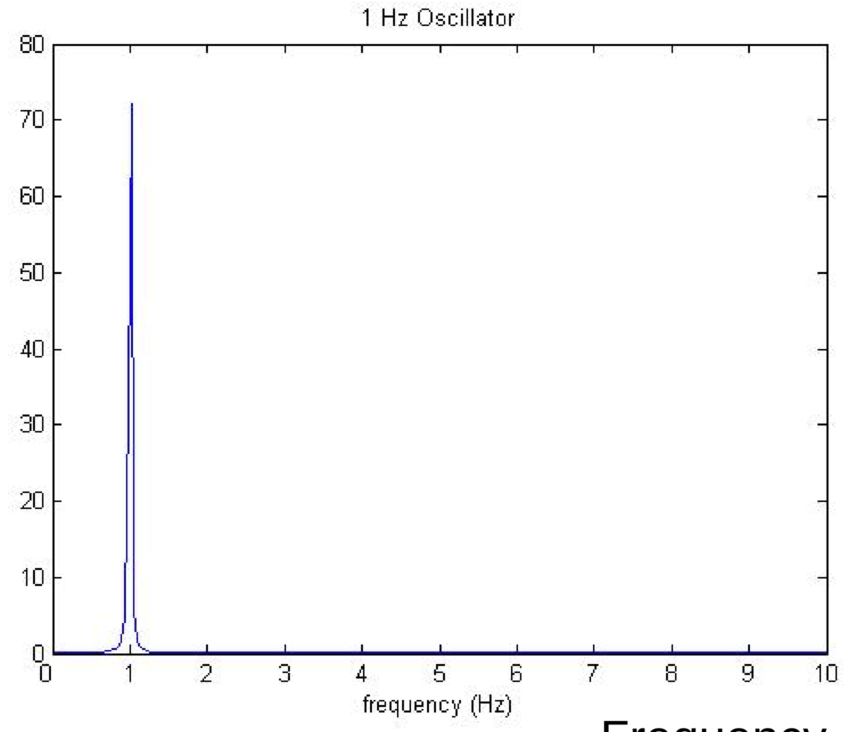
# How?

- Power spectra: White, Brown and Pink Noise
- Bacteria show Pink-like Noise
- Bacteria Adapt to Signals varying by orders of magnitude – efficient memories?
- Toy example: efficient memories can generate Pink noise and are useful in adaptation
- Conclusions – the mystery of heart time series

# Power Spectrum of a Clock

Plot Power vs Frequency

Power



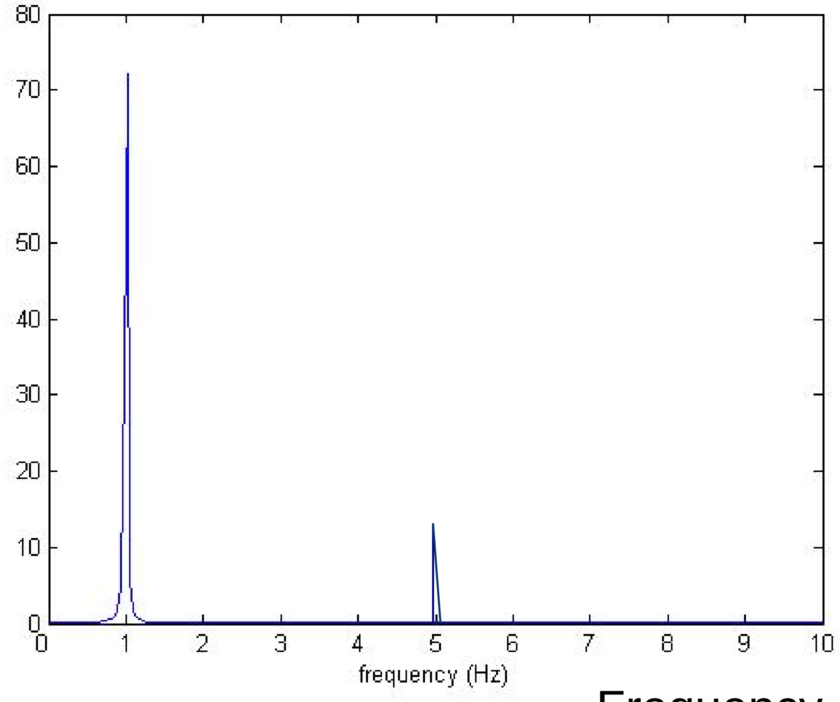

Frequency

Clock: No Noise

# Power Spectrum of two Clocks

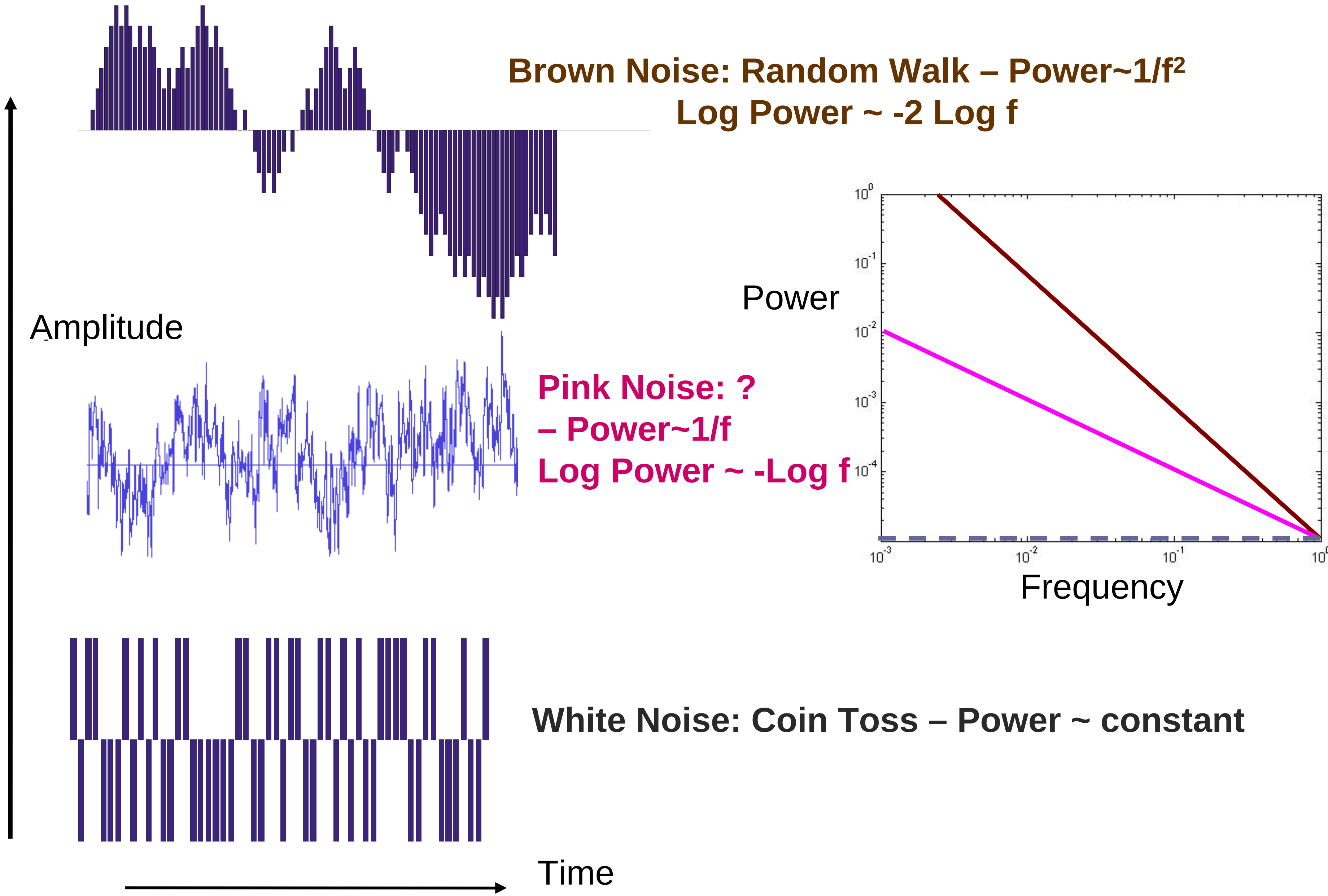
Plot Power vs Frequency

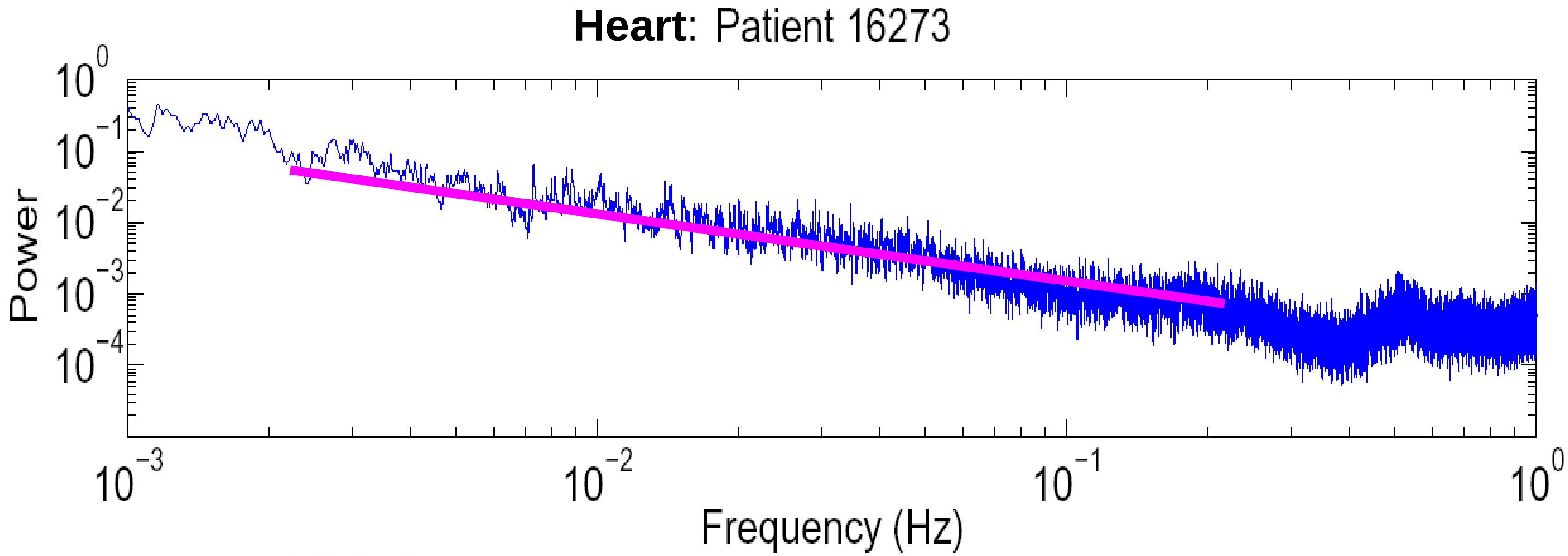
Power

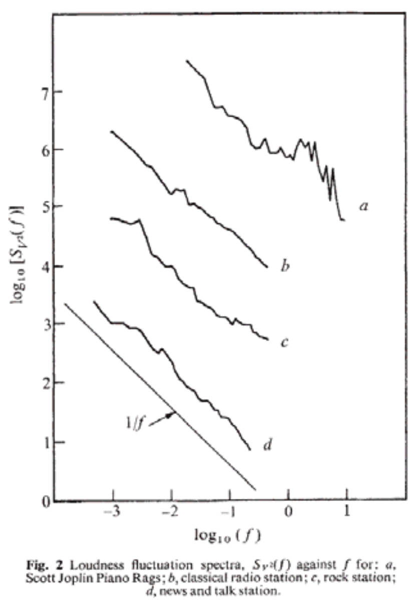



Frequency

Loud clock at 1 tick per second and quiet clock at 5 ticks per second


Brown Noise: Random Walk – Power~1/f²
Log Power ~ -2 Log f
Amplitude
Pink Noise: ?
– Power~1/f
Log Power ~ -Log f
Power
$10^{0}$
$10^{-1}$
$10^{-2}$
$10^{-3}$
$10^{-4}$
$10^{-3}$
$10^{-2}$
$10^{-1}$
$10^{0}$
Frequency
White Noise: Coin Toss – Power ~ constant
Time



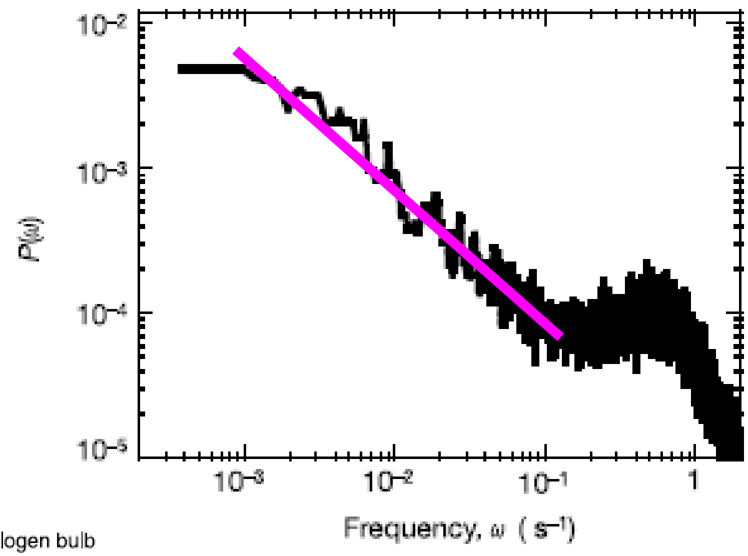




Spectra for Music and Speech: Pink noise Voss and Clarke Nature 1975

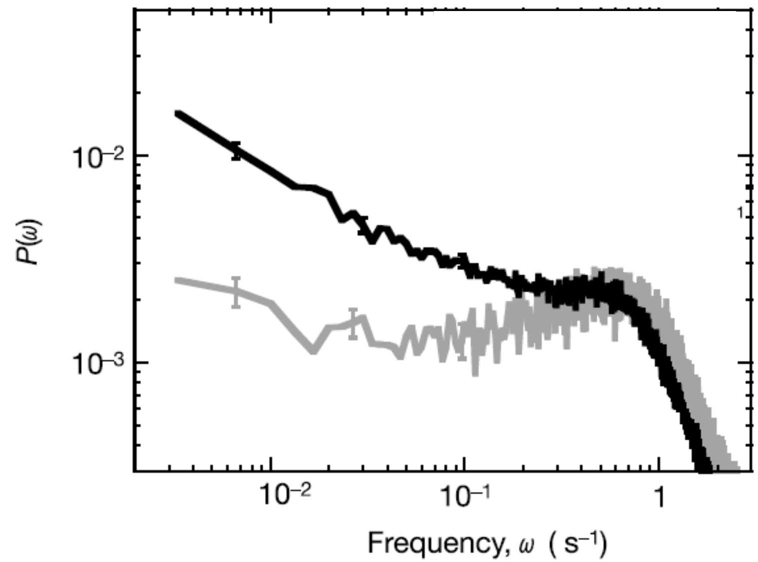
- Music and Heart time series show 1/f fluctuations in their power spectra. Pink noise.
- Ion Channels also show this behavior.(eg. Bezrukov and Winterhalter Phys. Rev. Lett. 2000)
- W. Li, http://www.nslij-genetics.org/wli/1fnoise/

# Power Spectra for the Rotations of Bacterial Tails

Power

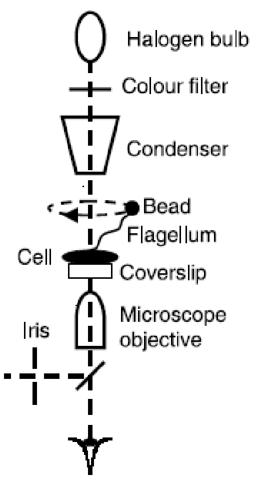



One bacterium




Black: Average of many bacteria
(Grey: motor only)

Pink noise =1/f




Bacteria show Pink-like noise in a constant environment

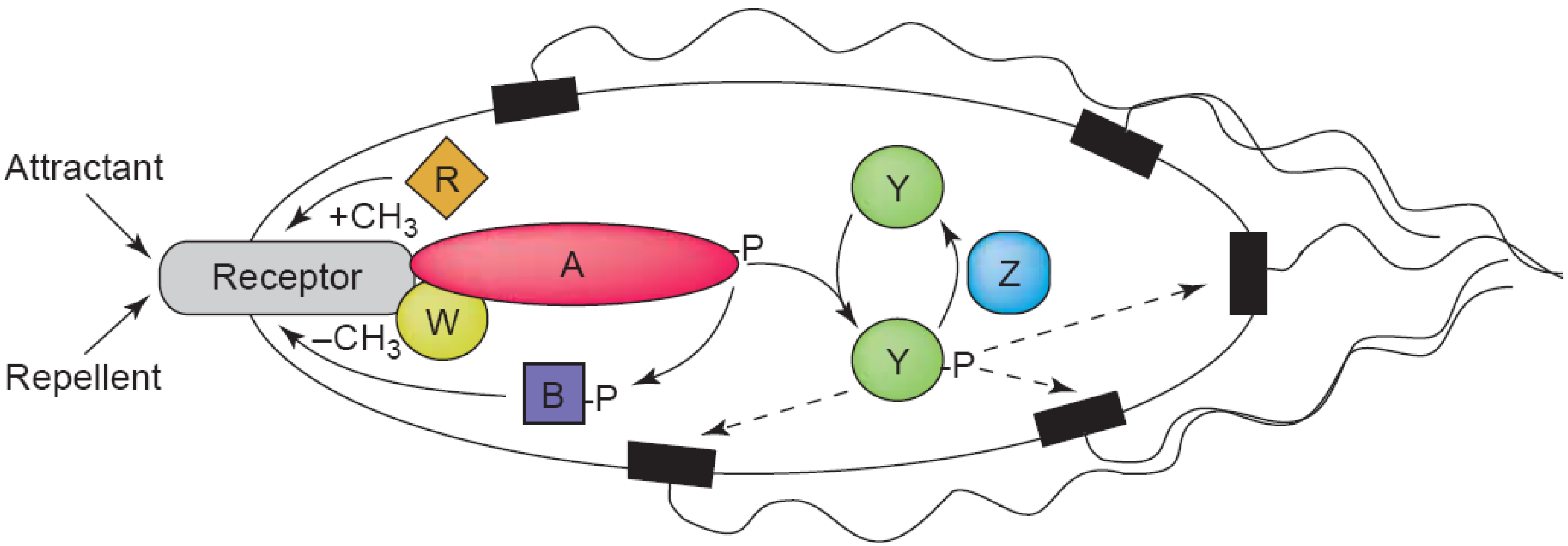
**Nothing in their environment changes and yet they fluctuate**

E. Korobkova *et al.*, Nature (London) **428**, 574 (2004).

# Bacteria Show Adaptation

- Adjust their baseline sensitivity to different concentrations of attractants.
- This baseline can be varied to respond to concentrations varying by five orders of magnitude.
- Methylation of receptors reduces their sensitivity to attractants. The more methylated the receptor the less sensitive it is (~$10^3$ receptors each with 4 sites)
- Methylation levels are a representation of the attractant concentration.
- Efficient representation of numbers varying by orders of magnitude requires non-unary memories.

# Picture of chemotaxis pathway



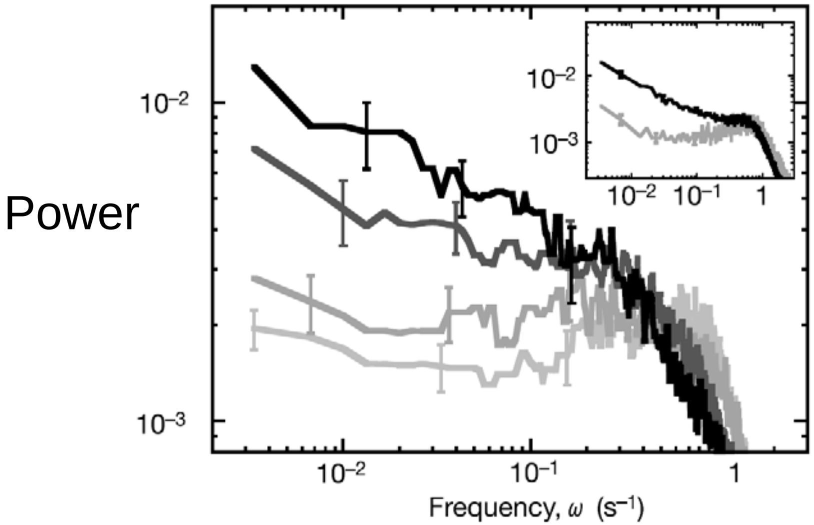

V. Sourjik, Trends in Microbiology **12**, 569 (2004)

# Some Numbers

- Bacteria can adapt to chemoattractant concentrations varying by five orders of magnitude ‘$1\text{-}10^5$’
- They have approximately $10^3$ receptors each with 4 sites.
- If each site is a more than unary memory then that allows a wider range for adaptation.

# Does the Adaptation machinery cause Pink Noise?

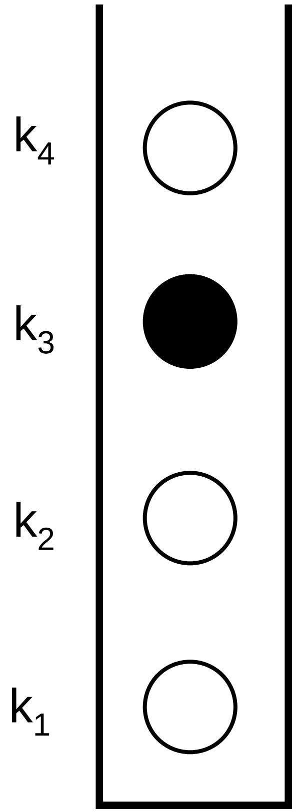
- Time scale of adaptation (and methylation) is similar to the time scale over which Pink noise is detected
- Changing concentrations of methylating chemical CheR causes changes to the spectrum
- Fixing the level of methylation eliminates the Pink Noise

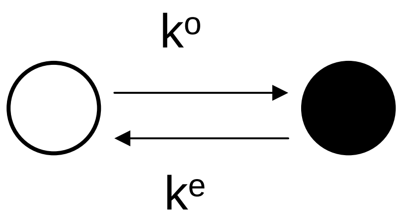


# But Why?

- Cluzel group did not provide a specific mechanism for the pink noise and mooted that these fluctuations might help with foraging.
- Tu and Grinstein PRL 2005 suggested methylation wasn't the cause but downstream fluctuations from [CheY-P]
- But perhaps the origin is more inevitable. Perhaps it is an unavoidable consequence of efficient memories used by bacteria in adaptation? A Toy Model. Memories in the membrane.

# A toy model that, in Steady-State, shows Pink Noise



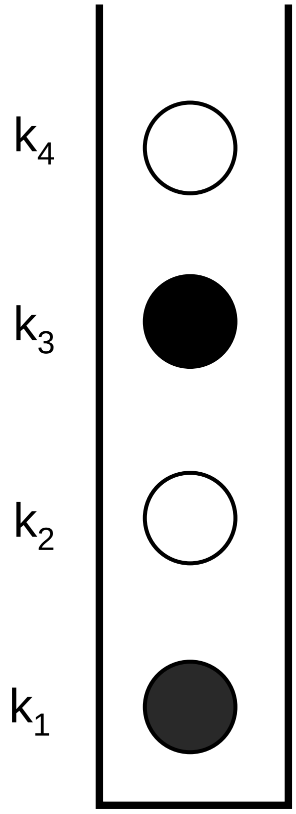

$k^o$ rate of occupation
$k^e$ rate of emptying

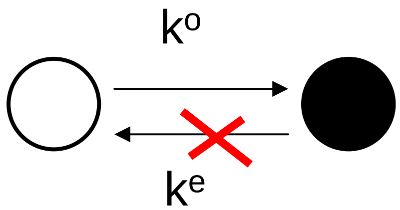
If $k^e=k^o$ and if $k_1/k_2=k_2/k_3=\ldots=k_i/k_{i+1}=C$ (C>1)

One can prove that the total number of sites occupied through time shows Pink Noise

Call $k^e=k^o$ the 'Steady-State' case

# Out of Steady-State it is an efficient memory: Stochastic Counting



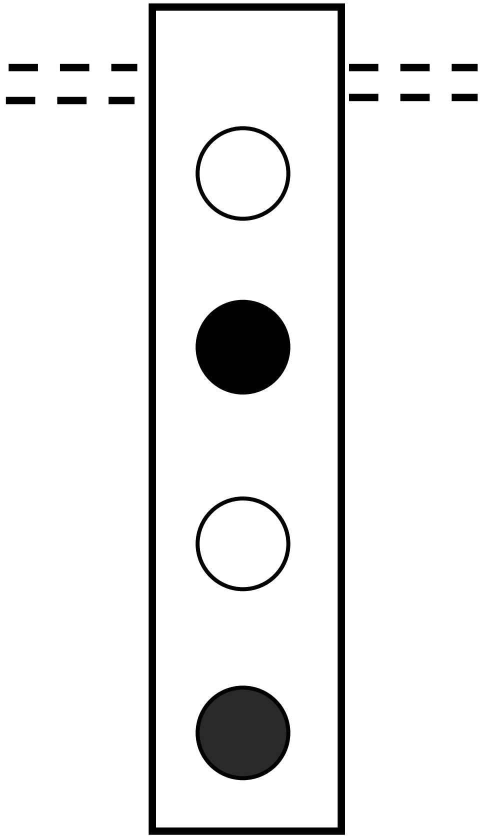

Non-Steady-State case

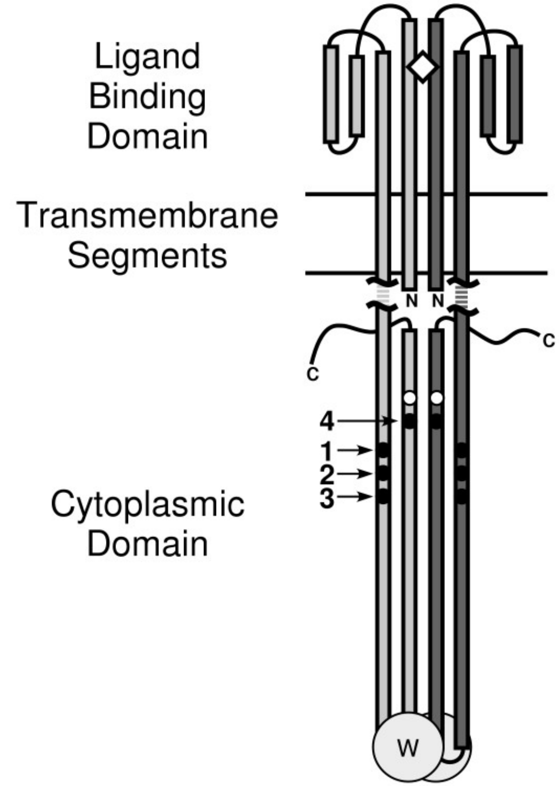
Can store the number ‘L’ efficiently even though each site is independent from all others.

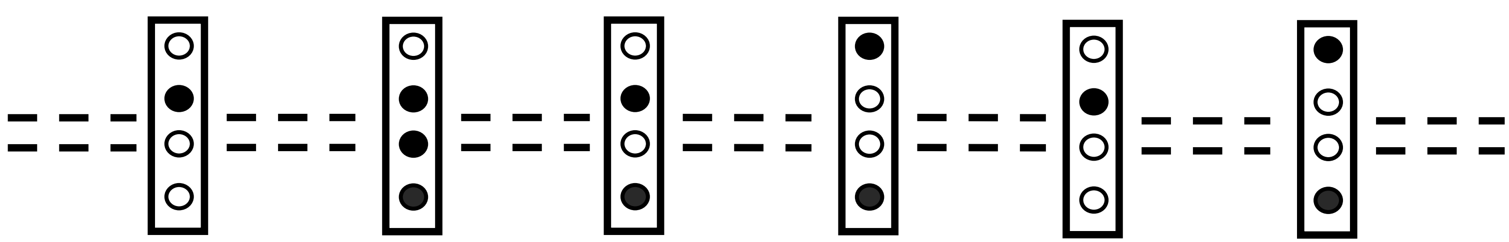
Set $k^e=0$ for a time ‘L’ (and keep $k_1/k_2=k_2/k_3=\ldots=k_i/k_{i+1}=C$ (C>1))

Then approximately log L sites will be methylated

# Toy and Reality?





# Toys and Reality

- Toy: in Steady-State it shows Pink Noise
- Toy: out of Steady-State it is an efficient memory. Useful for representing the wide range of numbers in adaptation
- Biochemical relevance? The toy system resembles the chemoreceptors of E. Coli. The methylation of these chemoreceptors is correlated with the tail rotations.
- In the ref below: $k_1/k_2=3.34$; $k_2/k_3=3.75$; $k_3/k_4=4.07$ for receptor methylation rates in bacteria. $k_1 \sim 50 * k_4$

  ($k_1=8.33*10^{-4}s^{-1}$)

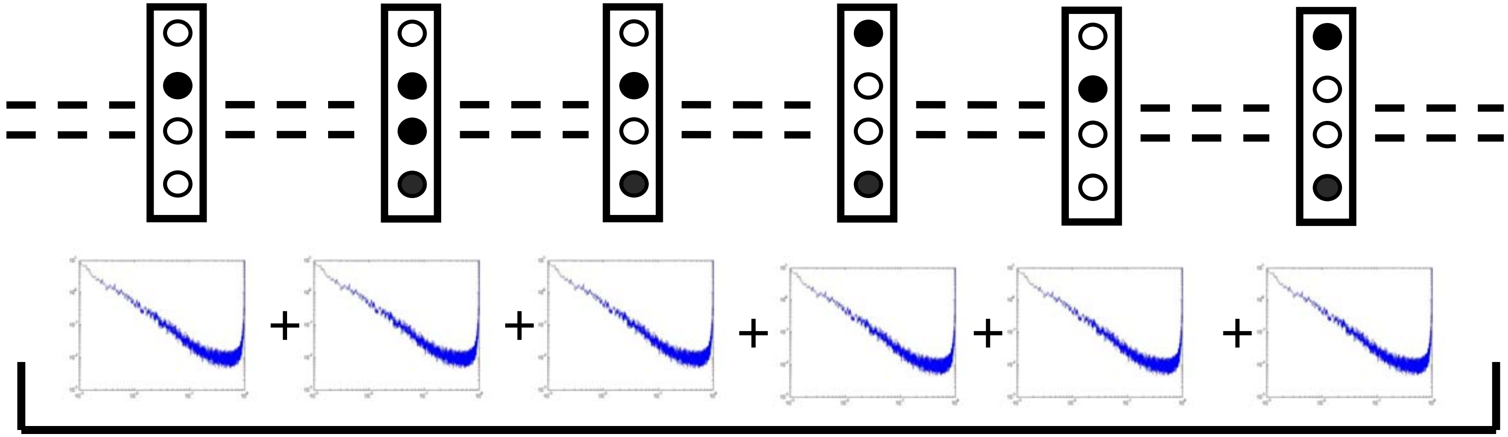
T.C. Terwilliger, J.Y. Wang and D.E. Koshland, J. Biol. Chem. **261**, 10814 (1986).

http://www.pdn.cam.ac.uk/groups/comp-cell/

# Strong Notes of Caution

- Reality is much more complex – toys like this are useful only to provoke richer understanding.
- No feedback in toy – in fact the more methylated a receptor the more it is demethylated
- Methylation and demethylation have different rates
- Strong evidence for co-operativity between receptors – memory effects could be to do with couplings between receptors rather than receptors themselves (eg. Work from Berg lab).
- Likely to be a complicated functional interplay between rates of each site and the corresponding activities.

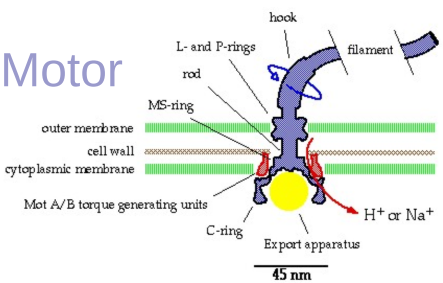
Membrane

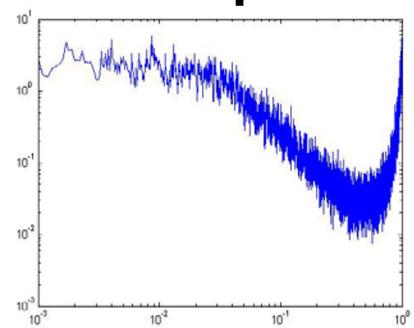


Receptor Noise

+

Motor

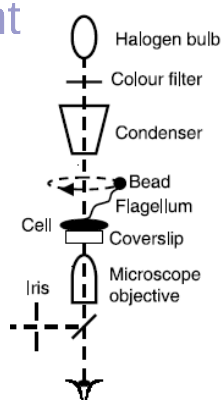


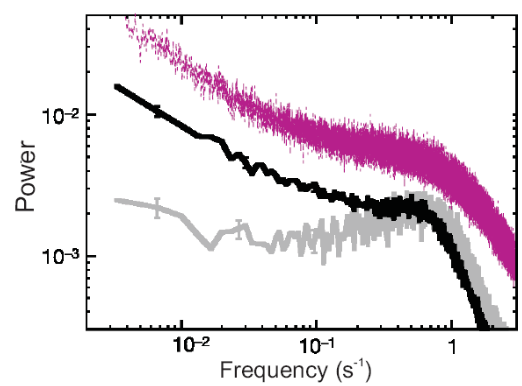



Motor Noise

=

Measurement



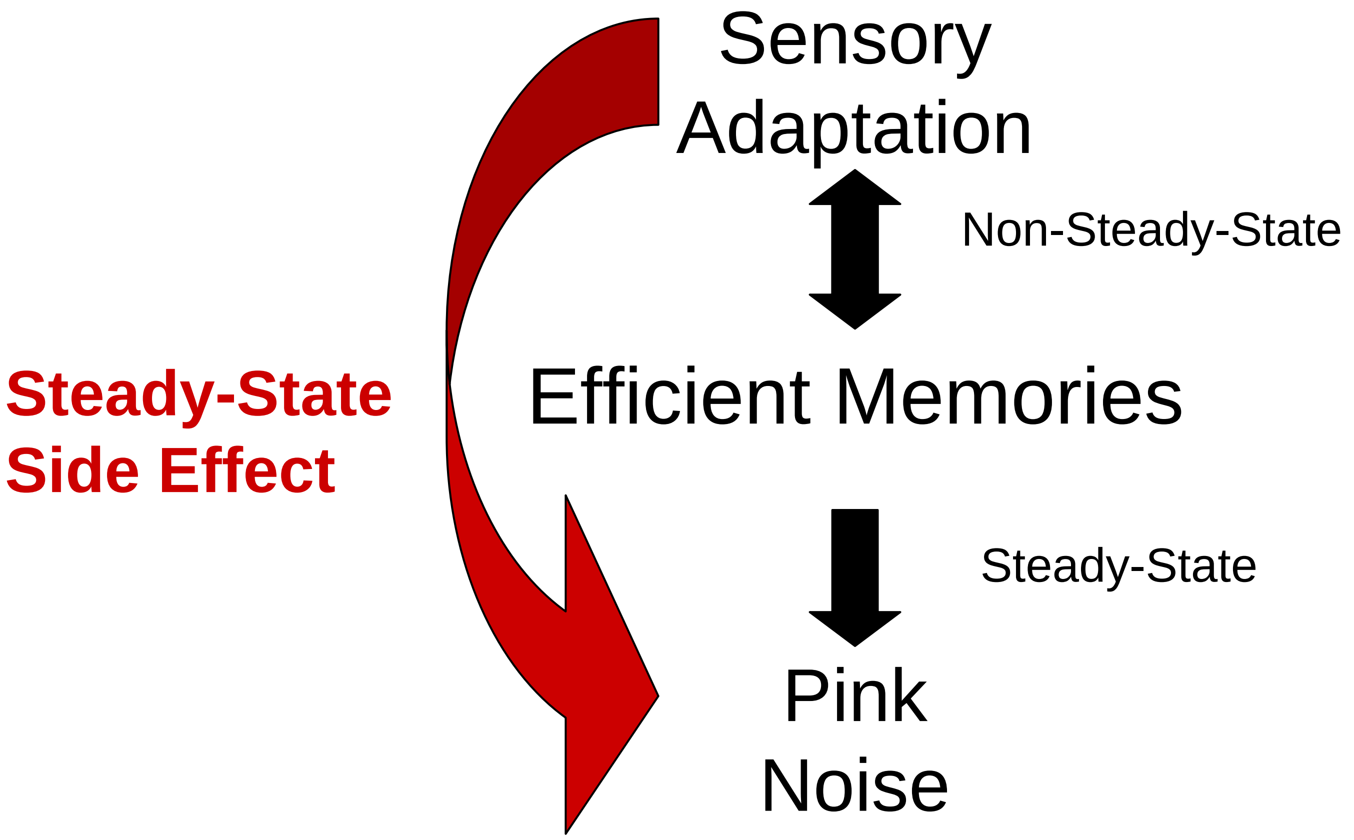




Observed Flagellal Noise?

# Connection with existing models of Sensory Adaptation

- This toy is not a model of sensory adaptation.
- Simply an example of a memory that generates non-trivial noise.
- It is basically compatible with existing models (eg. Barkai & Leibler Nature ‘97).
- Here I am arguing that memory effects mean that the reservoir of sites that can be methylated could be structured.

# Is Pink Noise a Side-Effect of Efficient Memories?



# 4 Ideas

- Two statements (one theoretical one experimental) and Two hypotheses.
- Efficient stochastic memories can yield Pink Noise
- In Bacteria Pink-like Noise is coupled to sensory adaptation
- Hypothesis: This is due to efficient memories in the receptors
- Hypothesis: Pink Noise in the heart is due to adaptation

# Hearts and Adaptation

- Heart rate time series show Pink Noise. Why they do this remains mysterious despite intense effort.
- Do they show Pink Noise because – like tail motors – they are coupled to an adaptive system? Is the source of these fluctuations a compact number representation?
- Patients who do not have Pink noise in their heart rate time series are more susceptible to heart attack (Peng Chaos ‘95). Is this because they lack the adaptive machinery to respond to large stresses?

# Experimental Tests and Predictions I

- Points, perhaps, to a modification of the parameters in StochSim – either in the weightings of the methylation sites or their rates – will this improve predictions?
- Noise from receptors should be pure compared to noise from the motor – because there are thousands of receptors and only one motor. Some kind of phase tagging? Might help identify where the memory effect lies – if it is a whole membrane effect then may be noisier.
- Fluctuations in the spectral gradient of the different bacteria explained by variability in [CheR]
- 'Power law' behaviors in intervals between rotation types – toy model produces them and loses them as the real system does.

# Experimental Tests and Predictions II

- Connection between raising methylation resting levels by raising [CheR] and changes to fluctuations.
- Connection between the range of timescales – $k_1 \sim 50 * k_4$ and the range of frequencies. Frequency cut off at high frequencies
- Could look at the range of adaptation as [CheR] is increased (should diminish).
- Would be interesting to repeat the Cluzel lab experiments for Rhodobacter Sphaeroides. Evidence of memory effects here?
- Physiological context: is it the mechanism of adaptation which is missing in patients who lack Pink Noise in their heart rate time series?

# Conclusion

- Pink Noise is a widespread type of noise which is not well understood.
- Efficient memories can produce Pink Noise
- Bacteria have an adaptive sensory apparatus and, in a constant environment, show pink-like noise.
- Empirical evidence for a connection between sensory adaptation and pink-noise.
- Hypothesis: sensory adaptation requires efficient memories. Fluctuations in these memories yield pink-noise as a side-effect. This might explain the presence of pink noise in a wide class of natural processes.

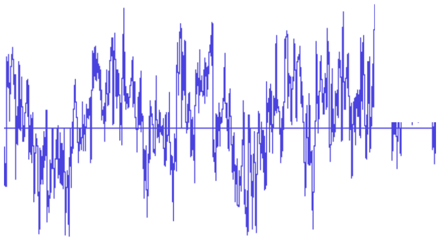
# Brown Noise can make Pink Noise

Random Walk

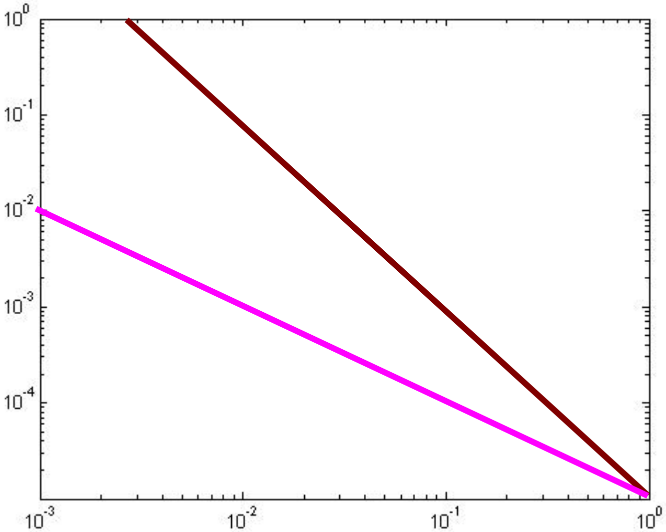
….321 320 319 320 319….

Digit Sum

….6 5 13 5 13 …



Pink Walk



# Computer Simulations: Pink or Brown?