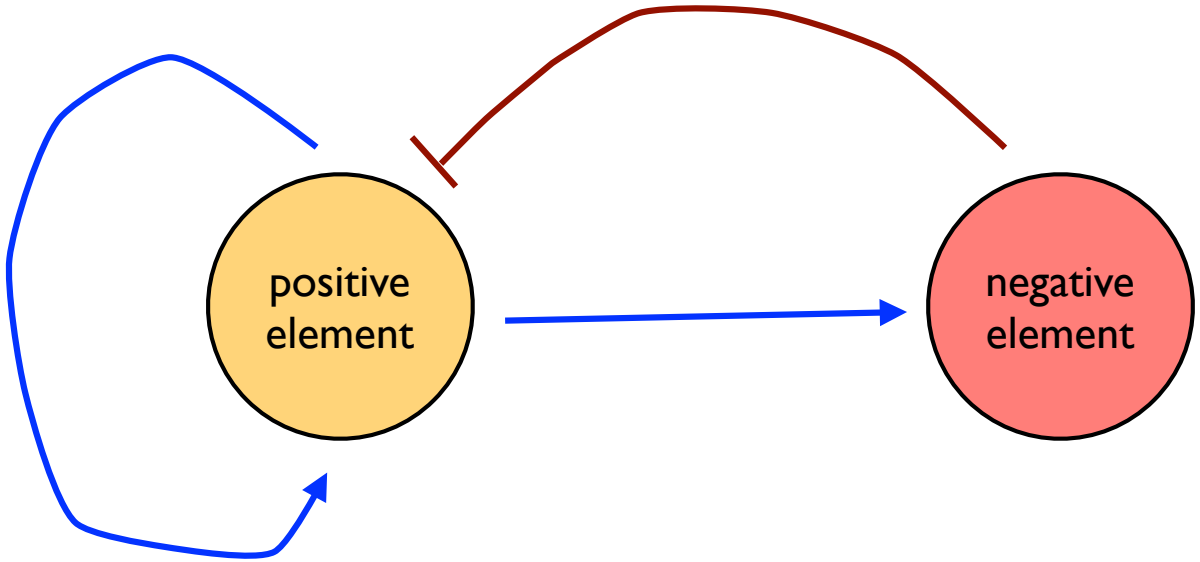
Relaxation oscillators are selected for their robustness

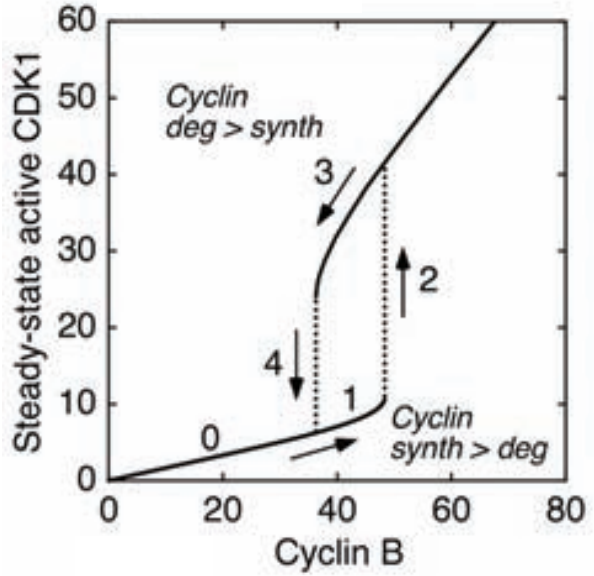
Circadian networks have a core structure of negative *and* positive feedbacks



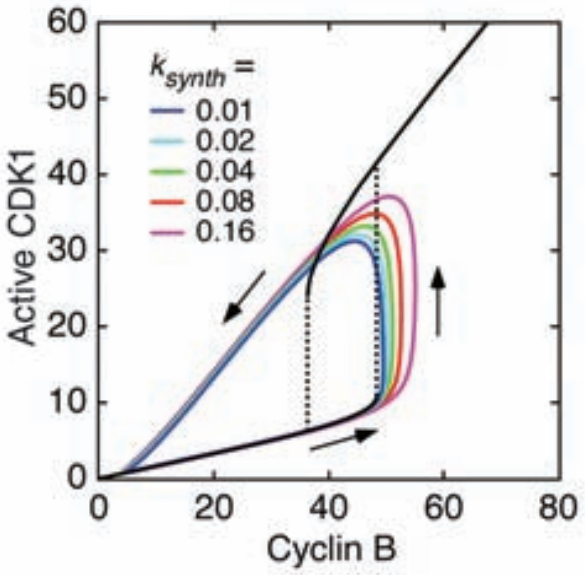
Why?

From Barkai & Leibler 2000 and Dunlap 1999

Relaxation oscillators operate around the hysteresis loop of an underlying, former bistability



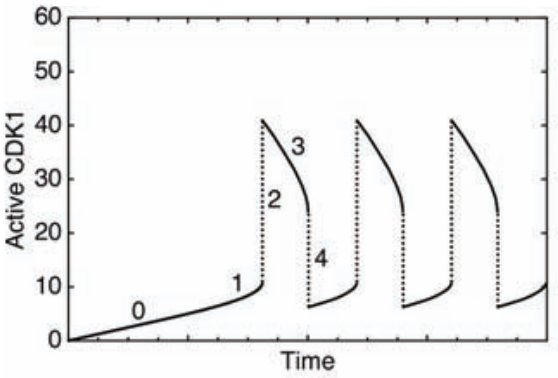
Steady-state response with only positive feedback has hysteresis.



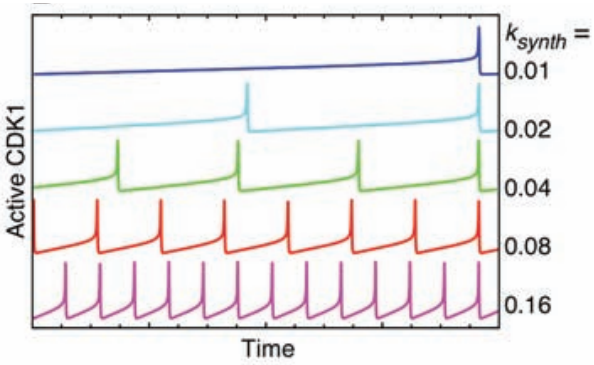
Relaxation oscillations occur with additional negative feedback.

A model of the cell cycle

Levels of CDK1 as cyclin B is slowly and periodically changed.

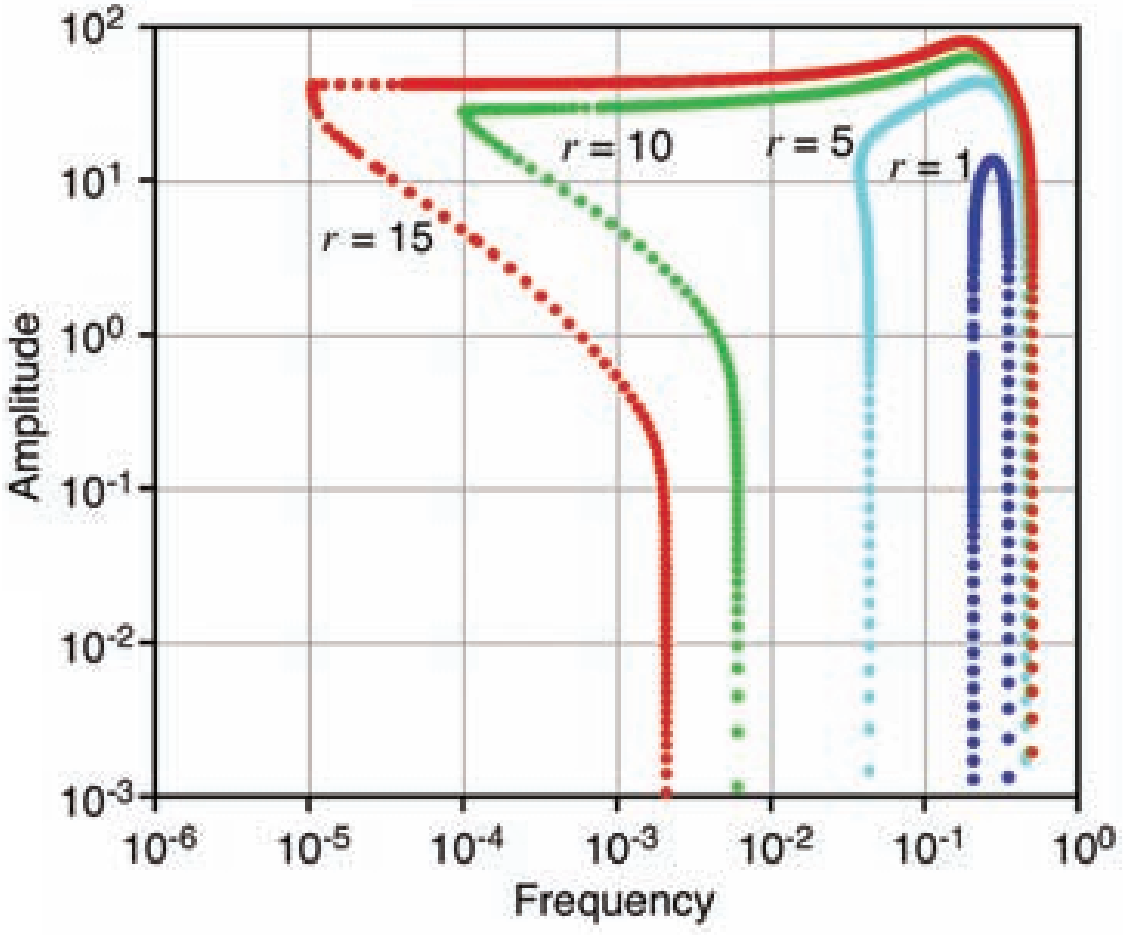


Relaxation oscillations



From Tsai *et al*, 2008

Relaxation oscillators can maintain the amplitude of oscillations as the frequency of the oscillations changes.

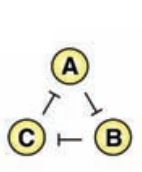


r controls the strength of positive feedback

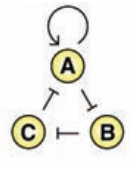
frequency is systematically changed by changing the synthesis rate

From Tsai *et al.*, 2008

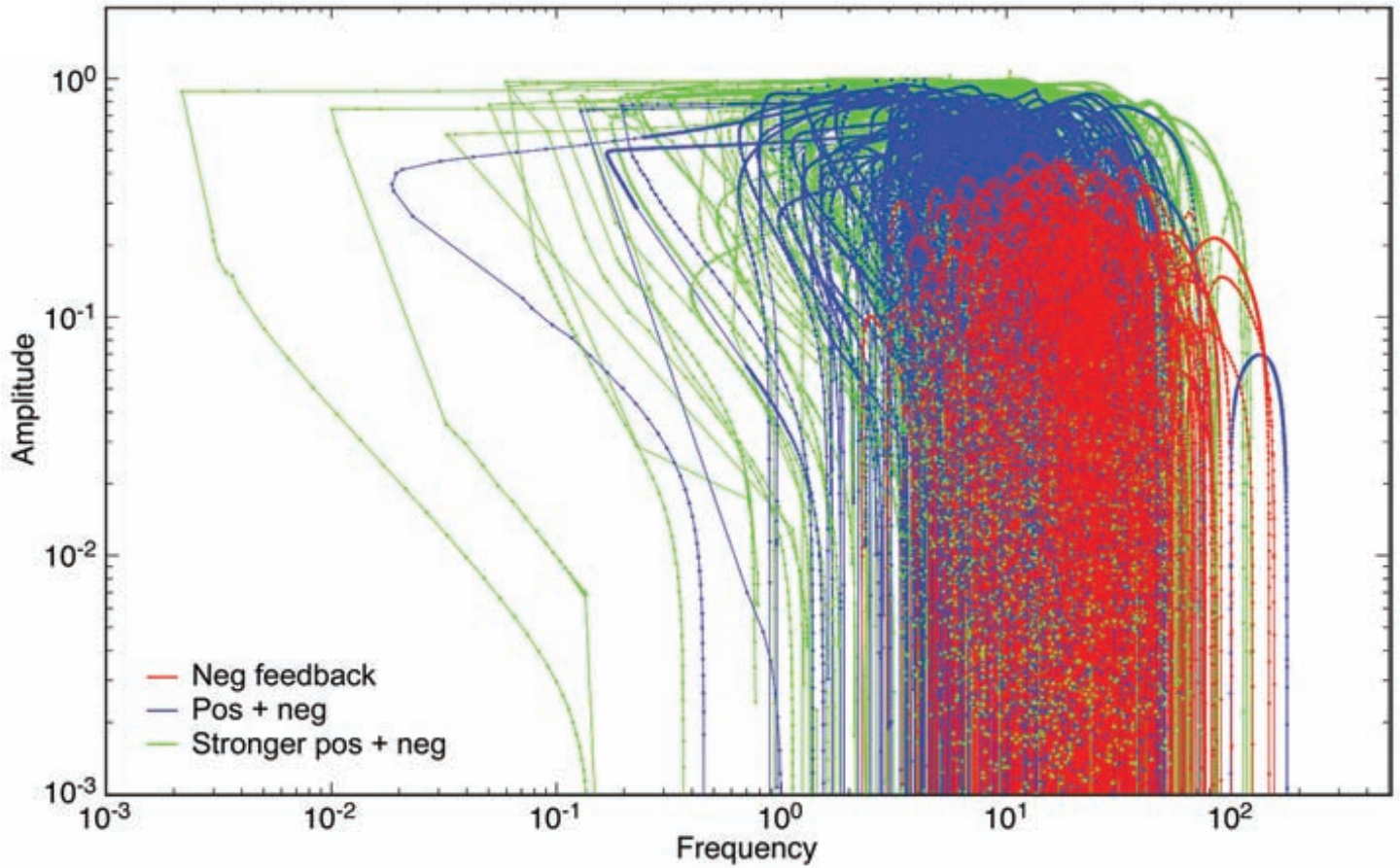
Relaxation oscillators can maintain the amplitude of oscillations more than negative feedback oscillators



negative feedback

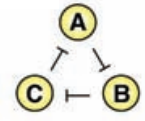


negative and positive feedback

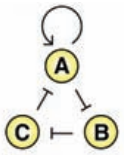


From Tsai *et al*, 2008

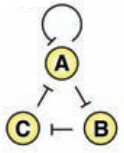
Relaxation oscillators are able to oscillate for wider ranges of parameters than negative feedback oscillators



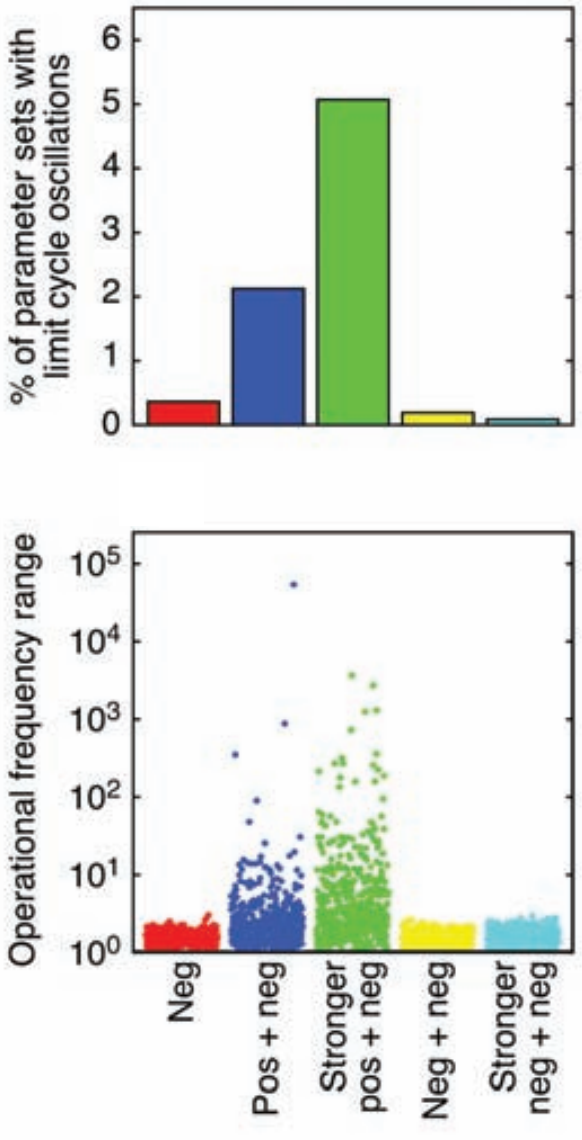
negative feedback



negative and positive feedback



negative and negative feedback



$\frac{freq_{max}}{freq_{min}}$

From Tsai *et al*, 2008