

# Identification of cell signaling pathways based on biochemical reaction kinetics repositories

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# Introduction

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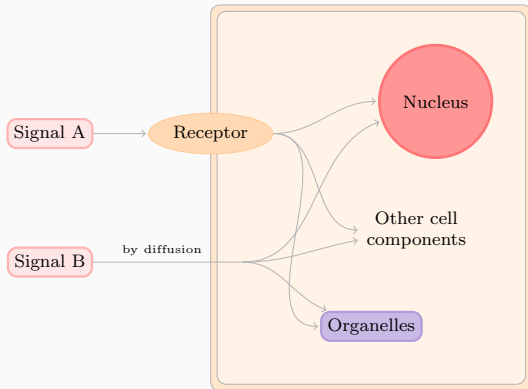
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Understanding the functioning of cell signaling is important in many biological areas.

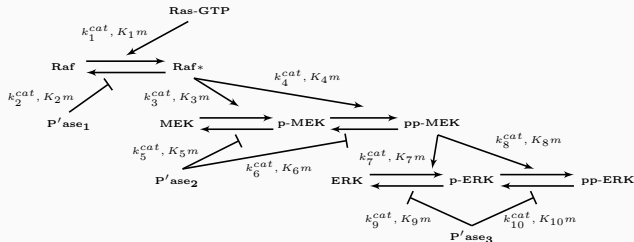
# Cell Signaling



**Figura 1:** A general cell signaling mechanism.

# Cell Signaling Pathways

A cell signaling network can be characterized by a sequence of chemical reactions that allows the presence of a signal to modify the state or behaviour of a cell.



**Figure 2:** An example of a signaling pathway.

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Using biochemical and enzymatic kinetics, we can write equations that represent the rate of change of concentration for a chemical species.

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Repeating this procedure for all reactions of a pathway allows us to derive a system of ordinary differential equations that can model the signaling pathway.

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- a model composed by a set of chemical reactions that are relevant for the biological experiment;
- information about the reaction rate constants of the model.

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One can search for the set of chemical reactions relevant for a biological experiment in repositories like the Kyoto Encyclopedia of Genes and Genomes (KEGG). However, the pathway maps from KEGG may be incomplete or have impertinent reactions for the biological experiment of interest.

Hence, it is desirable to construct a method that can systematically modify these models and choose the one that better represents the experiment.

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On her work, the problem of identification of cell signaling pathways is treated as a feature selection problem.

# Feature Selection Problem

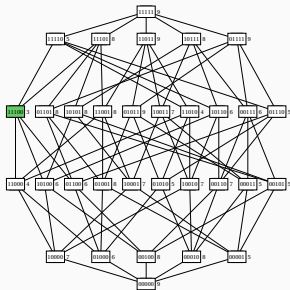
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Given a set of features  $S$  and a cost function  $c$ , find subset  $X \in \mathcal{P}(S)$ , with minimum cost  $c(X)$ .

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**Figure 3:** An example of feature selection search space with 5 features.



## Feature Selection for Identification of Signaling Pathways

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The methodology proposed by Wu defines the set of features as a set of chemical reactions that can be added to a starting model. This set of chemical reactions is fetched from KEGG and stored in a database of interactions.

## Wu's Search Algorithm for Feature Selection

The search algorithm used by Wu is the Sequential Forward Selection (SFS).

## Wu's Cost Function for Feature Selection

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The  $R(M)$  term is implicitly defined by imposing a time limit to the Simmulated Annealing procedure used to calculate the cost function. As a result, the penalization of the cost function is random.

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We can point three aspects of Wu's work that could explain its limitation.

- the database of interactions used could be more nearly complete;
- the search algorithm could also consider removing interactions;
- the cost function could implement a proper penalization of models;

## What we Propose on this Project

We propose to create a methodology that uses a feature selection approach for identification of signaling pathways, tackling the difficulties encountered by Wu.

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To create better search algorithms, we intend to use more general algorithms that can also remove interactions.



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To define better cost functions, we intend to use Bayesian approaches of model selection that allow us to create estimates of probabilities such as  $p(M|D)$  or  $p(D|M)$ .

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- Create search algorithms for the feature selection problem.
- Test the methodology on known signaling pathways.
- Apply the methodology on a real case.

# Fundamental Concepts

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# Model Selection

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# Experiments on Model Selection

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## Next Steps

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