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

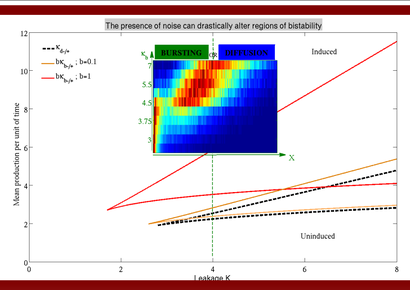
Self-Regulation ⇄ Nonlinear Regulation

White noise ⇄ Two different sources of noise

Using Sample paths simulation

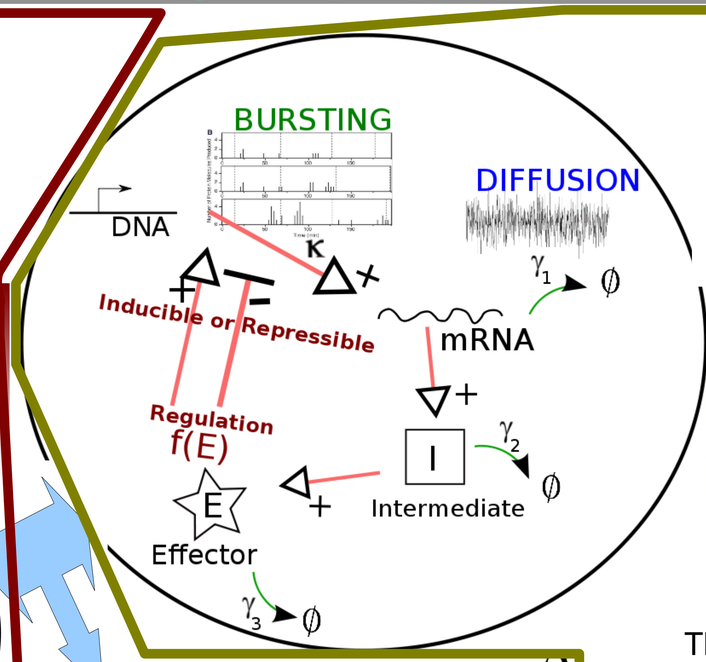
*The **reduced 1-dimensional stochastic model** has been analytically characterized when either one source of noise is present:*

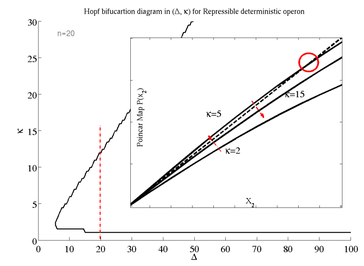
- ✓*Uni/Bimodal asymptotic density in the positive regulation;*
- ✓*Noise-induced bi-stability*
- ✓*Unimodal asymptotic density in the negative regulation.*



Questions that remains:

- **Transient Behaviour?**
- **Difference between the two source of noise?**





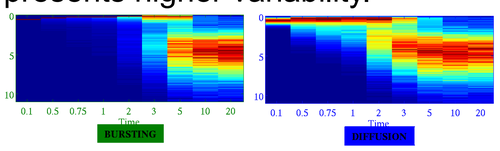
*The **full 3-dimensional deterministic model** is well known.*

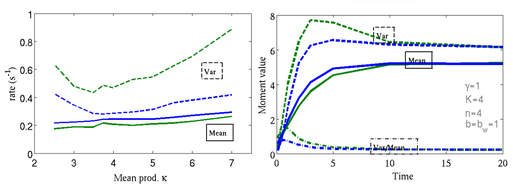
- ✓*Mono/Bistable behaviour*
- ✓*in the positive regulation;*
- ✓*Monostable/Limit cycle in the negative regulation.*

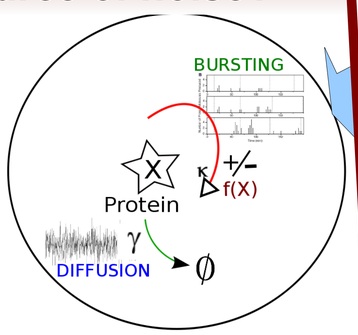
Questions that remains:

- **Adiabatic elimination when noise is present?**
- **Oscillation property when noise is present in the negative regulation?**

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

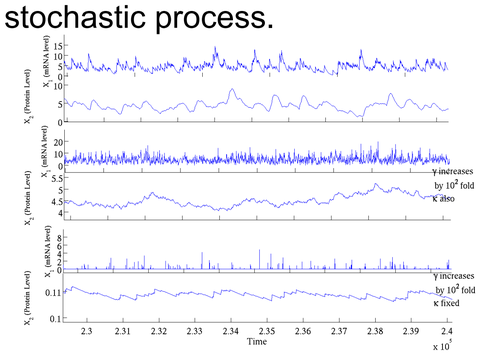




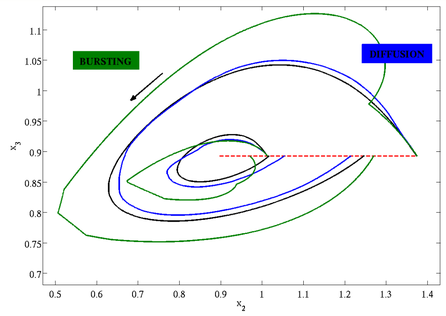


The **variance** converges slower and the **mean** value converges faster for the diffusion noise.

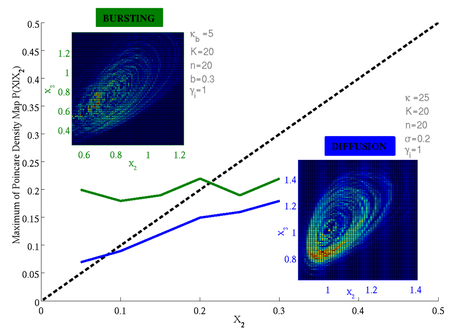
Adiabatic elimination. Depending on the scaling chosen, one can obtain different stochastic process.



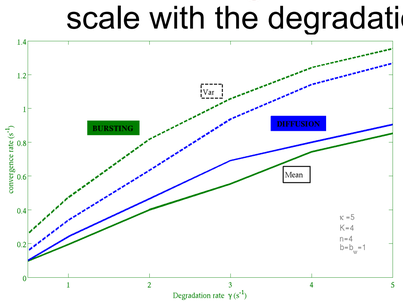
The **stochastic limit cycle** may be identified through a **stochastic Poincaré map**

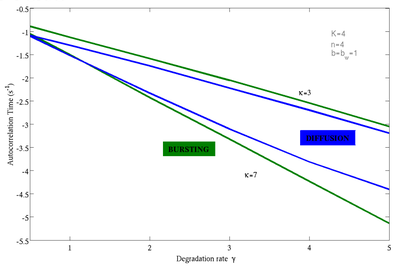


Asymptotic density, Power Spectra, And Poincaré Map Gives different information. The latter may be the most reliable to characterize **stochastic oscillations**

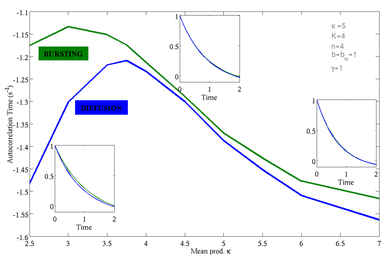


Both **convergence rate** and **autocorrelation time** scale with the degradation rate

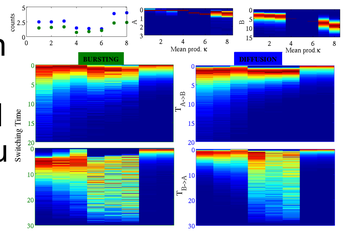




The bursting noise gives rise to higher or slower **autocorrelation time** depending on the respective value of the mean production rate and the degradation rate.

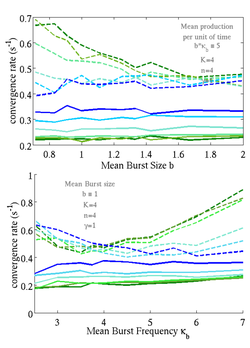


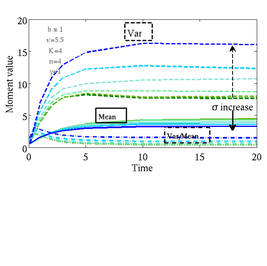
The diffusion model **switch** more an faster, specifically due to a non-refractory time in the bursting model while going from a high to a low valu (the bursting noise is asymmetric)

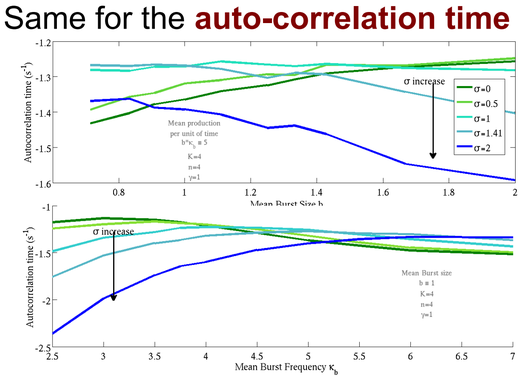


When both noise are present, the strength of the noise governs mainly the **convergence rate** of the **mean**. For the **variance**, we can observe non-monotonic behaviour and more complex dependencies of the two source of noise.

Same for the **auto-correlation time**







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