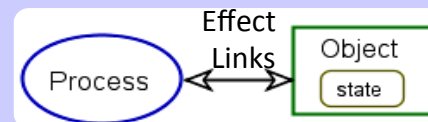




# Conceptual Model-based Systems Biology

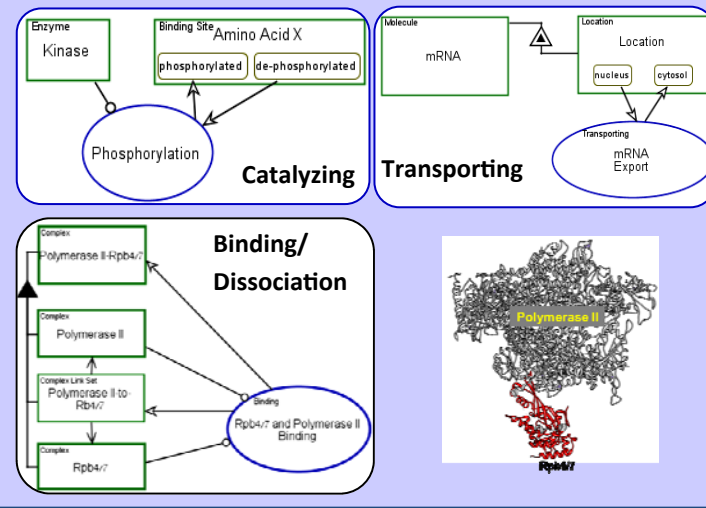
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OPM Basics:



Results:

OPM templates for modeling Molecular Biology:

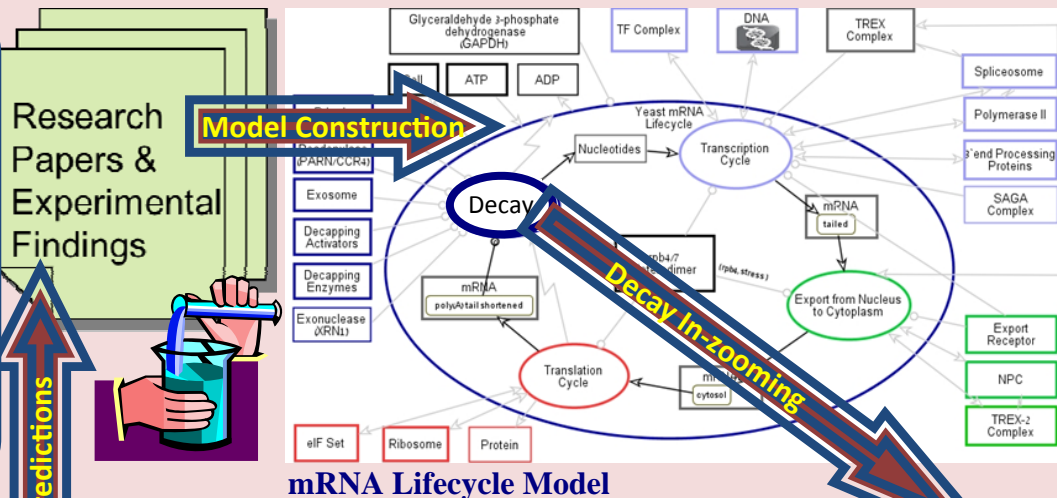


## Introduction

Biological wet-lab experiments are costly and long-lasting

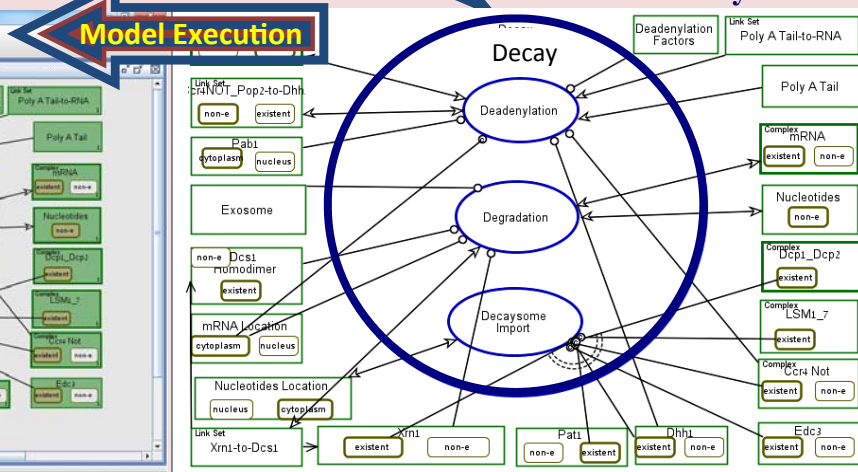
Additionally, there is a need for making system-level sense from the countless pieces of biological information, which can be used to refine biological experiments

OPM—Object-Process Methodology, originated in specifying information systems



mRNA Lifecycle Model

## mRNA Decay Process



## Model Construction

Decay model construction based on 70 mechanistic qualitative facts

Conjectures incorporated

Using in-zooming mechanism to handle big models

Decay model includes 130 objects and 60 processes

## Model Execution and Analysis

Compare the mechanistic model execution to qualitative experimental findings (desired input and output)

Adjust the model when inconsistencies are found and evaluate conjectures

## Results—mRNA Decay Model:

1. Find knowledge gaps—26 knowledge gaps were found
2. Evaluate Conjectures—the conjecture about Dcp1/2 complex recruiting Xrn1 and stays bound to it during degradation complies with current experimental findings
3. Predict New Hypotheses—we predict that Pat1 deletion effects on Xrn1, Dhh1 and Rpb4/7 import into the nucleus

## Conclusions

Our conceptual method enables user-friendly graphical, qualitative and executable representation of complex biological processes and structures from the lower level molecular functions to the entire mRNA decay process  
Conceptual modeling can help evaluate the correctness of biological hypotheses before conducting a wet-lab costly experiments  
Conceptual modeling can predict new testable hypothesis

## Selected References

- Fisher, J., Henzinger, T. A. (2007). Executable cell biology. *Nature Biotechnology*, 25(11), 1239-1249.
- Dori, D. (2002). Object-process methodology: A holistic systems paradigm. Springer Verlag.
- Houseley, J., & Tollervey, D. (2009). The many pathways of RNA degradation. *Cell*, 136(4), 763-776.

