

# Biotechnology and Computational Biology

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MITRE Sponsored Research

The logo for the MITRE Technology Program, featuring a stylized graphic of stacked blocks in yellow, orange, and blue on the left, and the text "MITRE Technology Program" in yellow and white on the right.

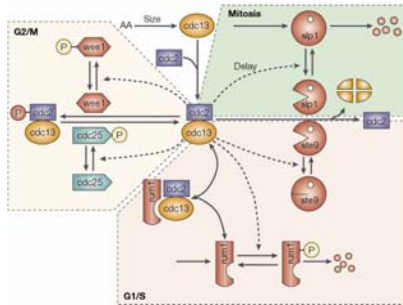
MITRE  
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# Problem

- **The barrier to entry for misusing biotechnology has been lowered, making it easier to construct designer biological agents for use in asymmetric warfare or terrorist activities.**
- **Modeling and simulation can be used to dramatically improve consequence management.**

# Background

## Qualitative Description



## Rate Equations

$$\begin{aligned}
 R + L &\xrightleftharpoons[S]{\tilde{S}} \tilde{R}L \\
 \tilde{R}L &\xrightarrow{I} RL \\
 [R]_T &= [R]_F + [\tilde{R}L] + [RL] \\
 r_b &= \frac{k_T([R]_T - [RL])[L]}{K_S^{-1} + [L]}
 \end{aligned}$$

## Quantitative Model

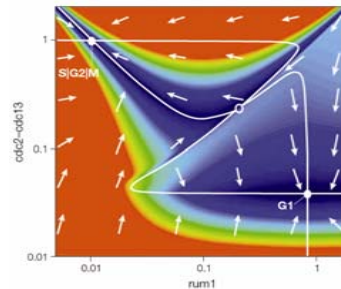
$$\begin{aligned}
 \frac{d[RL]_T}{dt} &= r_b - \mu[RL]_T & \frac{d[c_{22}]_T}{dt} &= \Omega_{22} - 2r_{22} - \mu[c_{22}] \\
 \frac{d[R]_T}{dt} &= \Omega_R - \mu[R]_T & \frac{d[c_{25}]_T}{dt} &= 2r_{25} - \mu[c_{25}] \\
 \frac{d[F]_T}{dt} &= \Omega_F - 2r_F - \mu[F]_T & \frac{d[c_{27}]_T}{dt} &= \Omega_{27} - \sum_{i=1}^n r_{i27} - \mu[c_{27}] \\
 \frac{d[RL.F]_T}{dt} &= r_r - \mu[RL.F]_T & \frac{d[c_{28}]_T}{dt} &= \sum_{i=1}^n r_{i28} - \mu[c_{28}] - r_{off} \\
 \frac{d[C_1]_T}{dt} &= r_c - r_{d1} - \mu[C_1]_T & \frac{d[b]_T}{dt} &= \Omega_b - \mu[b]_T \\
 \frac{d[AI]_T}{dt} &= \Omega_{AI} - \mu[AI]_T & \frac{d[l_2]_T}{dt} &= \Omega_{l_2} - \mu[l_2]_T \\
 \frac{d[AI.C_2]_T}{dt} &= r_{d1} - \mu[AI.C_2]_T & &
 \end{aligned}$$



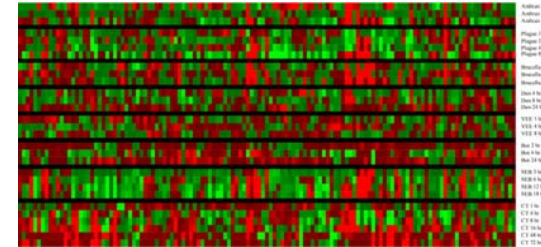
## Experimental Validation



## Model Exploration



## Parameter Estimation



*Iteratively refining computational modeling with experimental techniques*

# Objective

## Utilize computational modeling techniques to speed response to pathogenic agents

- Identify how a biological warfare agent is acting to disrupt normal cellular processes
- Develop and test intervention strategies computationally
- Estimate pathogenicity so countermeasures can be mounted that are commensurate with the posed threat

*Developing computational tools, informatics infrastructure, and interdisciplinary expertise to model cellular systems*

# Activities

- **Role in organization of BioTEM II**
- **Initiation of bio cluster meetings/speaker series**
- **Collaborative efforts with UC Berkeley, NYU, and Columbia**
- **Two NIH (NIAID) grant submissions**
- **Participation in experimental studies ongoing at Walter Reed Army Institute of Research**

# Highlight



| GENE                   | Anthrax |   |   | SEB |   |    |    |
|------------------------|---------|---|---|-----|---|----|----|
|                        | T=      |   |   | 3   | 6 | 12 | 18 |
| ADP-ribosylation fac   |         | ■ | ■ |     |   |    |    |
| guanine binding pr     |         |   |   |     |   |    | ■  |
| guanine nucleotide re  |         | ■ | ■ |     |   |    |    |
| guanine nucleotide-bi  |         | ■ |   |     |   |    | ■  |
| guanine nucleotide-bi  |         |   |   |     | ■ | ■  |    |
| neuro epithelioma tran |         | ■ | ■ |     |   |    |    |
| Ral A; GTP-binding pr  |         |   |   |     |   |    | ■  |
| RalB GTP-binding pro   |         | ■ | ■ |     | ■ | ■  |    |
| ras-related C3 botulin |         | ■ | ■ |     | ■ | ■  |    |
| ras-related protein R  |         | ■ | ■ |     |   | ■  | ■  |
| ras-related protein R  |         |   |   |     | ■ |    |    |
| ras-related protein R  |         | ■ | ■ |     |   |    |    |
| ras-related protein R  |         |   | ■ | ■   |   |    |    |
| ras-related protein R  |         | ■ | ■ |     |   |    |    |
| ras-related protein R  |         | ■ | ■ |     |   |    |    |
| transducin beta 5 su   |         |   |   |     |   |    | ■  |
| transforming protein r |         |   | ■ | ■   |   |    |    |
| vav oncogene           |         |   |   |     |   | ■  | ■  |
| GTPase-activating pr   |         | ■ |   |     |   | ■  | ■  |
| RalGDSB; GTP/GDP       |         | ■ | ■ |     |   |    |    |
| ran GTPase activatin   |         |   | ■ |     |   |    |    |
| rho GDP dissociation   |         |   |   |     |   |    |    |

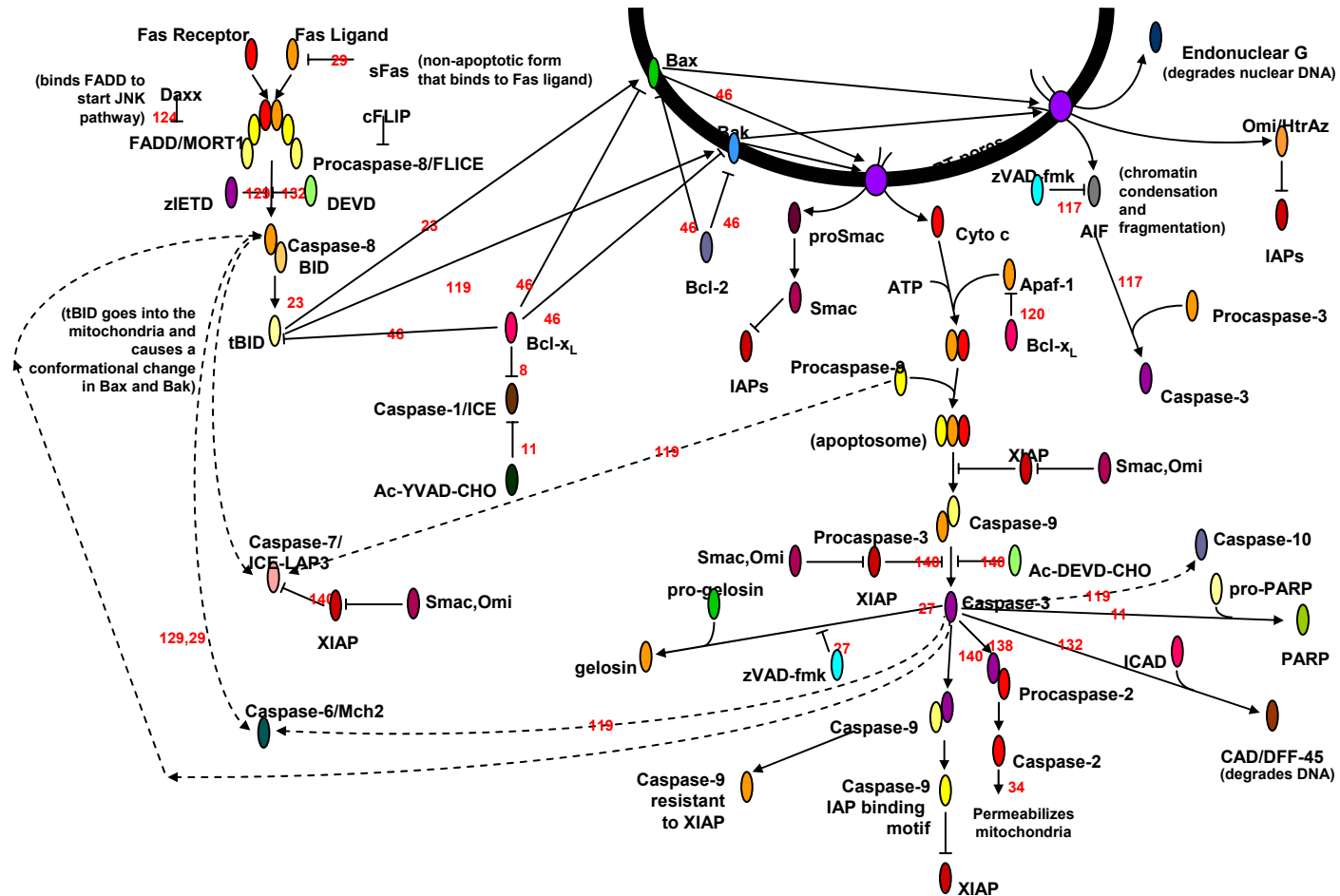
**Training on many state-of-the-art experimental techniques**



# Impacts

- **Participation in broader MITRE biotechnology work program**
- **Collaborative efforts and potential grant opportunities**
- **Introduction of MITRE into the biological modeling and simulation community**
- **Involvement in new homeland security initiative**

# Future Plans



**Enhancing sophistication and predictive power of current model**