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Getting to understand more and more a (simple?) model of stochastic gene expression

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► **To cite this version:**

Romain Yvinec. Getting to understand more and more a (simple?) model of stochastic gene expression. 7th International Congress on Industrial and Applied Mathematics (ICIAM 2011), Jul 2011, Vancouver, Canada. hal-03114889

HAL Id: hal-03114889

<https://hal.science/hal-03114889>

Submitted on 7 Feb 2021

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Getting to understand more and more a (simple?) model of stochastic gene expression

Self-Regulation

Nonlinear Regulation

White noise

Two different sources of noise

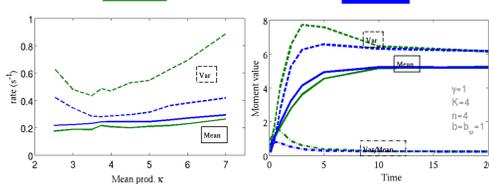
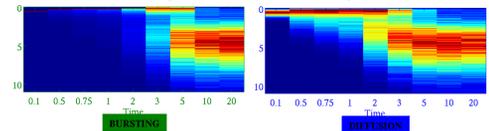
Yvinec Romain (ICJ)

Using Sample paths simulation

The **reduced 1-dimensional stochastic model** has been analytically characterized when either one source of noise is present:

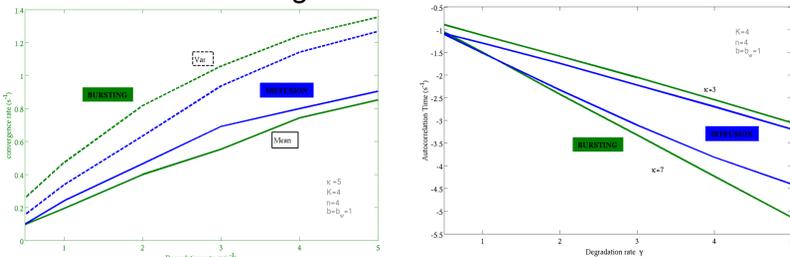
- Uni/Bimodal asymptotic density in the positive regulation;
- Noise-induced bi-stability
- Unimodal asymptotic density in the negative regulation.

Time-dependent densities are different for the two sources of noise. The bursting model presents higher variability.

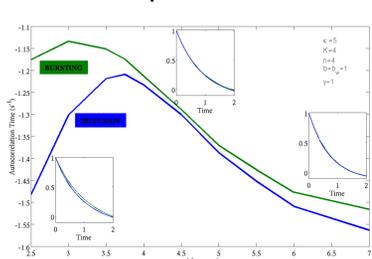


The **variance** converges slower and the **mean** value converges faster for the diffusion noise.

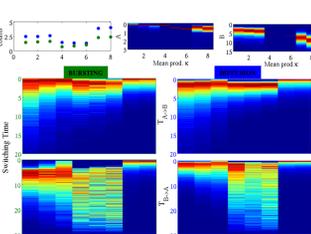
Both **convergence rate** and **autocorrelation time** scale with the degradation rate



The bursting noise gives rise to higher or slower **autocorrelation time** depending on the respective value of the mean production rate and the degradation rate.

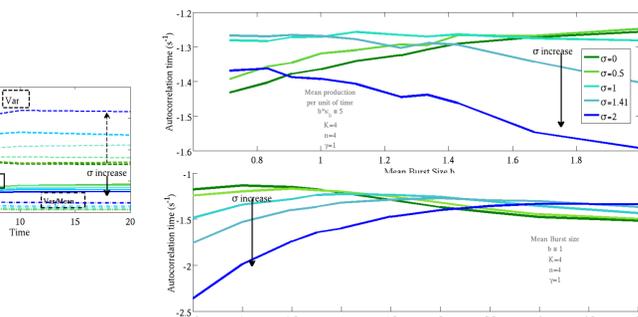
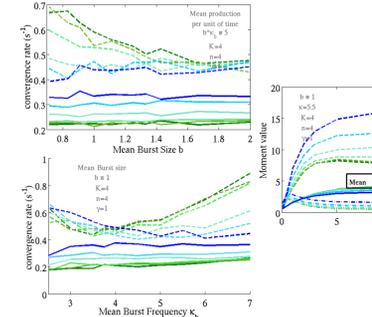


The diffusion model **switch** more an faster, specifically due to a non-refractory time in the bursting model while going from a high to a low value (the bursting noise is asymmetric)

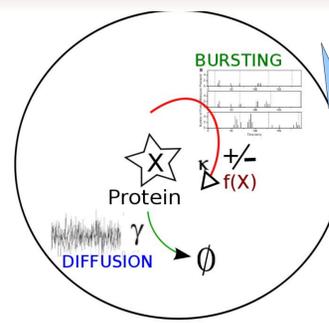


When both noise are present, the strength of the noise governs mainly the **convergence rate** of the **mean**. For the **variance**, we can observe non-monotonic behaviour and more complex dependencies of the two source of noise.

Same for the **auto-correlation time**



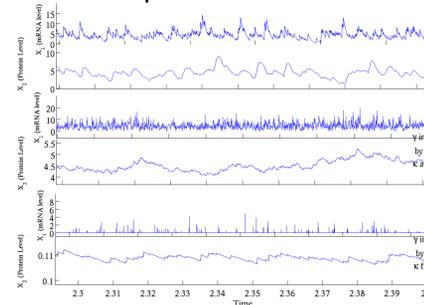
Questions that remains:
 → **Transient Behaviour?**
 → **Difference between the two source of noise?**



Adiabatic elimination.

Depending on the scaling chosen, one can obtain different stochastic process.

$$X=2$$



Asymptotic density, Power Spectra, And Poincaré Map Gives different information. The latter may be the most reliable to characterize **stochastic oscillations**

The **stochastic limit cycle** may be identified through a **stochastic Poincaré map**

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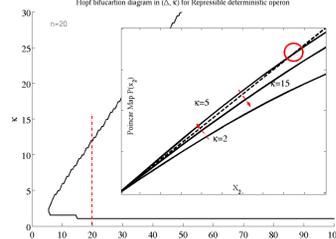
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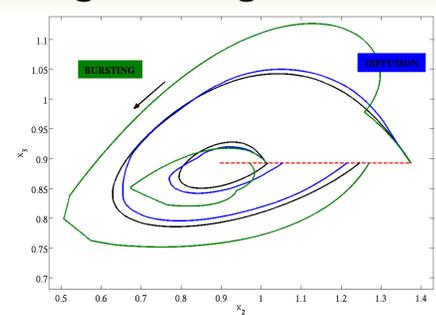
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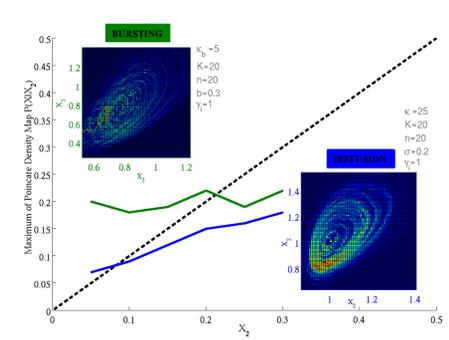


The **full 3-dimensional deterministic model** is well known.
 • Mono/Bistable behaviour
 • in the positive regulation;
 • Monostable/Limit cycle in the negative regulation.

Questions that remains:
 → **Adiabatic elimination** when noise is present?
 → **Oscillation property** when noise is present in the negative regulation?



Asymptotic density, Power Spectra, And Poincaré Map Gives different information. The latter may be the most reliable to characterize **stochastic oscillations**



CONCLUSION:

- The two sources of noise have distinct **transient** properties as well as different **convergence rates** toward equilibrium; **Memory** and **switch** property also differs;
- Noisy and bistable regime may occur **transiently**;
- Key **scaling** parameters has been identified;
- **Oscillations** and **limit cycle** property is being characterized.

- **Interplay** between the **two** source of noise is still mysterious;
- Interpretation in terms of biology: possible interpretation as **Intrinsic** and **Extrinsic noise**?
- **Adiabatic reduction** not fully understood. Will some properties such bistable regime be transmitted?
- Analytical results....

References:
 Molecular distributions in gene regulatory dynamics. Mackey MC, Tyran-Kamińska M, Yvinec R. J Theor Biol. 2011 274(1):84-96
 On the Poincaré–Hill cycle map of rotational random walk: locating the stochastic limit cycle in a reversible Schnakenberg model. Vellela M. and Qian H., Proc. R. Soc. 2010 vol. 466 no. 2115 771-78