Chemical Transistor Motif

Introduction

Systematically implementing biochemical control loops is a key aim in synthetic biology.[1] This would allow complex circuit functions to be built.Cellular functions like information processing,organization of metabolism, mechanical structure etc., are all fundamentally implemented by the proper "wiring" of protein reaction networks. Gene-regulatory networks arise at a higher level of system organization and the workings of chemical circuits are most fundamentally seen at the protein reaction level.[2]
Designing a protein reaction motif to achieve a specified form of dynamics has similarities to designing analog circuits.Both involve the control of flows (currents) and accumulations (voltages) of "charge"(electrons/chemical species) to achieve signal processing.[3]

Molecular "Currents" and Concentration "Voltages"

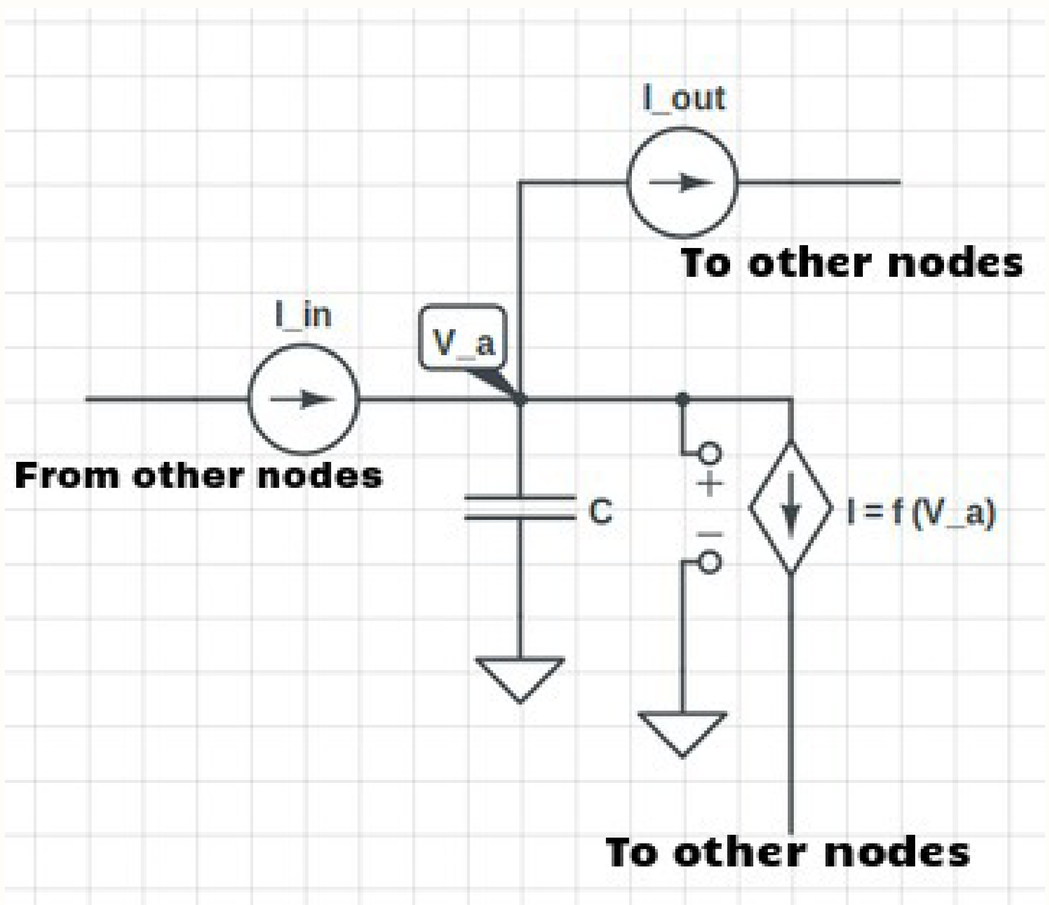

Figure 1: Electrical Circuit Node

$$\mathrm{I_{in}} = \mathrm{f}(V_A, other\ voltages) + \mathrm{I_{out}} + \mathrm{C}\frac{\mathrm{d}V_A}{\mathrm{dt}} \tag{1}$$

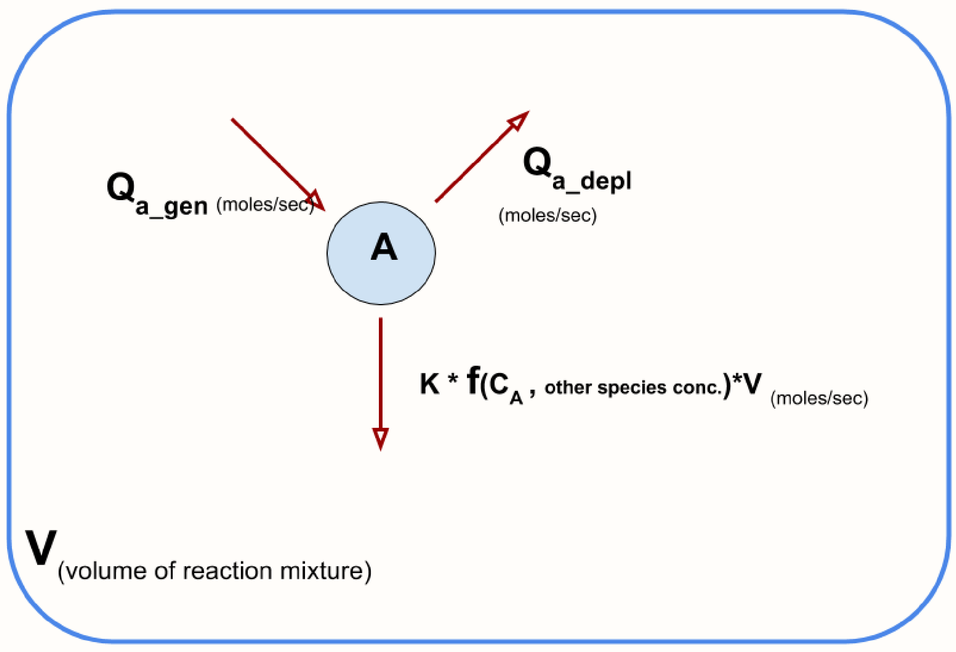

Figure 2: Chemical Species as a Circuit Node

$$\begin{gathered} Generation\ =\ Depletion\ by\ this\ reaction + \\ Depletion\ due\ to\ other\ reactions\ +\ Accumulation \end{gathered}$$

$$\mathrm{Q_{gen}}\ = \mathrm{k}\cdot\mathrm{f}(\mathrm{C_A}, other\ concentrations)V + \mathrm{Q_{depl}} + V\frac{\mathrm{dC_A}}{\mathrm{dt}} \tag{2}$$

Equation (1), charge conservation equation is analogous to Equation(2) mass balance. Dividing equation (2) by the Volume of the reaction mixture (V) results in an equation in terms of only intensive variables.Volumetric Generation/Depletion rate can be interpreted as a "current" entering/leaving the "node".Concentration of the species A at Chemical Node A [fig.(2)] is analogous to the Voltage of the Electrical Node A [fig.(1)].The reaction which is being separately represented in [fig.(2)] is analogous to a nonlinear voltage controlled current source in [fig.(1)]. The restriction on the analogy is that every electrical node must have an identical capacitor to the ground and the reaction volume,V,be fixed.

Implementing a Biochemical Transistor

The idea of the transistor has been implemented using technologies as different as vacuum tubes and solid state devices.Its extraordinary importance in circuit design is due to its following properties -

- Serves as a signal amplifier.
- The device is unilateral - 2 input nodes, 1 output node.
- It is the most elementary controlled source ("current valve") available as a single block for design.
- Enables implementation of both type of feedback loops. One node voltage actuates the output current positively,other node voltage actuates it negatively and the third node has no effect.
- Operates at 2 well separated time scales - DC Bias (Steady state), Small signal (Perturbations).The former is used to tune the latter.

I propose the following elementary interaction network which appears to share these above properties.The network is inspired from a sub-motif in the TOR signalling pathway of *S.cerevisiae*[4].

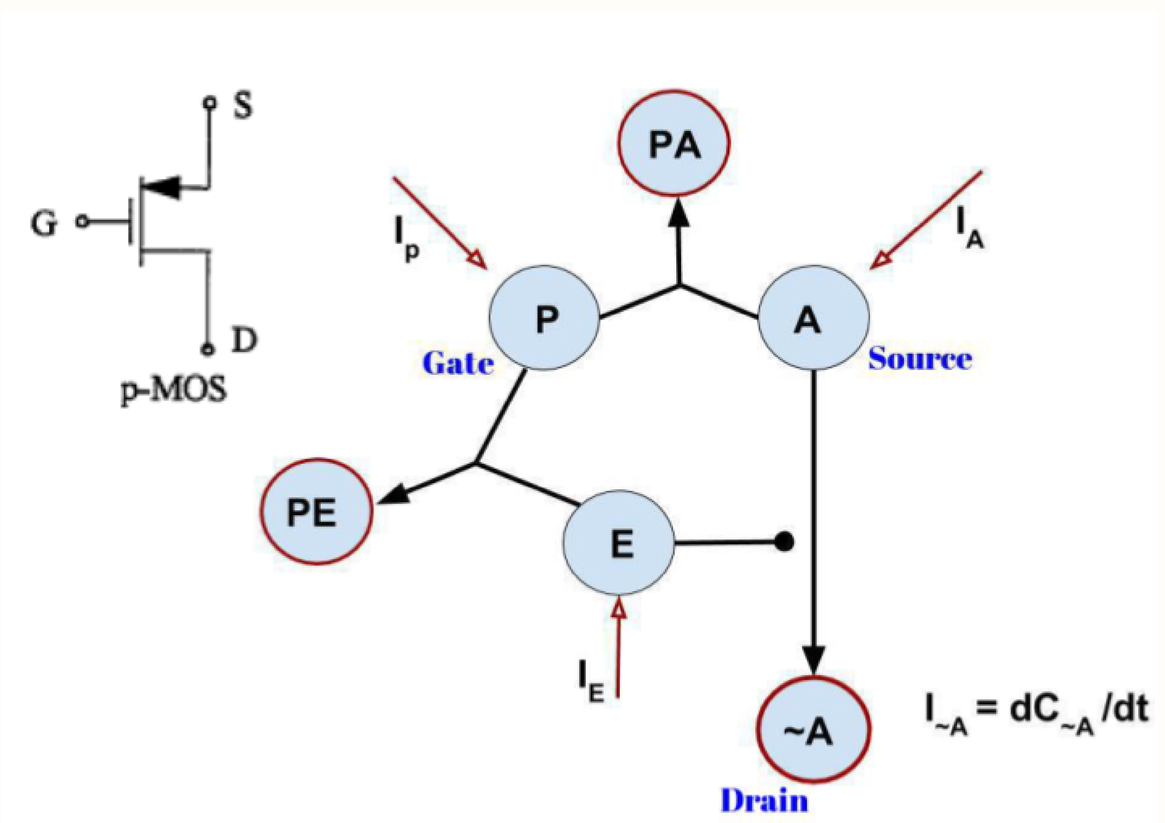

Figure 3: Proposed Motif: P associates with E and A : E is the enzyme

Similarities to P-MOSFET Action in Saturation

1. **Unilaterality**: AE(Enzyme-substrate complex) $\rightarrow$ A is extremely irreversible. Any imposed perturbation to $\mathrm{C_A}$ has no influence on the remaining network. A is an "Output node" - similar to the drain in common source PMOS transistor.
2. **BIAS**: Assume a constant molecular current goes into node P, node A and node E. Also assume the currents can be sourced from other reactions which generate these molecules. In steady state, PA , PE and A will be generated at a constant rate.This can be interpreted as an emerging current which may be routed to other reactions. In the absence of any further reactions downstream,these molecules would accumulate in the volume.In steady state, nodes P, A and E will settle to a constant concentration("Voltage"),while a constant "drain current" emerges from A.The network is thus "biased" to an "operating point".
3. **Gate Control**: P is the Gate, A is the Source, A is the drain. If a molecular current is pushed into node P, its concentration (Gate Voltage) increases. This increase will pull down the enzyme concentration $\mathrm{C_E}$. This decreases A -> A rate. (Source-Drain current.)
4. **Source Control**: If a molecular current is pushed into node A (Source), its concentration (Source Voltage) increases. This increase will pull down $\mathrm{C_P}$ in turn pushing up the enzyme concentration $\mathrm{C_E}$. This increases A -> A rate. (Source-Drain current.)
   This is particularly important as it implements negative feedback action - An increase in "Source Voltage"($\mathrm{C_A}$) causes a larger "Source-Drain Current" to be pulled out of that node thus pulling the "Source voltage" ($\mathrm{C_A}$) down.

P.T.O

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