COMPUTING WITH MOLECULES
(SOLOVEICHIK ET. AL.

REGISTER MACHINE: ABSTRACT COMPUTING MACHINE

(FSM WITH A FIXED NUMBER OF REGISTERS. EACH REGISTER STORES A NON-NEGATIVE INTEGER)

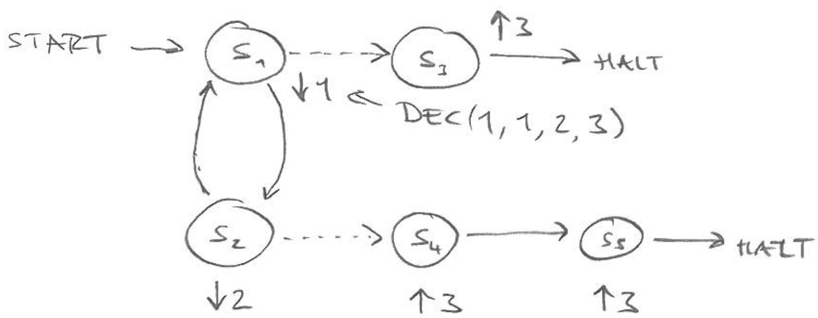
STATES: $S_0, S_1, \ldots S_n$

REGISTERS: $R_0, R_1, \ldots R_m$

TRANSITIONS: (i) INCREMENT $inc(i,r,j)$

(ii) DECREMENT $dec(i,r,j,k)$

EXAMPLE:



IF $R_1 \leq R_2$ THEN OUTPUT 1 IN R_3

ELSE OUTPUT 2 IN R_3

REGISTER MACHINES ARE TURING UNIVERSAL.

STOCHASTIC CHEMICAL REGISTER MACHINE

STATE MOLECULE S_i (ONE SPECIES/STATE, <u>ONE</u> AT A TIME)
REGISTER SPECIES: R_r (M_r / REGISTER)

INC(i,r,j): $S_i \xrightarrow{k} S_j + R_r$ $(M_r \rightarrow M_r + 1)$

DEC(i,r,j,k) $S_i + R_r \xrightarrow{k} S_j$

$S_i \xrightarrow{\varepsilon} S_j$

ERROR: $\frac{\varepsilon}{\varepsilon + M_r k/V}$

CHEMISTRY IS TURING UNIVERSAL (WITH SMALL BUT FINITE ERROR)

$n > 1$, $P_{eq} >> K$:

$$P \sim \left(\frac{4\alpha}{K\gamma_P}\right)^{1/(n+1)}$$

PARAMETER SENSITIVITY

$$S(P,\alpha) = \frac{\Delta P / P}{\Delta \alpha / \alpha} = \frac{\alpha}{P}\frac{dP}{d\alpha}$$

NO FEEDBACK:

$$S(P,\alpha) = \frac{\alpha}{(\alpha/\gamma_P)}\,\frac{1}{\gamma_P} = 1$$

FEEDBACK, $n = 1$; $P_{eq} >> K$:

$$S(P,\alpha) = \frac{\alpha}{\sqrt{\alpha\gamma_P K}} \cdot \frac{\sqrt{\gamma_P K}}{2\sqrt{\alpha}} = \frac{1}{2}$$

$$\dot{m} = \alpha_m - \gamma_m m \quad \Rightarrow \quad m_{eq} = \alpha_m / \gamma_m$$

$$\dot{P} = \alpha_p m - \gamma_p P = \frac{\alpha_p \alpha_m}{\gamma_m} m - \gamma_p P = \alpha - \gamma_p P \qquad \alpha := \frac{\alpha_p \alpha_m}{\gamma_m}$$

$$\Rightarrow P_{eq} = \alpha / \gamma_p$$

GENE EXPRESSION IS STOCHASTIC $\Rightarrow$ α NOISY!

$\Rightarrow$ P_{eq} FLUCTUATES WITH α

$$\longrightarrow P \longrightarrow \emptyset$$

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$$\dot{P} = \frac{\alpha}{1 + (P/K)^n} - \gamma_p P$$

$n = 1$: (STEADY STATE)

$$\frac{\alpha}{1 + P/K} - \gamma_p P = 0 \quad \Rightarrow \quad \gamma_p / K \, P^2 + \gamma_p P - \alpha = 0$$

$$P = \frac{K}{2\gamma_p}\left(-\gamma_p + \sqrt{\gamma_p^2 + 4\alpha/K}\right) = \frac{K\cancel{\gamma_p}}{2}\left(-1 + \sqrt{1 + \frac{4\alpha}{K\gamma_p}}\right)$$

$$P_{eq} = \alpha/\gamma_p \ll K$$

$$\sqrt{1+x} \sim 1 + x/2 \quad (x \ll 1)$$

$$P \sim \frac{K\cancel{\gamma_p}}{2}\left(-1 + 1 + \frac{2\alpha}{K\gamma_p}\right) = \frac{\alpha}{\gamma_p} \qquad 1/K \sim \text{FEEDBACK STRENGTH}$$

$P_{eq} \gg K$:

$$P \sim \frac{K\cancel{\gamma_p}}{2}\sqrt{\frac{4\alpha}{K\gamma_p}} \quad \Rightarrow \text{LESS SENSITIVE TO } \alpha!$$

$$= \sqrt{\frac{\alpha K \gamma_p}{\gamma_p}}$$