

## Cell Cycle

Dividing cells undergo a cell cycle in which the concentrations of various proteins correlate with the stage of the cell in the division process. Two such proteins, Cdk1 (alternatively, called cdc2) ( $u$ ) and cyclin ( $v$ ) can be modeled as having chemical rate equations of the following dimensionless form:

$$\begin{aligned}\dot{u} &= b(v - u)(a^2 + u^2) - u \\ \dot{v} &= c - u.\end{aligned}$$

$a$  and  $b$  are related to the properties of cdc2 and cyclin and can't be changed readily by the cell;  $c$  is fairly easy for the cell to change.

Roughly speaking, experimentalists can observe the concentration of cdc2 increase greatly as the cell is entering mitosis and cytokinesis (this means, dividing); after the cell divides, the concentration of cdc2 decreases greatly, and only increases again when mitosis in these daughter cells begins. Let's assume that the dynamics of the cdc2 are fast compared to the cyclin. This implies that  $b \gg 1$ .

- (a) Sketch the null-clines and draw the flows in the  $u$ - $v$  plane.
- (b) Without any quantitative analysis, describe under what conditions this system is a relaxation oscillator.
- (c) Is the behavior of this oscillator sensitive to any of the choices of  $a$ ,  $b$ ,  $c$ , as long as  $b \gg 1$ ?

For the remainder of the problem, assume that the system is acting a relaxation oscillator. The analysis becomes simpler if we assume that  $a \ll 1$ , and  $ab \ll 1$ , so we'll assume these things as well.

- (d) Show that the system only is a relaxation if  $c_1 < c < c_2$ , and find approximate expressions for  $c_1$  and  $c_2$ .
- (e) Now suppose that  $c_1 < c < c_2$ , and  $c$  is not "too close" to either value. Find a (somewhat crude) approximation for the period of the oscillator.
- (f) Does the cell spend most of its time in the division stages of the cell cycle or not? Does the answer make sense?