

Synthetic Biology

Engineering at the Sub-cellular Level

John Dileo, Ph.D

703.983.7913 • jdileo@mitre.org

MSR



Problem



- **How do you know if a facility is producing chemical weapons (CW)?**
 - **Existing methods for proving chemical weapons production are limited**
 - **Remote detection is almost impossible**
- **Solution: Local monitoring of facility emissions with a remotely observable output**
 - **Detect the presence of signature chemicals or suggestive combinations of chemicals**

Background

**Legitimate operations
and CW production
facilities look nearly
identical**

Shifa Pharmaceutical Plant, Sudan



**Announced, on-site
inspections are only
way to verify under
Chemical Weapons
Convention**

Objective



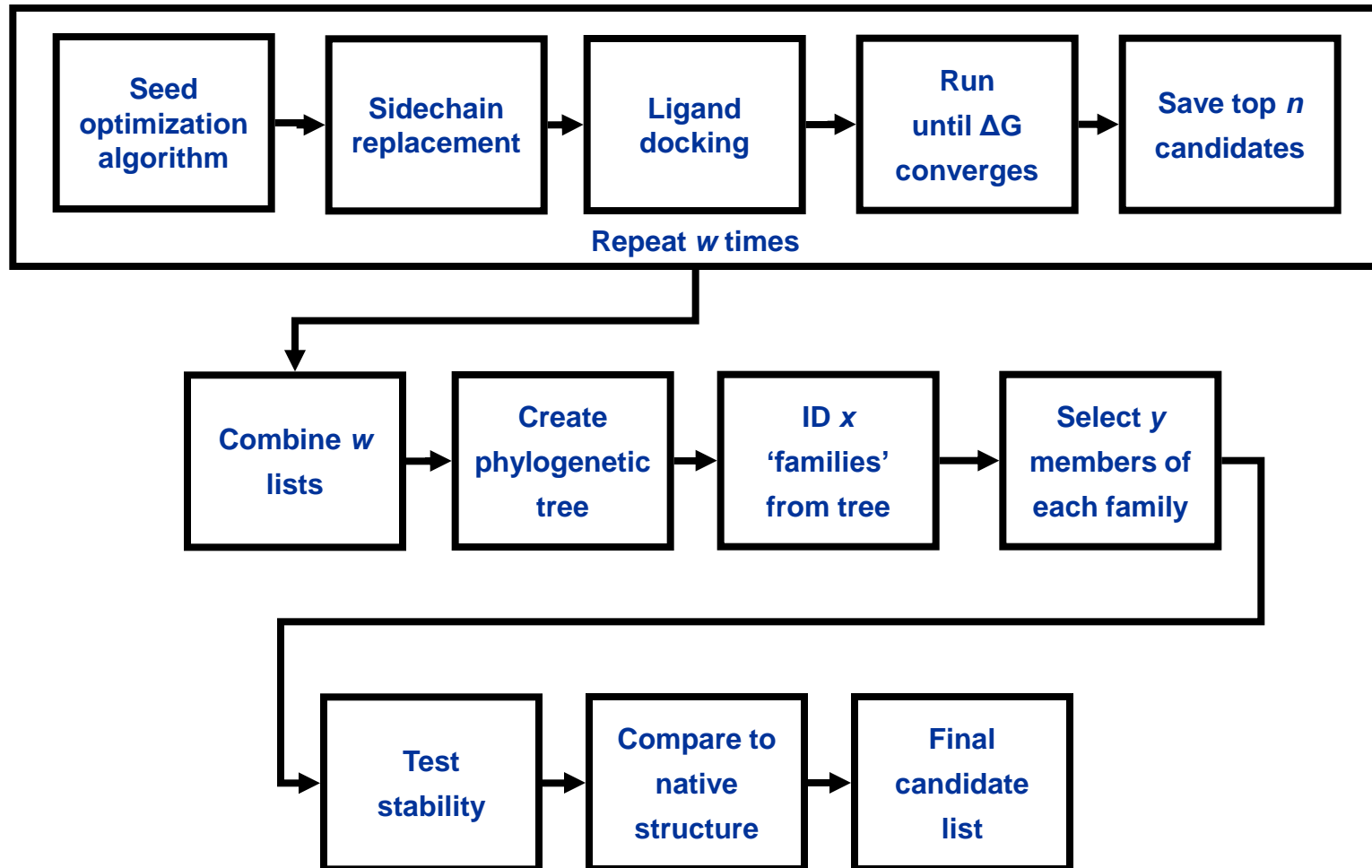
- **Engineer a cell-based system that can detect a chemical signature suggestive of VX production and produce a remotely observable signal in response**
- **Specific activities**
 - **Design protein detectors that recognize CWs and initiate a cellular response**
 - **Implement complex logical information processing circuitry in DNA (multiplexing and output)**
 - **Integrate protein and DNA elements into a unicellular system**

Activities

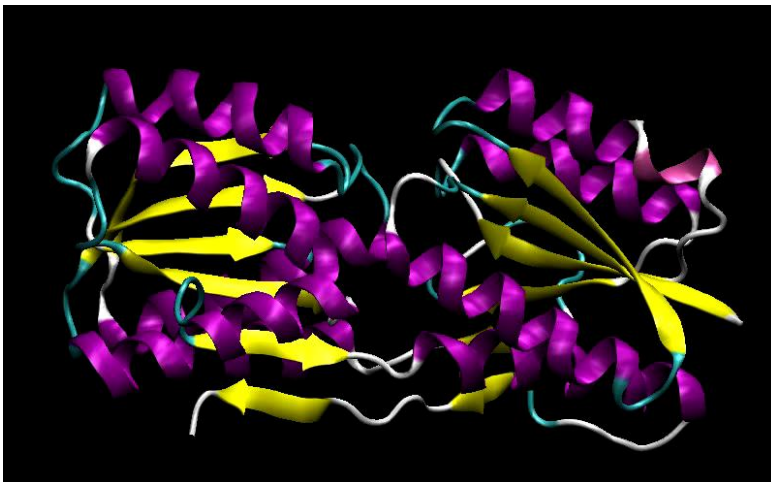
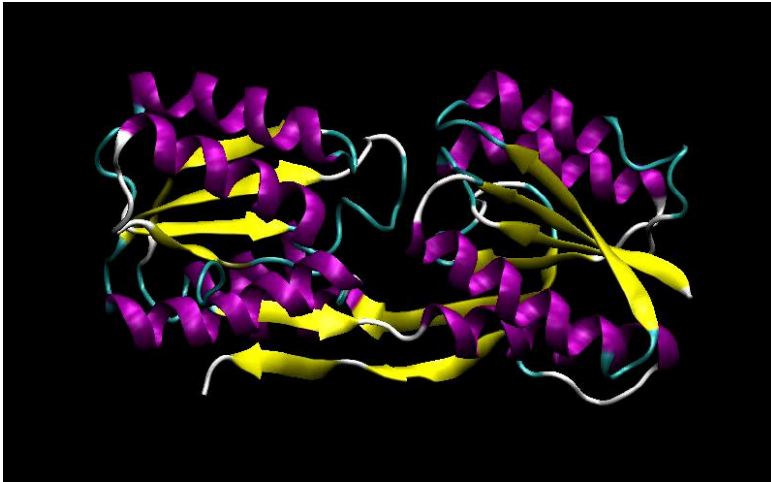


- **Constructed a Protein Design Pipeline with core functionality**
 - **Adapted methods to run on HPC systems**
 - **Implemented a strategy for directed search**
 - **Implemented molecular dynamic simulations**
 - **Developed an open source web service for protein design**
- **Designed candidate detectors for VX precursor**
 - **Determining stability, expressibility, and functionality of initial designs**
- **Fabricating a second round of proteins**
- **Developing an in-house repository of reusable cellular parts and biological design tools**

Designing Protein Based Detectors



Simulating Protein Structures



- **Molecular dynamic simulations of protein structures using the AMBER software package on 144 node HPC system**
- **Utilize Newton's equations to model atomic movements over 2ns**
 - **Top: unstable mutations**
 - **Bottom: stable mutations**
- **Gauge stability by RMSD to original protein structure**

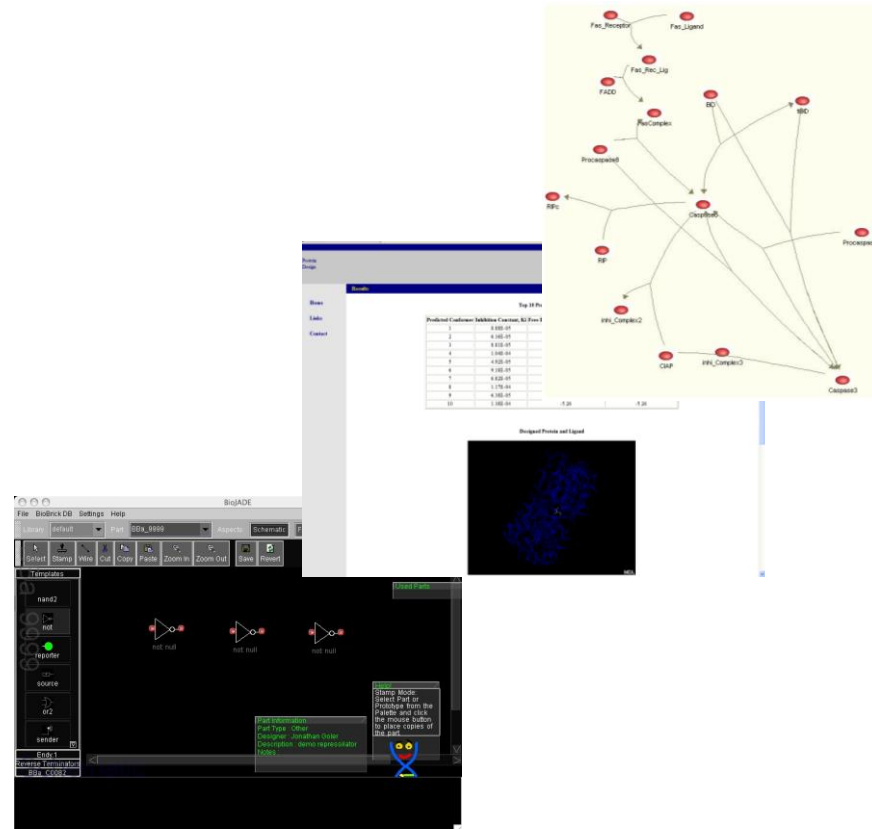
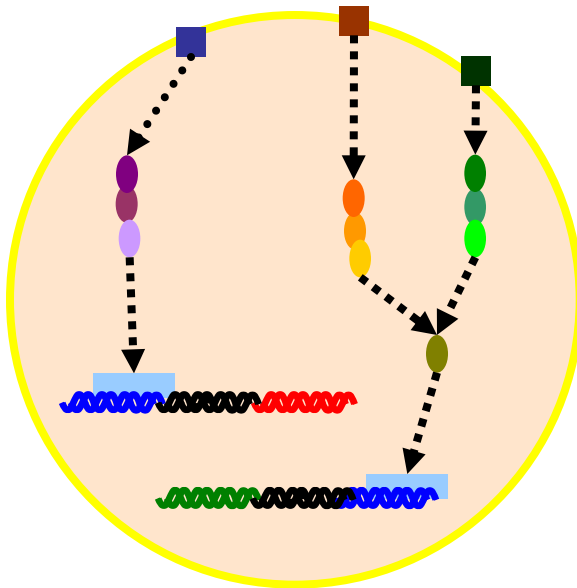
Impacts



- **Application of technology to CW countermeasure design in support of USAMRICD**
- **Recognition as a resource in the field**
- **Advancement of the state of the art**
- **Ability to influence emerging technical standards and codes of conduct via interaction with BioBrick Foundation and ICPS**
- **Peer reviewed publications & conference presentations**
- **Establishing a new field of engineering at MITRE**
- **Applying established MITRE expertise into biotechnology**
- **Extending existing MITRE investments**
- **Building relationships with leading academic researchers & institutions**

Future Plans

Cell-based sensor systems



Tools for engineering cells on the genome, protein, and systems level