Abstract interpretation of cellular signaling networks

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Biological Signaling Pathways

• Signaling pathways regulate sending and receiving extra-cellular signals and trigger cell activities

• Understanding the pathways will allow greater incite on controlling the inner workings of the cell
Signaling Pathways

- Pathways function through kinetic interactions between ligands and proteins
- Often not possible due to the high number of combinations that the pathways can form
Overview

• Like BioNetGen, k-Calculus Uses a formalized mathematical language to look at signaling pathways through a collection of rules

• Danos worked within the framework of k-Calculus to provide a criteria to prove a pathway finite
$EGF(r^1), EGF(r^2), EGF(l^1, r^3, Y1048^4_p, Y1148_p), EGF(l^2, r^3, Y1048_u, Y1148^5_p), GRB2(SH2^4, SH3^6), SOS(a^6), SHC(PTB^5, Y317^7_p), GRB2(SH2^7, SH3)$
K-Rules

- $\text{EGFR}(r), \text{EGFR}(r) \rightarrow \text{EGFR}(r_1), \text{EGFR}(r_1)$

- $\text{EGF}(r_1), \text{EGFR}(l_1, r), \text{EGFR}(r, l_2), \text{GF}(r_2) \rightarrow \text{EGF}(r_1), \text{EGFR}(l_1, r_3), \text{EGFR}(r_3, l_2), \text{EG}(r_2)$
Reachable complexes

• The set of complexes is denoted by $\Gamma$ and the reachable complexes $\Gamma^*$

$$\text{POST}_c(X) = X \cup \{ c \in \Gamma \mid \exists [c_1], \ldots, [c_m] \in X \exists r \in R \exists S \in \Sigma : [c_1, \ldots, c_m] \rightarrow_r S \land c \in S\}$$

$$\Gamma^* \subseteq \text{lfp}_{\alpha_c(S_0)} \text{POST}_c$$
Views and complexes

\[ \beta(EGF(r^1), EGFR(l_1, r^2), EGFR(r^2, l^3), EGF(r^3)) = EGF(r^{l_{EGFR}}, EGFR(l^{r_{EGF}}, r^{r_{EGFR}}), EGFR(l^{r_{EGF}}, r^{r_{EGFR}}), EGF(r^{l_{EGFR}}) \]

- Complex:
- View
Views and complexes

\[ \alpha: \wp(\Gamma) \rightarrow \wp(\Delta) \quad \gamma: \wp(\Delta) \rightarrow \wp(\Gamma) \]

\[ \gamma \alpha([A(a^1, b^1)]) = \{ [A(a^n, b^1), \ldots, A(a^{n-1}, b^n)]; \ n \in \mathbb{N} \} \]
Reachable views

$$\text{POST}_v(Z) := Z \cup \{u_i \in \Delta \mid \exists v_1, \ldots, v_n \in Z \exists r \in R : v_1, \ldots, v_n \rightarrow_r^\# u_1, \ldots, u_n\}.$$ 

$$\text{lfp}_{\Gamma_0} \text{POST}_c \subseteq \gamma(\text{lfp}_{\alpha(\Gamma_0)} \text{POST}_v).$$
Summary

• WTS when a reachable complexes $\Gamma^*$ is finite

• We know

$$\Gamma^* \subseteq \text{lfp}_{\alpha_c(S_0)}\text{POST}_c$$

• And

$$\text{lfp}_{\Gamma_0}\text{POST}_c \subseteq \gamma(\text{lfp}_{\alpha(\Gamma_0)}\text{POST}_v).$$

• Also

$$\text{lfp}_{\alpha(\Gamma_0)}\text{POST}_v$$ is by definition finite

• All that is left is to fine criteria when $\gamma$ maps to a finite set
Questions?