Noise-induced rhythmicity in an ensemble of circadian oscillators

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Content

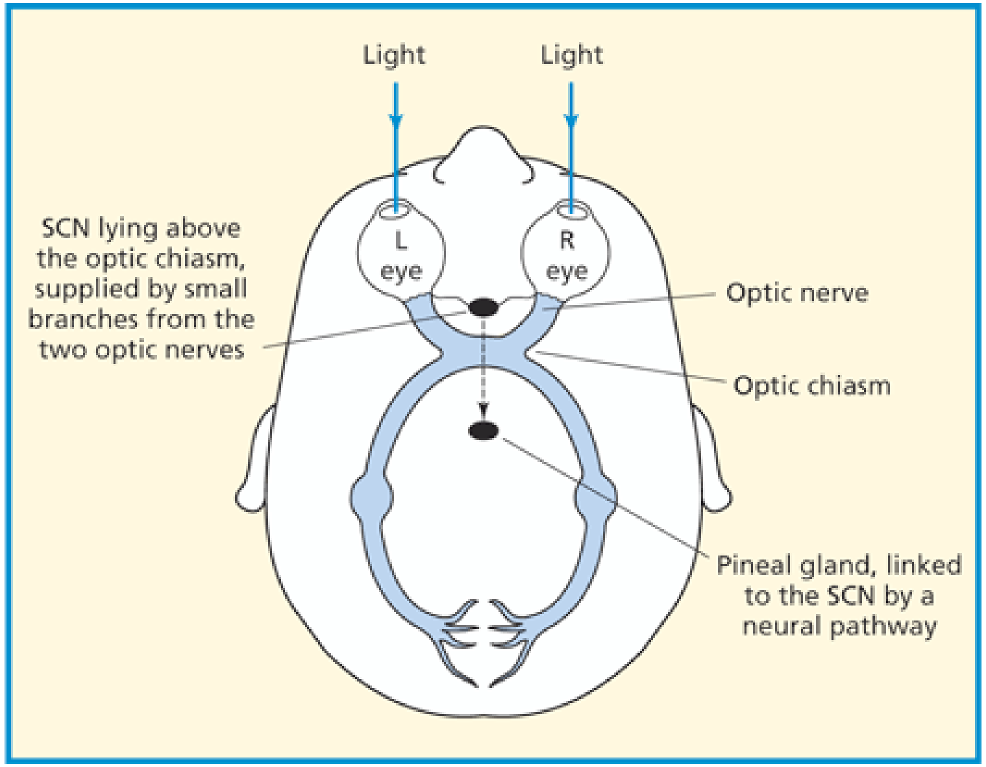
The normal Circadian Rhythm

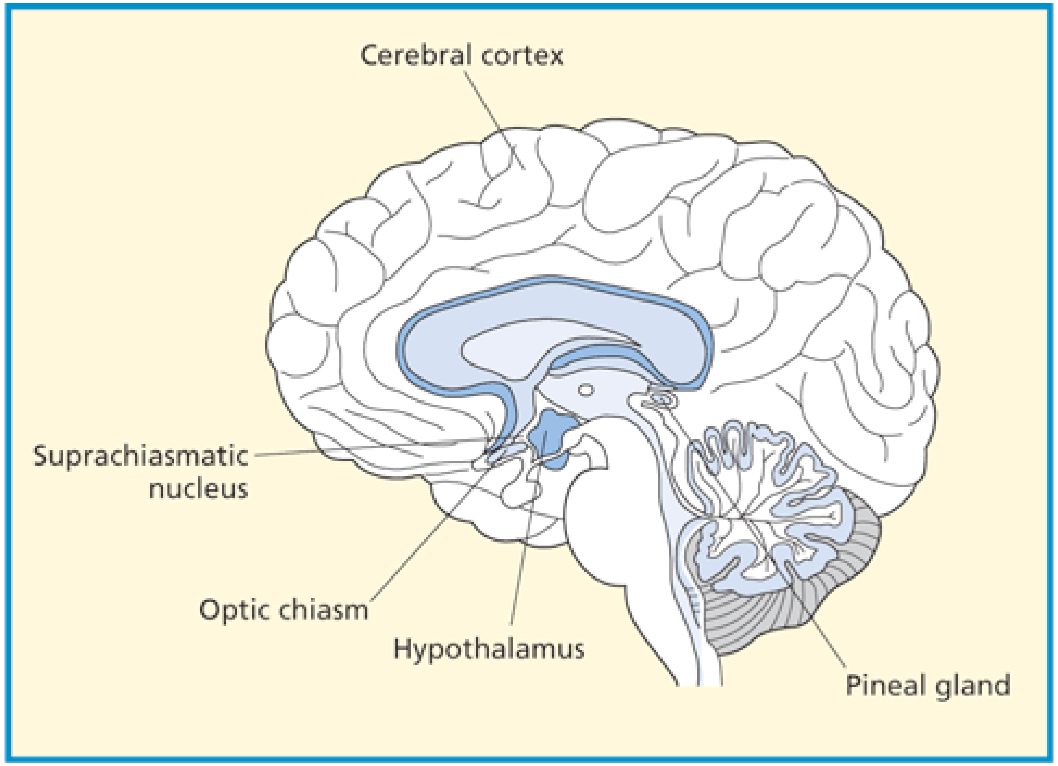
a roughly-24-hour cycle in the biochemical, physiological or behavioral processes of living beings

www.fotocommunity.de

The circadian pacemaker

The Suprachiasmatic Nucleus

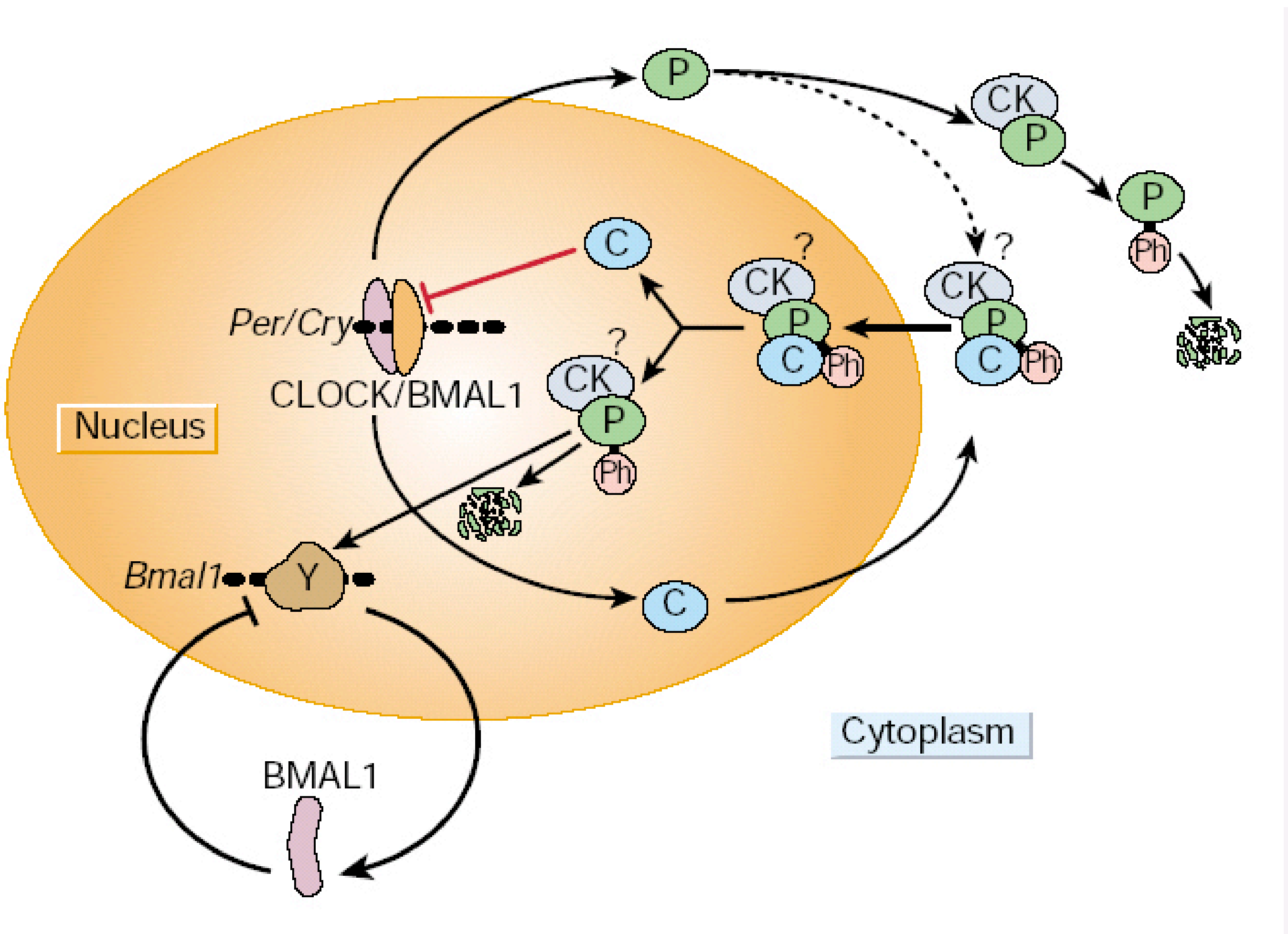




www.a-levelpsychology.co.uk/online/a2

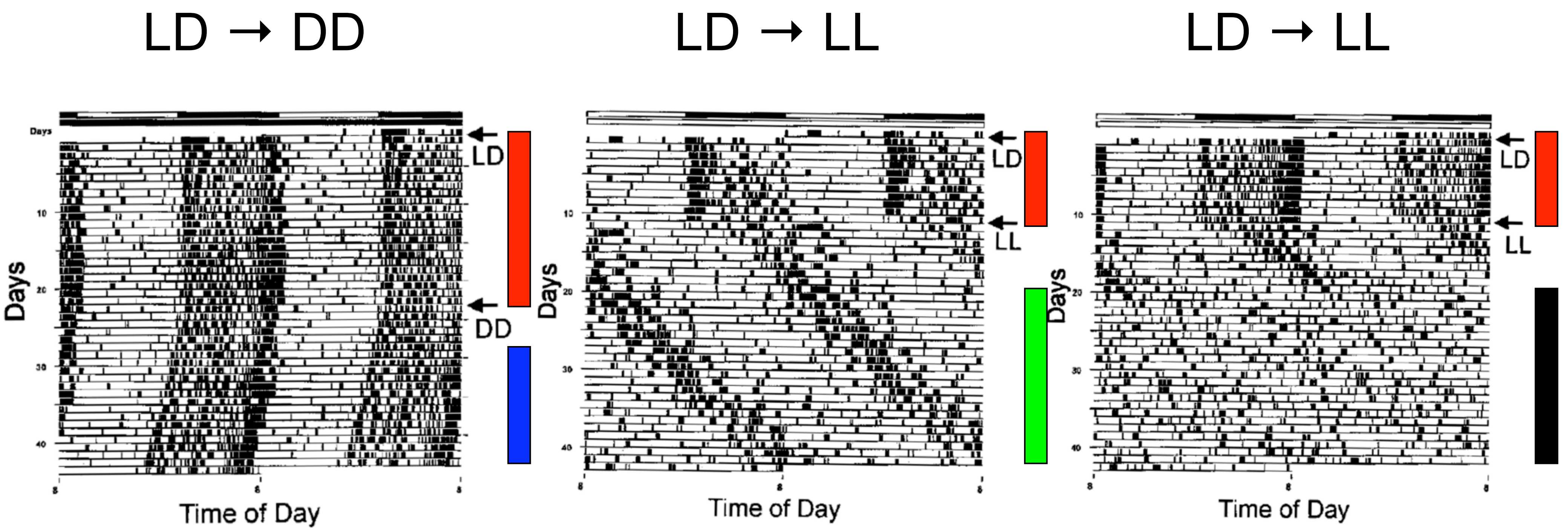
The circadian pacemaker

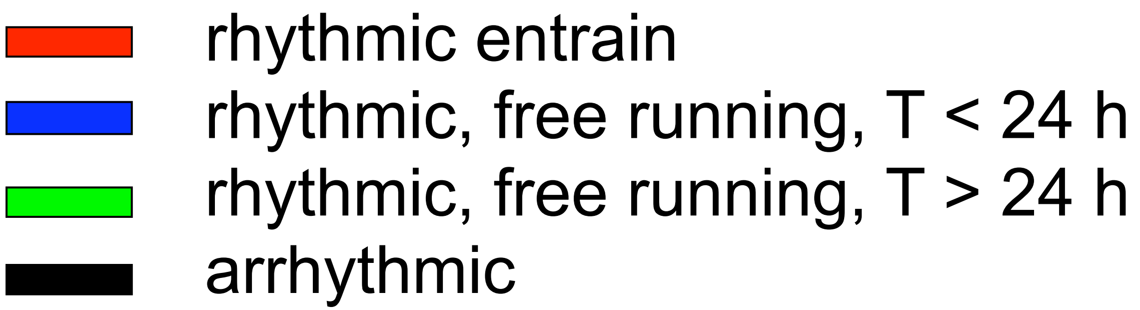
Mammalian circadian clock



S. Panda, J.B. Hogenesch and S.A. Kay,
Nature, 2002, **417**, 329-335

The transitions

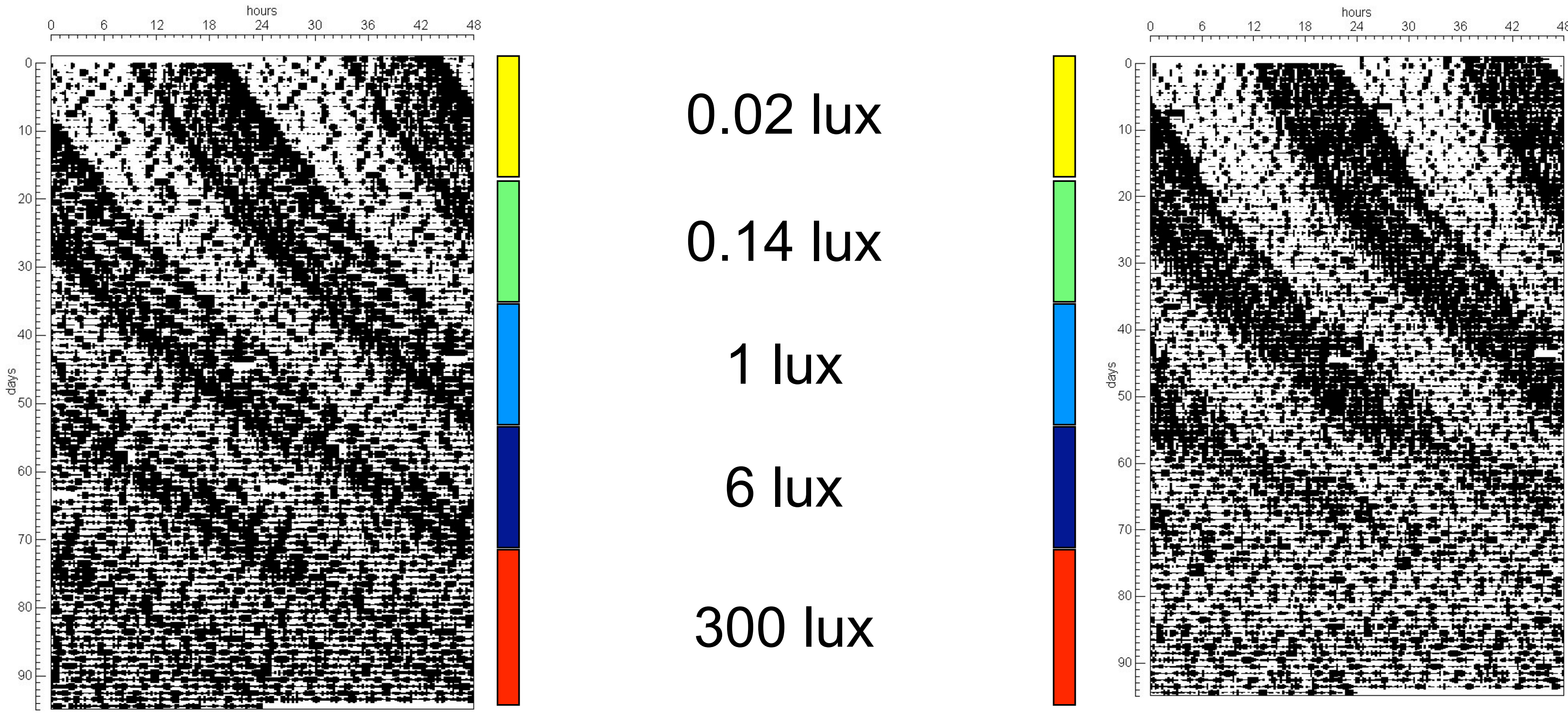




T. Moriya et al., Journal of Neuroscience Research, 2000, **60**, 212-218

The transitions in experiments

stepwise light increase



Trinitat Cambras Riu and Antoni Díez Noguera, Department of Physiology, Faculty of Pharmacy, University of Barcelona, Spain

The transition on the genetic level

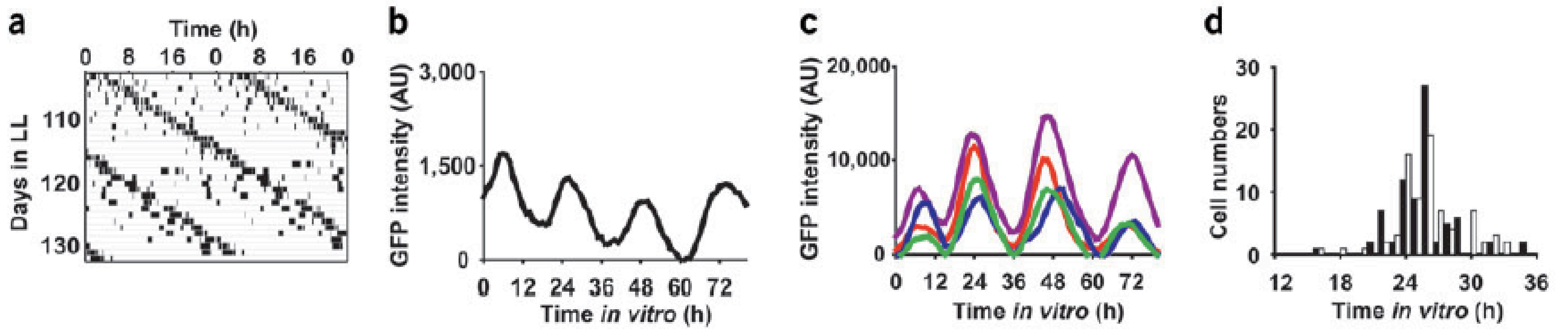


Figure 2 Behavioral and SCN rhythms from a rhythmic constant light–treated mouse. (**a**) Actogram of wheel running activity from a mouse that remained rhythmic in LL. (**b**) Time-lapse SCN *Per1:GFP* fluorescence signals. (**c**) Individual SCN neuronal *Per1:GFP* rhythms from SCN in **b**. (**d**) Peak time histograms of individual neuronal rhythms. $n = 154$ cells.

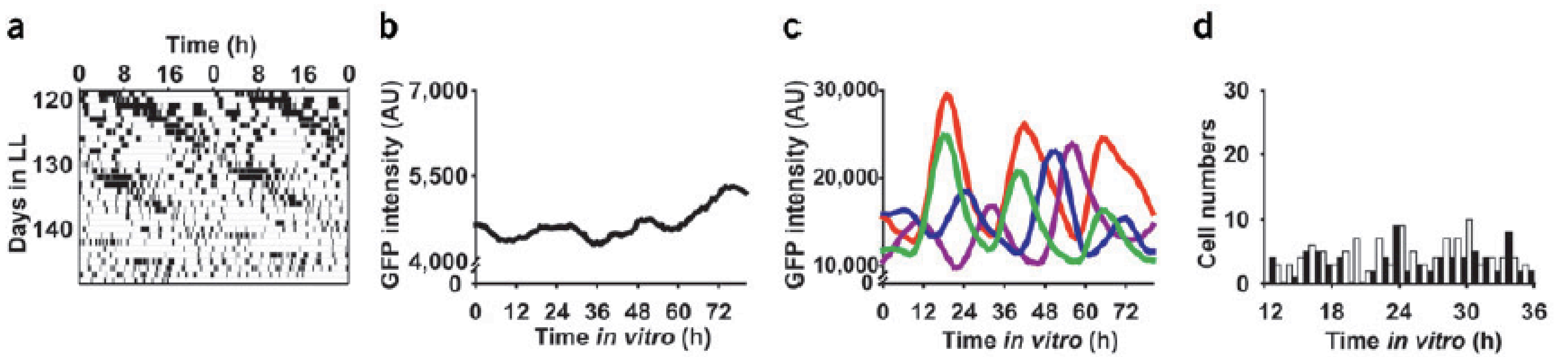


Figure 1 Behavioral and SCN rhythms from an arrhythmic constant light–treated mouse. (**a**) Actogram of wheel running activity. Black marks indicate wheel revolutions. Note loss of temporal organization in latter portion of record. (**b**) Time-lapse SCN *Per1:GFP* fluorescence signals for 3.5 d *in vitro*. (**c**) Individual SCN neuronal *Per1:GFP* rhythms from SCN in **b**. Four representative cells are plotted for clarity (colored lines). (**d**) Peak time histograms of individual neuronal rhythms. Peak times of neurons in the right SCN are plotted with black bars, whereas those in the left SCN are plotted with open bars. Histograms for this and the following figures are for hours 12–36 *in vitro*. $n = 193$ cells. Animal care and use was reviewed and approved by the Vanderbilt University IACUC.

H. Ohta, et al., Nature Neuroscience, 2005, **8**, 267-269

From the nature to the model

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- Each genetic oscillator is self-oscillatory
- Light influences the coupling
- The circadian rhythm is a joint effect of all oscillators

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- Individual elements remain in the oscillatory regime

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- Individual elements remain in the oscillatory regime
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- Coupling strength is the bifurcation parameter and can be effected by light
- Can noise restore a rhythm in the arrhythmic state?

The modified Goodwin model

$$
\begin{aligned}
\frac{dX_i}{dt} &= \nu_1 \frac{K_1^n}{K_1^n + Z_i^n} - \nu_2 \frac{X_i}{K_2 + X_i} + \nu_c \frac{KV_i}{K_c + KV_i} && \text{clock gene} \\
\frac{dY_i}{dt} &= k_3 X_i - \nu_4 \frac{Y_i}{K_4 + Y_i} && \text{clock protein} \\
\frac{dZ_i}{dt} &= k_5 Y_i - \nu_6 \frac{Z_i}{K_6 + Z_i} && \text{active protein} \\
\frac{dV_i}{dt} &= k_7 X_i - \nu_8 \frac{V_i}{K_8 + V_i} - \eta(V_i - (Q_0 + \zeta(t))F) && \text{neurotransmitter} \\
F &= \frac{1}{N} \sum_{i=1}^{N} V_i
\end{aligned}
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$$F = \frac{1}{N}\sum_{i=1}^{N} V_i$$

$\nu_{1,2,4,6,8}$ and $k_{3,5,7}$ individually rescaled by τ_i

τ_i normal distributed with diversity σ_τ

→ individual eigen-frequencies

The measures

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$$R_{syn} = \frac{\langle \bar{Y}^2 \rangle - \langle \bar{Y} \rangle^2}{\frac{1}{N}\sum_{i=1}^{N}(\langle Y_i^2 \rangle - \langle Y_i \rangle^2)} = \frac{Var(\bar{Y})}{Mean_i(Var_t(Y_i))}$$

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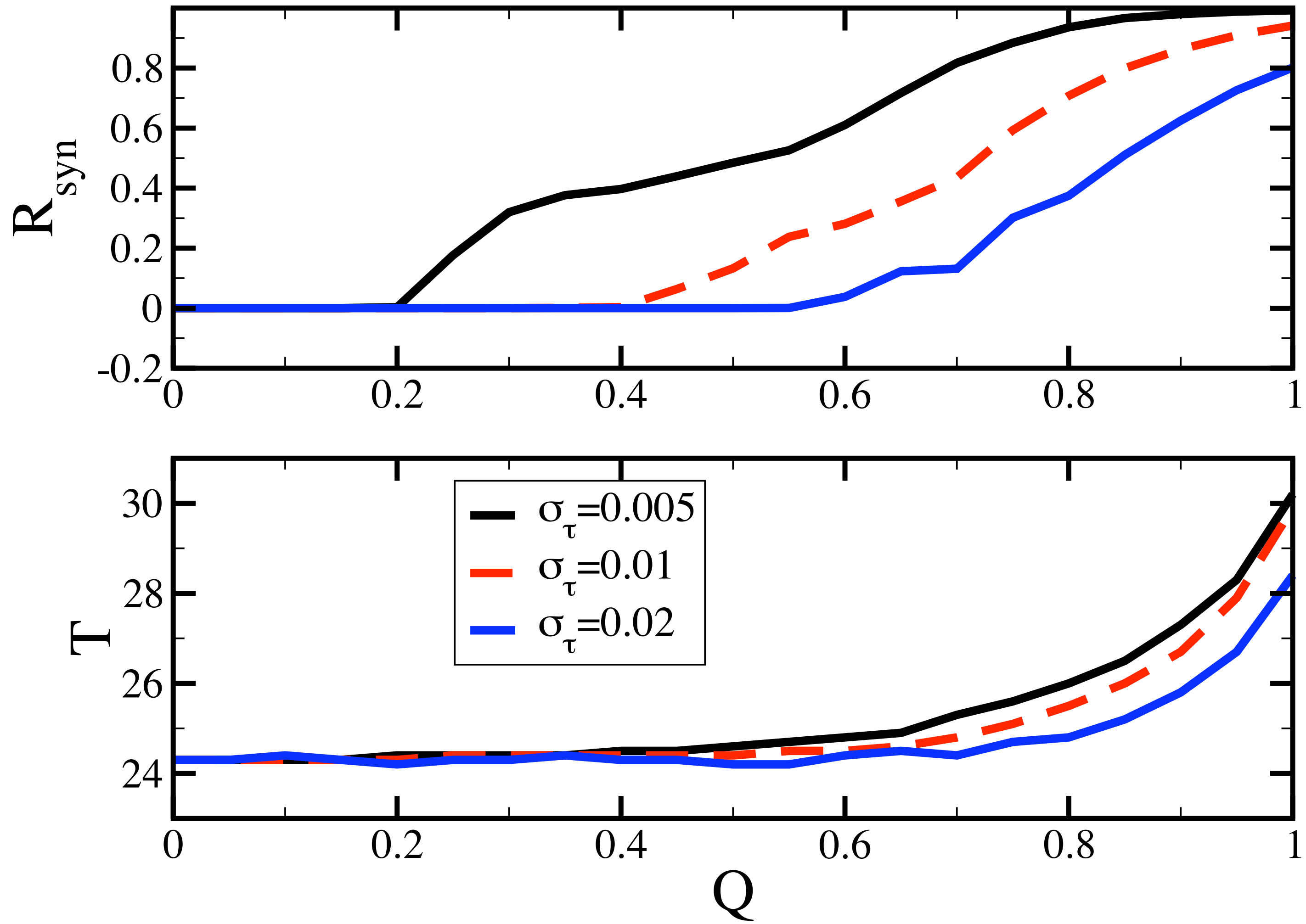
- The coherence measure:

the decay time of the envelope of the autocorrelation function of the overt rhythm

The transition

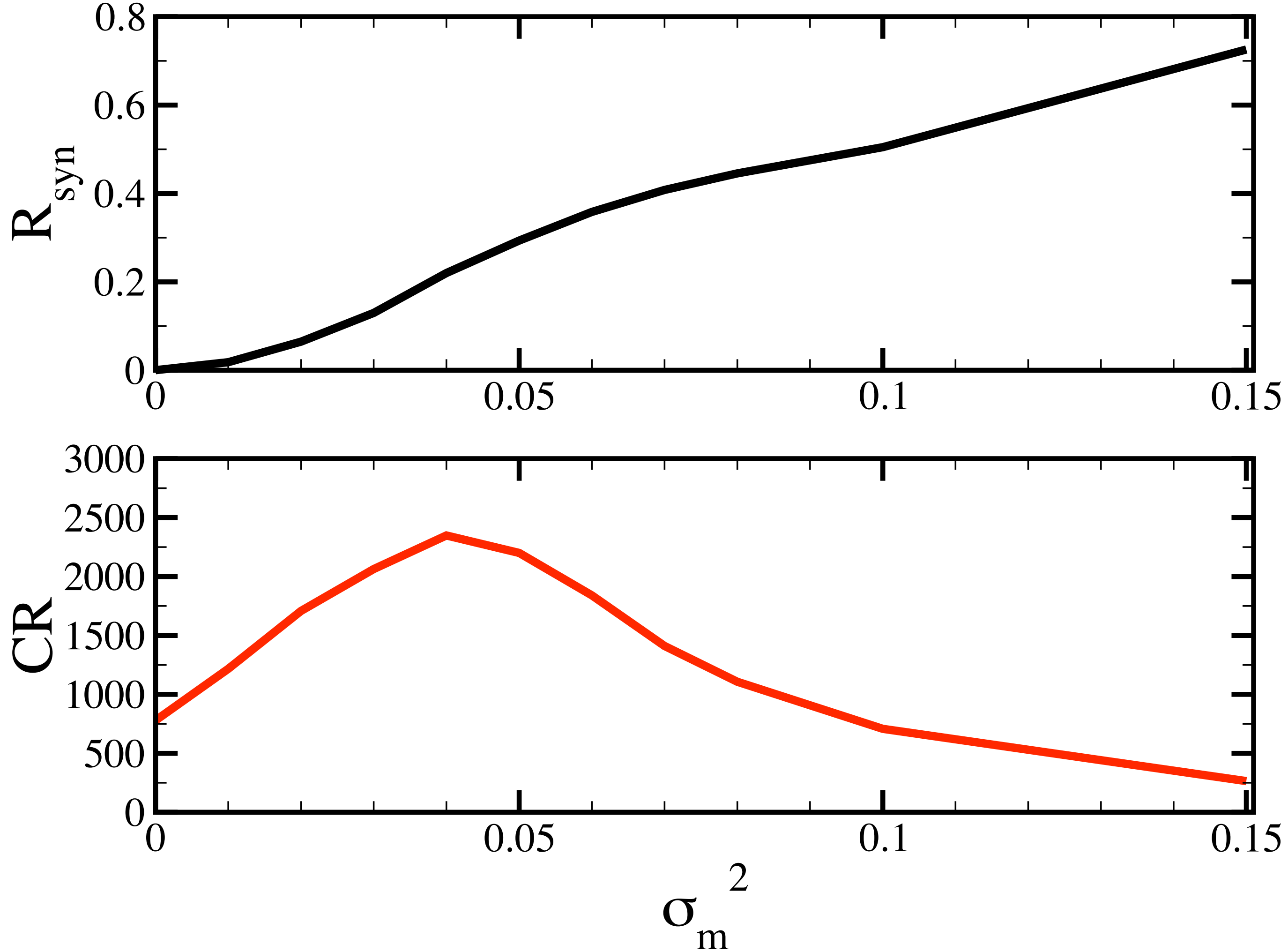
arrhythmic ↔ rhythmic

unsynchronized ↔ synchronized



The Coherence Resonance
Noise-induced rhythmicity

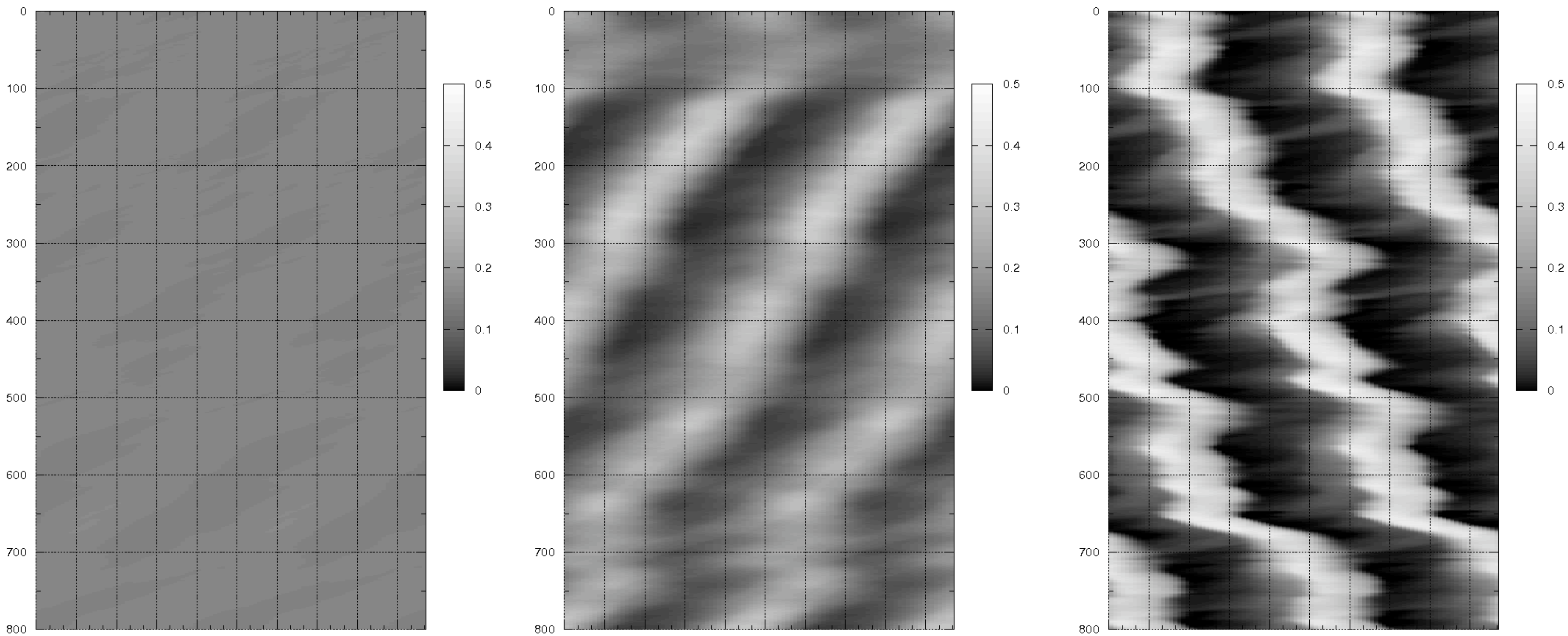
$\sigma_\tau = 0.005$, $Q_0=0.15$



CR in Double plotted actograms

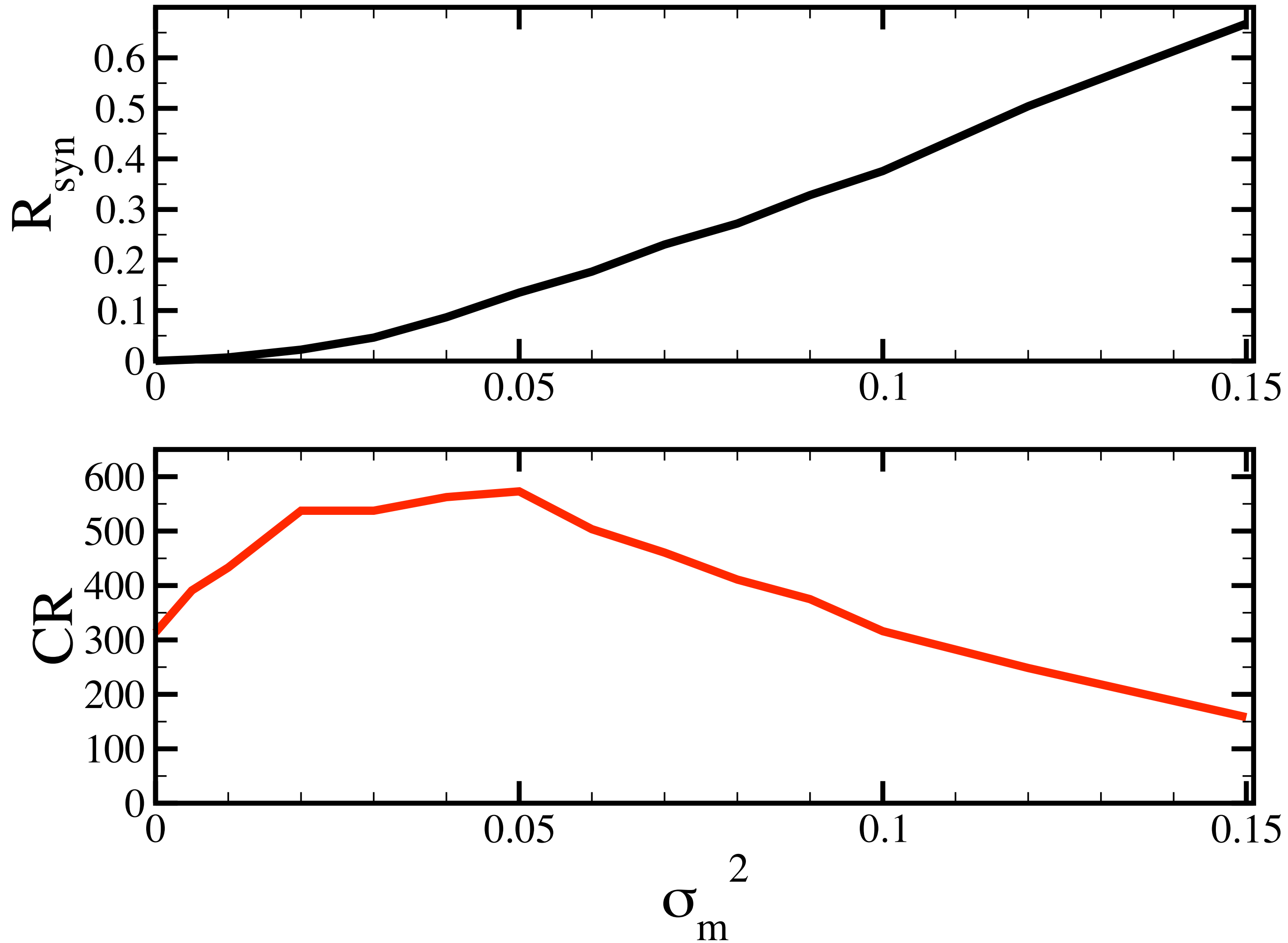
$\sigma_\tau = 0.005$, $Q_0=0.15$

$\sigma^2_m = 0.0$ $\sigma^2_m = 0.04$ $\sigma^2_m = 0.1$



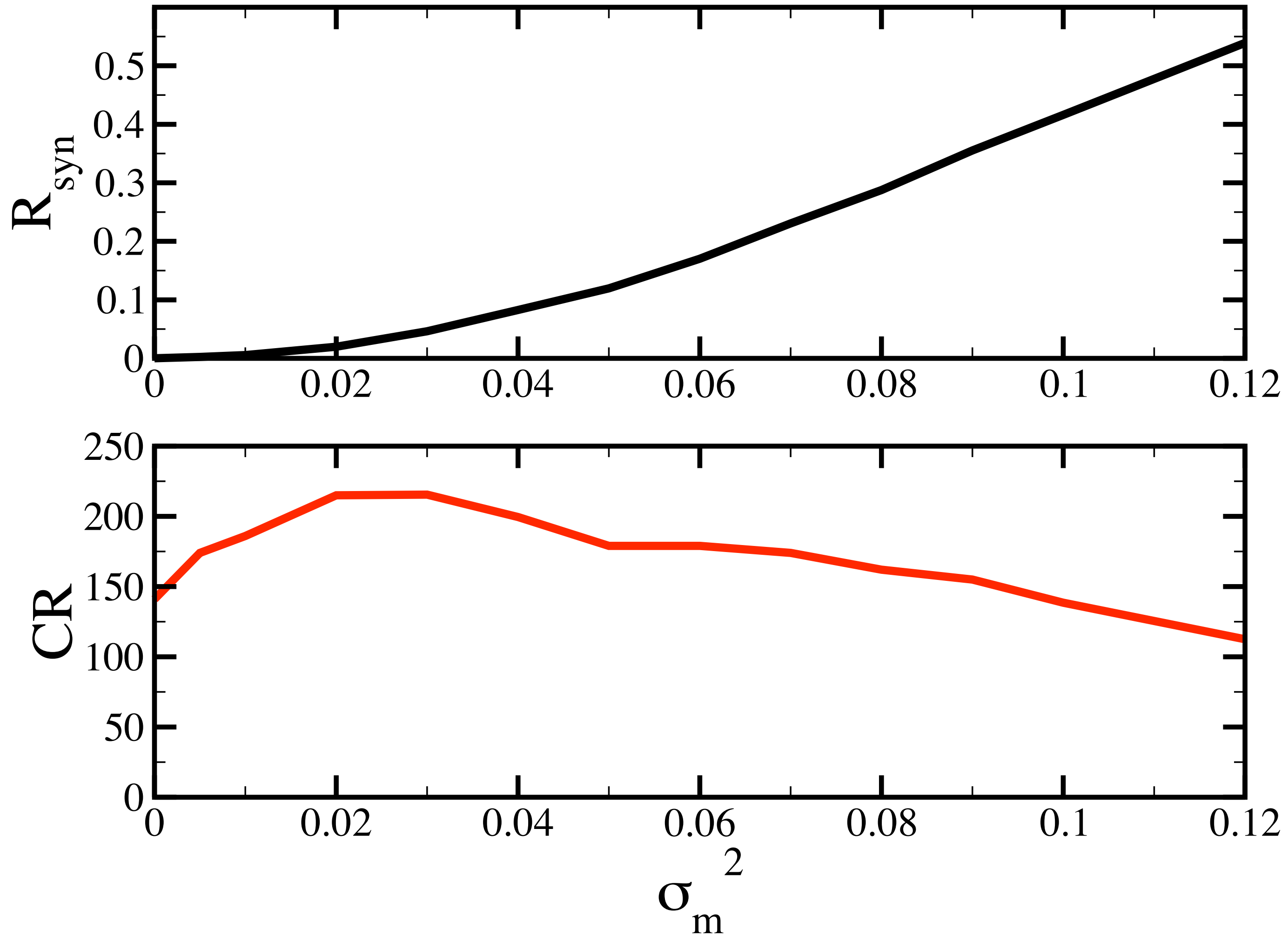
The Coherence Resonance
Noise-induced rhythmicity

σ_τ = 0.01, Q_0=0.25



The Coherence Resonance Noise-induced rhythmicity

$\sigma_\tau = 0.02$, $Q_0=0.4$



Conclusion

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- A large ensemble is required
- A kind of Coherence Resonance / Stochastic Coherence
- Noise is multiplicative and affects the coupling strength

Open Problem on Noise

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Open Problem on Noise

- CR is very sensitive to system properties
- The hypothesis of light-dependent coupling is critical for CR in the model
- Would a hypothetical noise-enhanced rhythmicity in *in vivo* experiments be sufficient to strengthen the hypothesis of light-dependent coupling?

Acknowledgements

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Centre for Research in Theoretical Chemistry, Parc Científic de Barcelona, University of Barcelona, Spain

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Thank you for your attention and interest