

# Hybrid Gene Networks: a new Framework and a Software Environment

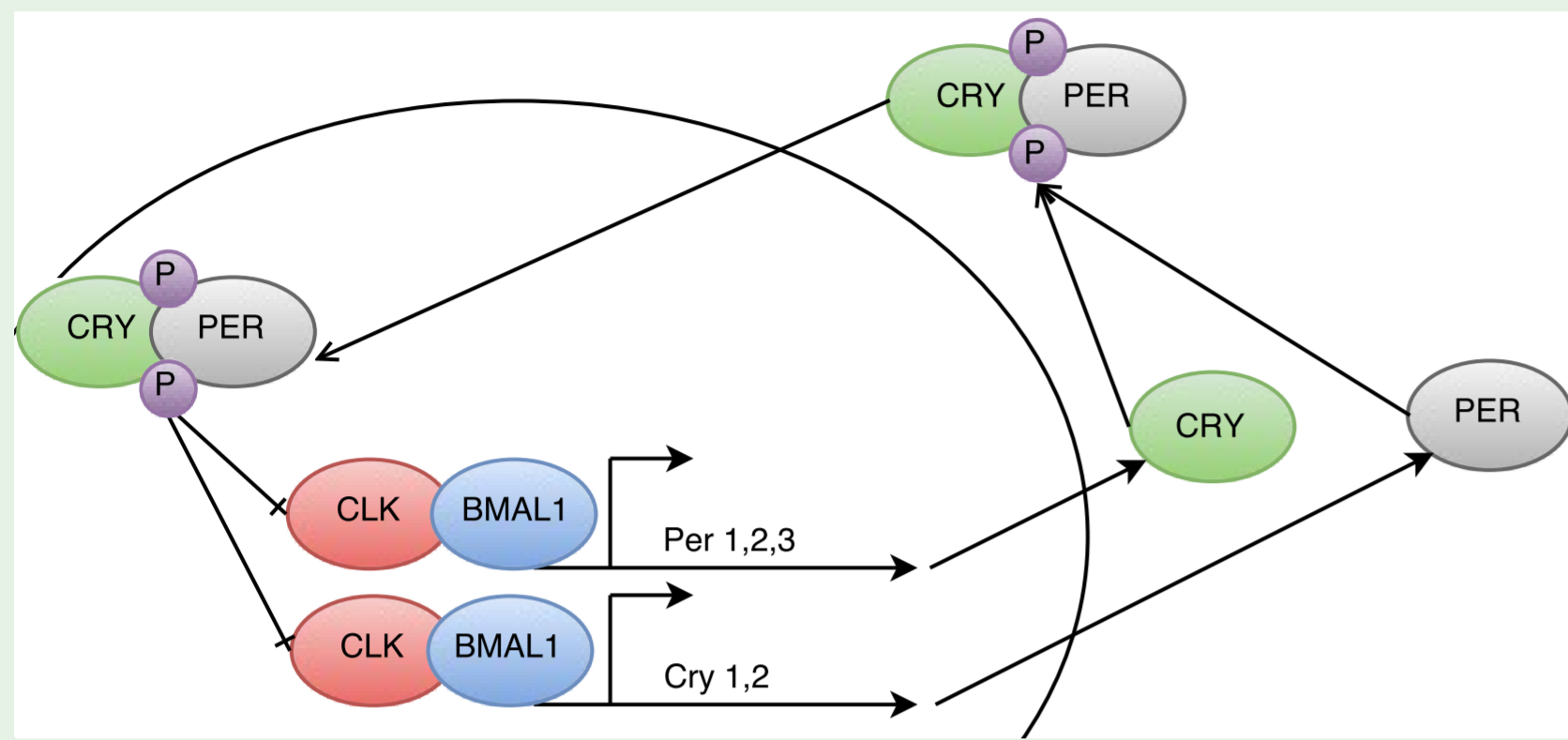
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The **modelling framework of René Thomas** [Tho73] allows one to design abstract models of gene regulatory networks. In this formalism, time is only represented by the succession of discrete events. However, for numerous gene networks, the delay between two events is of primary interest like for the circadian cycle. This poster introduces a hybrid Thomas' formalism, allowing to take into account **chronometrical information**, and presents a first version of a user-friendly software platform named **HyMBioNet**. We illustrate our approach on an extremely simplified network of the circadian clock.

## 1 - The Molecular Circadian Clock

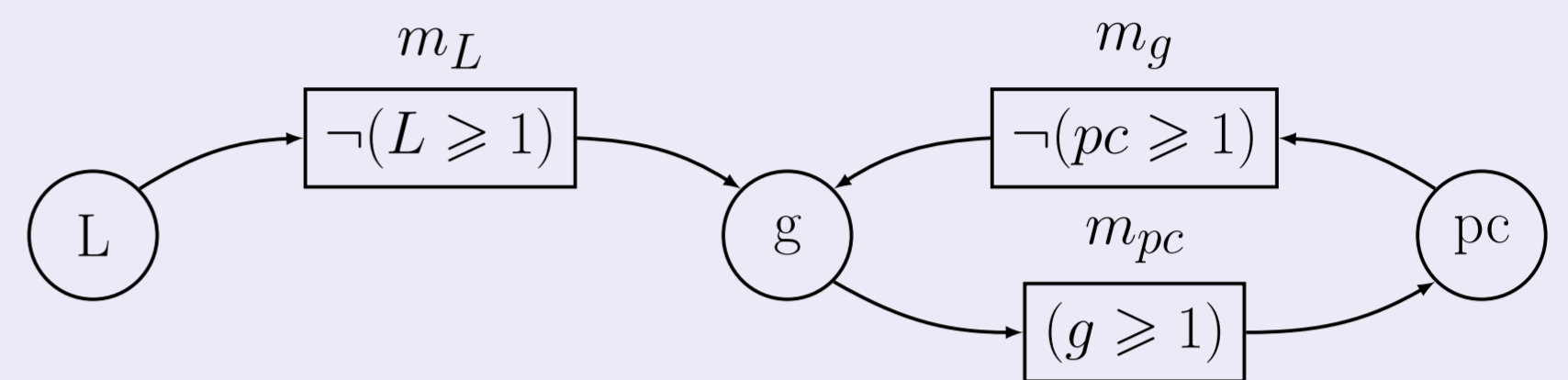
The circadian clock relies on a gene network that oscillates with a 24 h period and regulates many physiological processes. Light is a universal synchronizer (Zeitgeber) to the external LD cycle in all species.



## 2 - Hybrid Gene Regulatory Network of Circadian Clock

Simplified network of circadian clock [CBD<sup>+</sup>12] :

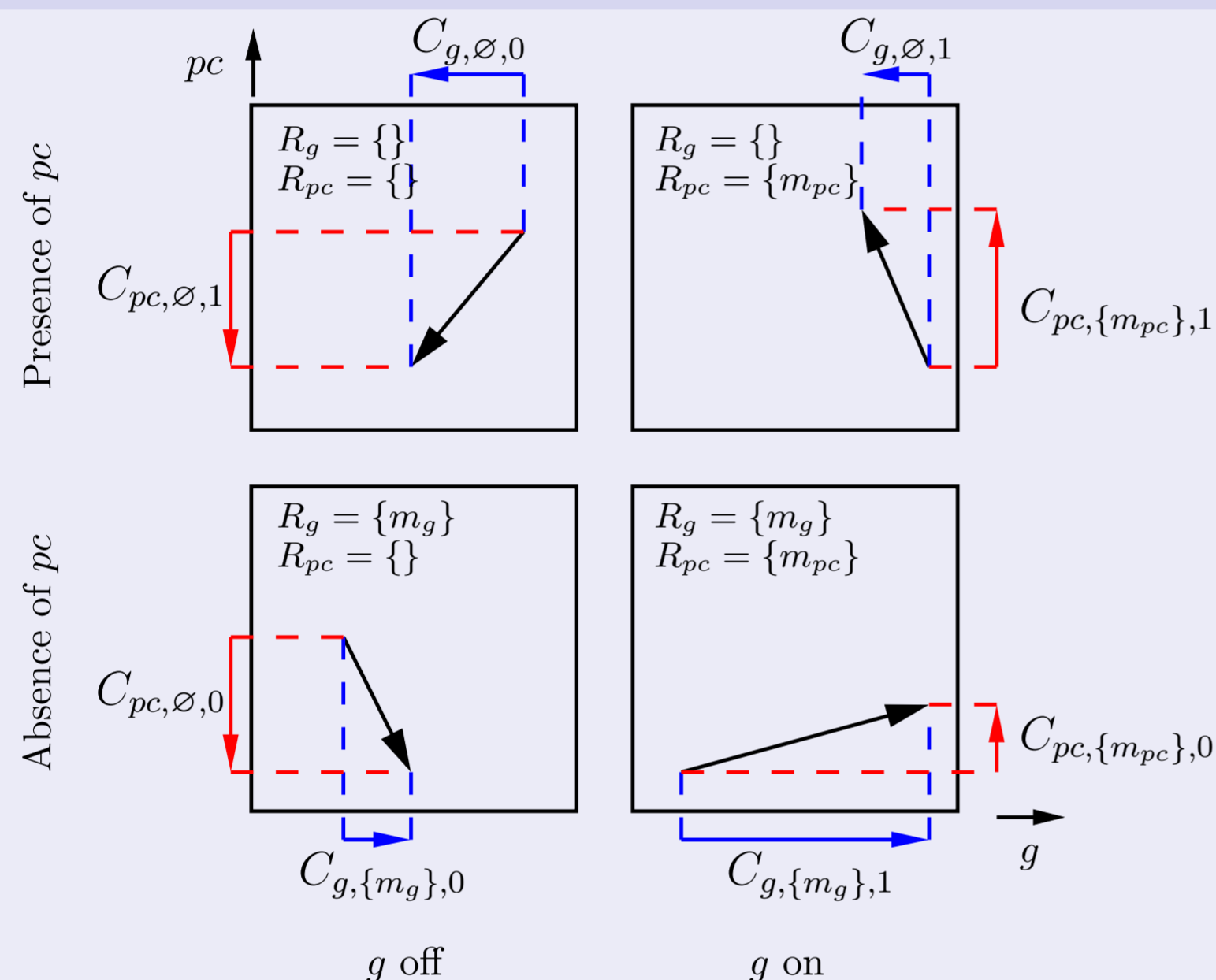
- $g$  : *per* and *cry* genes
- $pc$  : phosphorylated PER-CRY
- $L$  : Light (zeitgeber)
- Circles : variables of the system
- Rectangles : multiplexes (encode the conditions of interactions)



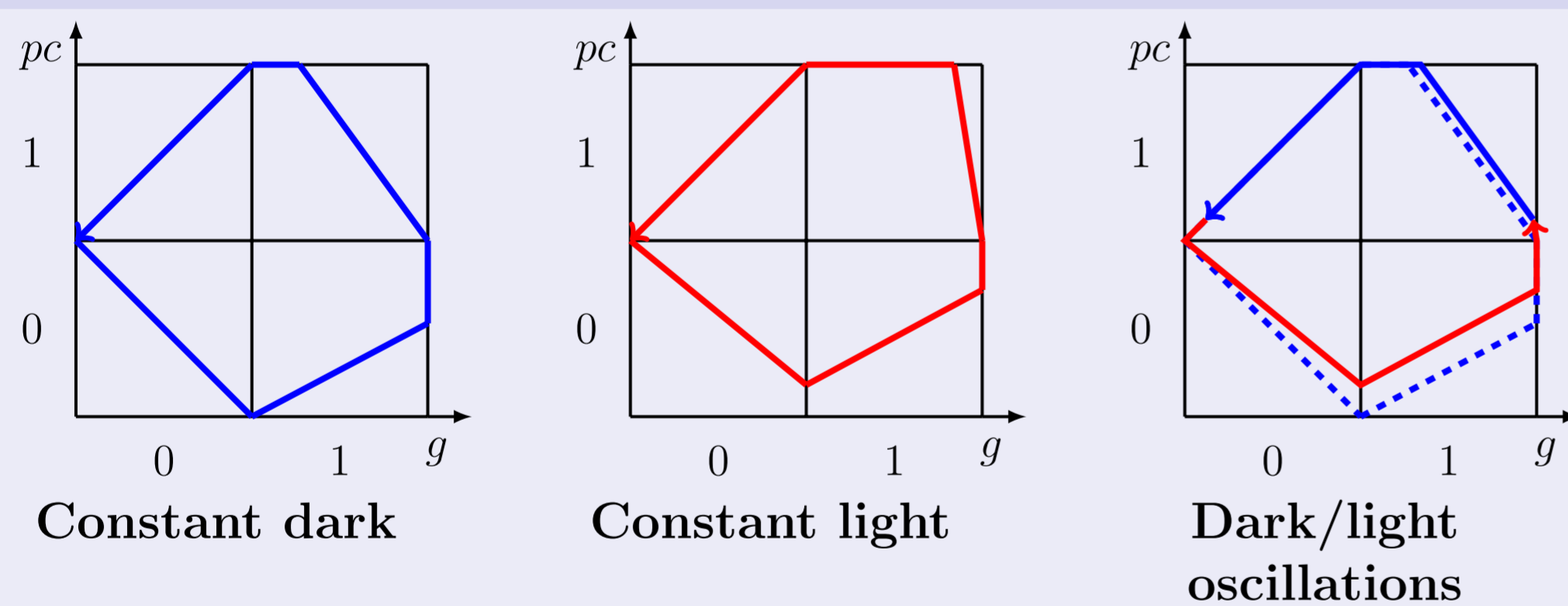
A **celerity**  $C_{v,\omega,n}$  represents the speed of a variable  $v$  inside a discrete state. It is indexed by :

- a variable of the system  $v$ .
- a set of resources,  $\omega$ : the set of multiplex predecessors of  $v$  whose formula is evaluated to true.
- a discrete level of  $v$ ,  $n$ .

## 3 - Dynamics of Hybrid Gene Regulatory Network



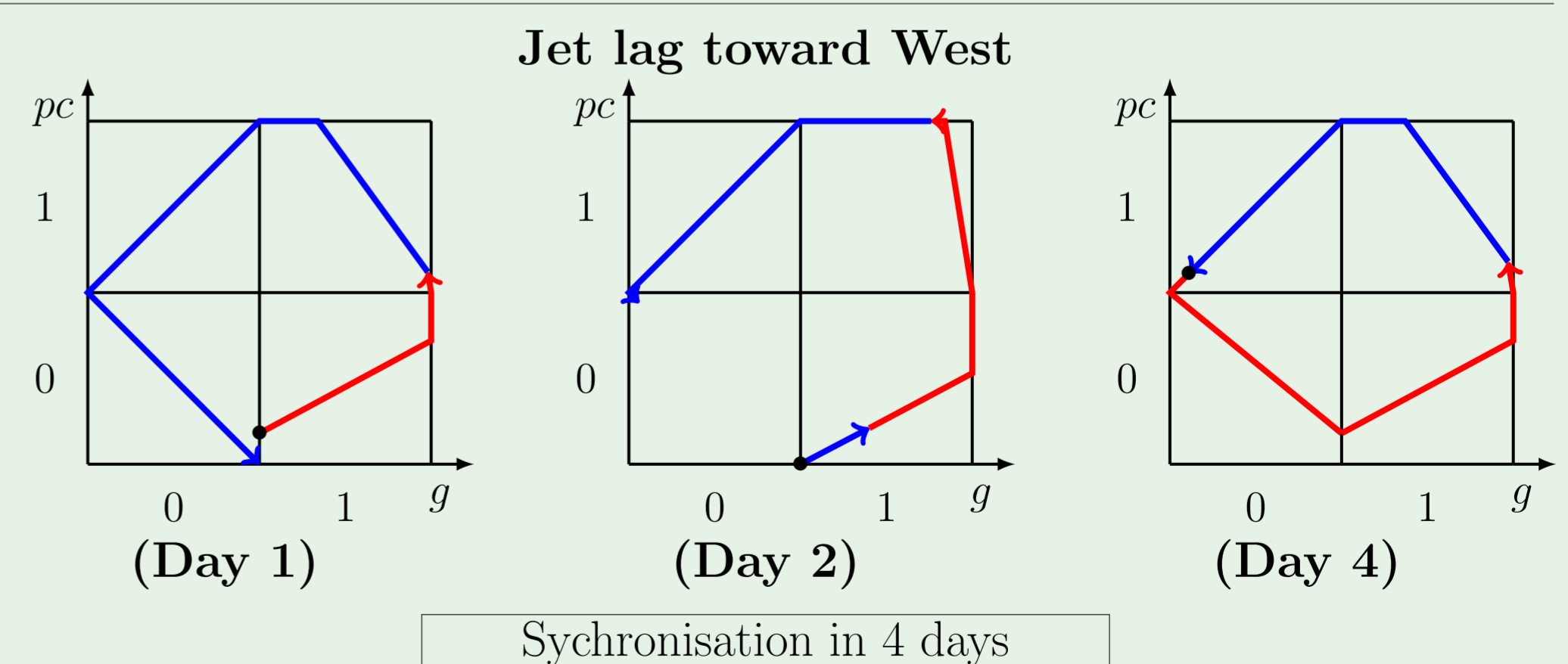
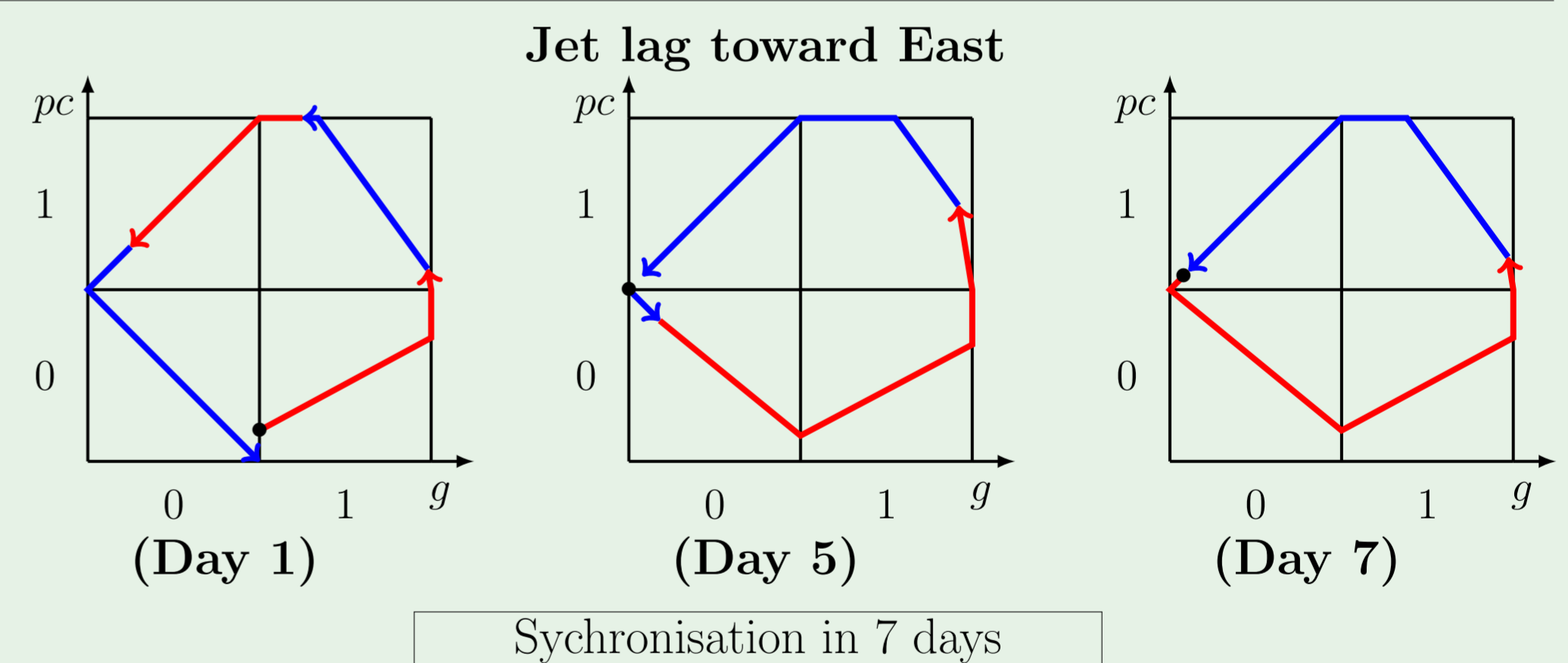
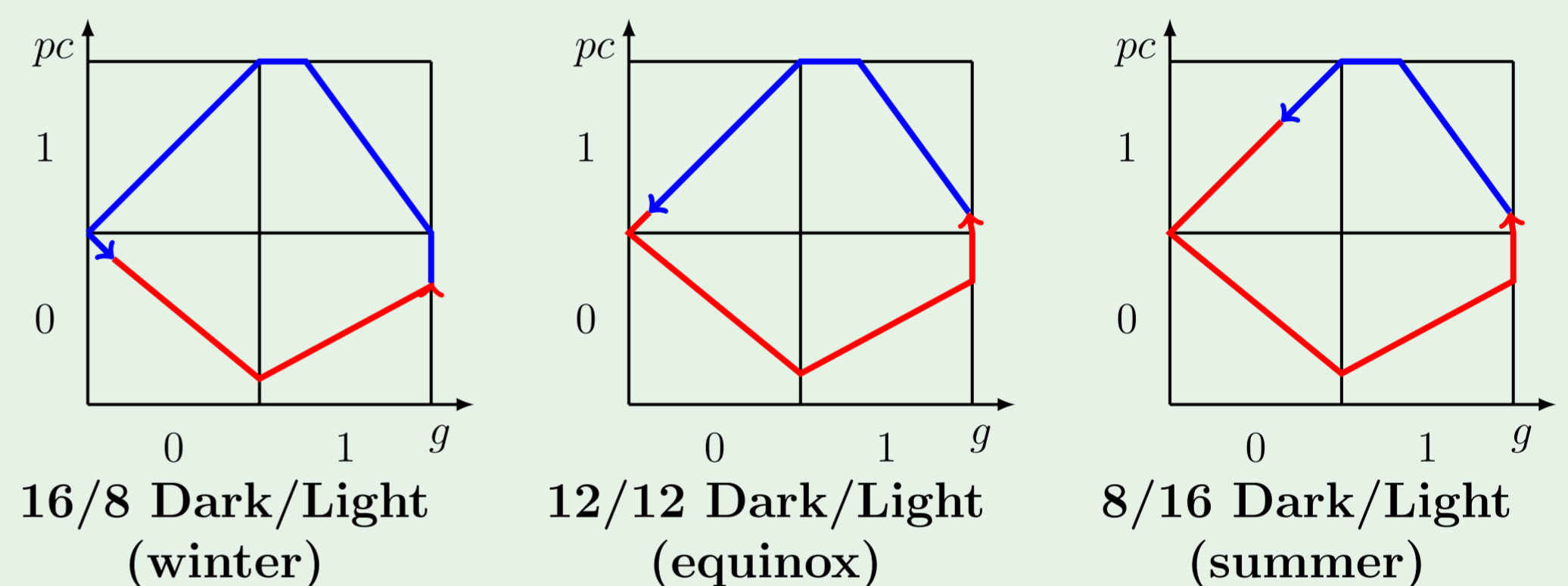
## 4 - Application to the Circadian Clock



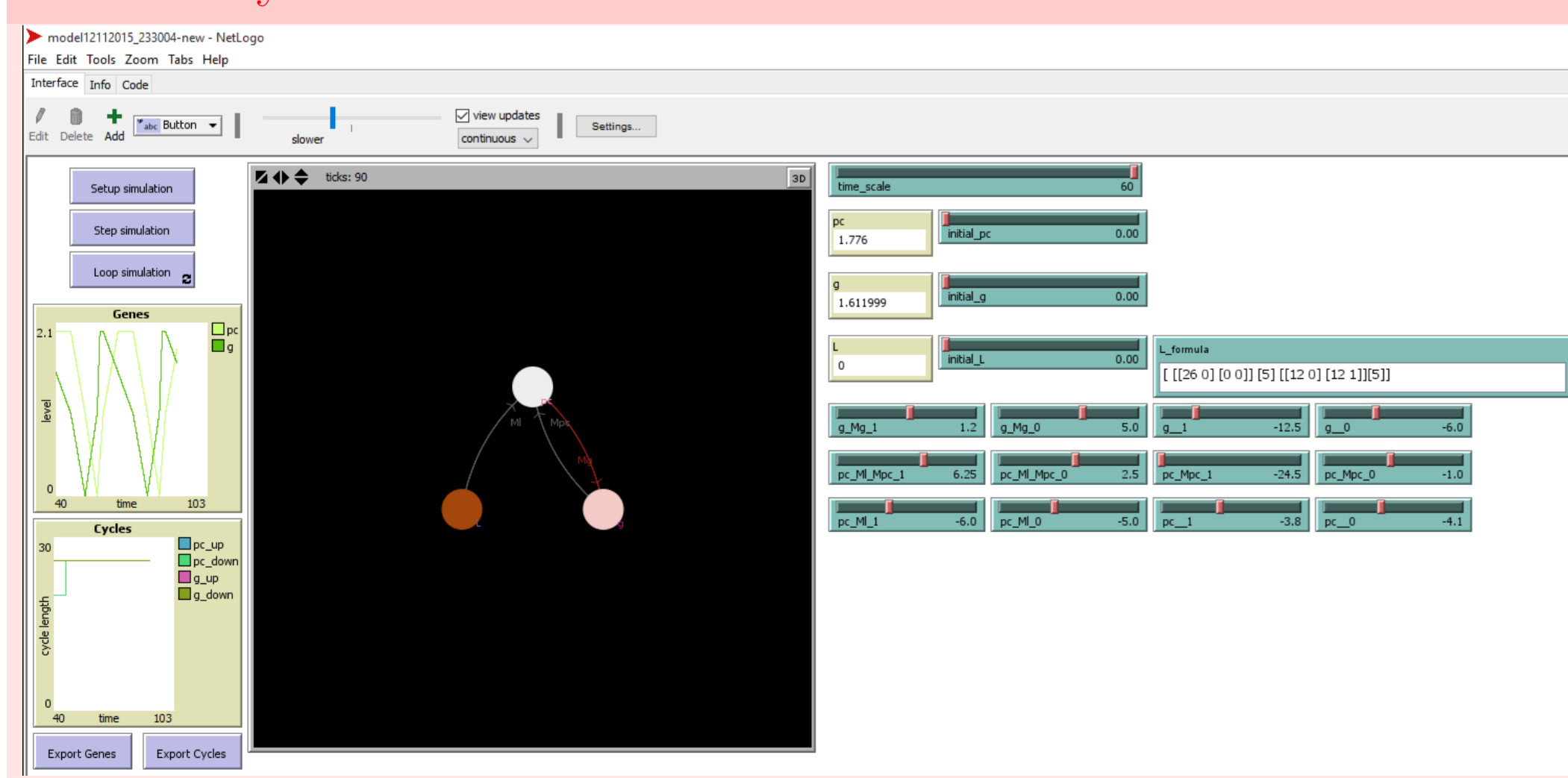
- **Constant dark** : sustained oscillations. The presence of a sliding on a boundary is the only one condition to obtain a limit cycle [CCBE16].
- **Constant light** : Very long period.
- **Dark/light oscillations** : The light change the trajectory and the oscillations get a period of 24h.

## 5 - Simulations

In this frame, all figures represent the trajectory of the system in 24 hours.



## 6 - The HyMBioNet Software



## References

- Jean-Paul Comet, Gilles Bernot, Aparna Das, Francine Diener, Camille Massot, and Amélie Cessieux. Simplified models for the mammalian circadian clock. *Procedia Computer Science*, 11(0):127 – 138, 2012. Proceedings of the 3rd International Conference on Computational Systems-Biology and Bioinformatics.
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- René Thomas. Boolean formalization of genetic control circuits. *Journal of Theoretical Biology*, 42(3):563–585, 1973.