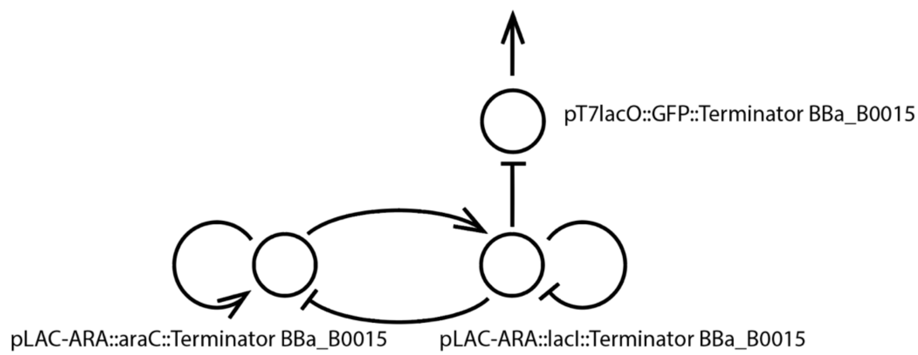
INTRODUCTION TO CELLULAR SYSTEM MODELING
FINAL PROJECT 2022 SUMMER
Due date: 30.6.2023

In this project you will virtually perform a bioengineering project. The objective of the project is to tune a system published in Nature by Stricker et al. in 2008. Note that in practice, tuning means changing the DNA sequence. In this project, the accompanying steps of DNA design, DNA assembly, and cell transformation are assumed to be automatic. In practice, however, each sequential genetic modification amounts to at least 1 week of laboratory work.



Mathematical modeling
The system described in the figure is a gene regulatory network comprising two interconnected single node motifs, a PAR connected to an NAR. If correctly tuned, the system generates oscillations in GFP. You will derive the differential equation model, construct a Matlab simulation, and find parameter values that result in oscillatory behavior. Note, the mathematical model introduced by Stricker et al. in 2008 is very detailed. In this section it is ok to use the simplified models introduced in lectures.

Break down modeling into the following steps and submit results from each part.

1) Describe the underlying chemical reaction network. Note, this chemical reaction network will indicate how activation and repression in the first gene jointly affect gene 1 expression (AND/OR gate).
2) Write down the system of differential equations using the mass action law.
3) Select physically relevant values for all reaction rates.
4) Simulate your system using MATLAB.
5) Identify reaction rates that yield oscillations in GFP. Oscillation period should be approximately 40min and the magnitudes of lacI and araC oscillation should be within an order of magnitude of each other.
6) Rank your parameter search by laboratory time required to arrive at this design. Assume 1 week for each sequential step. (Hint: tuning steps can also be performed in parallel)

7) (BONUS, not mandatory) Simulate the same system using SSA and compare the trajectories. Do you see the same oscillatory behavior?