



BAA 01-26

Bio-Computation

DARPA/ITO



Bio-Computation Program



Explore, Develop, and Exploit

- Computational Mechanisms in Bio-Substrates
 - Information processing using bio-molecular coding and manipulation
 - Leverage massive parallelism, Harvest Nature's toolkit
- Computational Models of Cells
 - Natural Computation



TECHNICAL RESEARCH AREAS



-
- **DNA COMPUTING**

 - **COMPUTATIONAL MODELS OF INTRA-CELLULAR PROCESSES AND SYSTEMS OF CELLS.**



DNA Computing: Technical Research Area I



TOPICS

- 1. Scalable DNA Computing**
- 2. Compact, content addressable storage**
- 3. Programmable, Self-assembled 2-D, 3-D Nano-structures**
- 4. Implementing computational elements and circuits that use in-vitro transcription and/or translation, and application demonstrations**
- 5. Other related ideas with significant promise.**

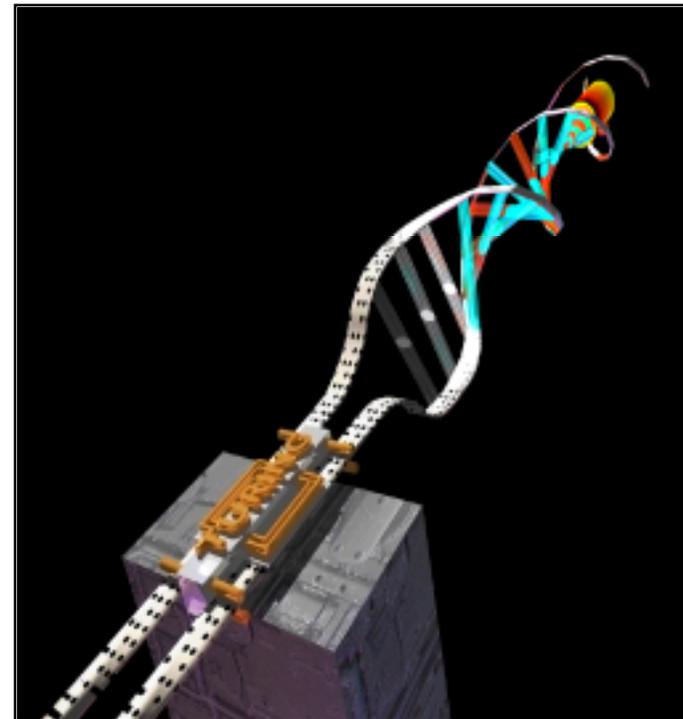


AREA 1: Topic 1

Scalable DNA COMPUTING



- **DNA, RNA, other Nucleotides**
- **Leap beyond toy problems**
- **Scaling**
 - **Coding. Bit -> nt**
 - **Automation of manual tasks**
 - **Prototypes**





AREA 1: Topic 2

Content Addressable Storage



- A gram of DNA can store Terra-bytes
- R&D Leading to
 - Wet Database system
 - Tagged DNA
 - Error Resiliency
 - Push up I/O speed
 - Prototype Development





AREA 1: Topic 3

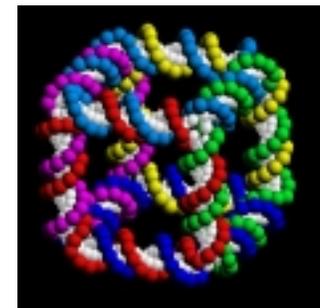
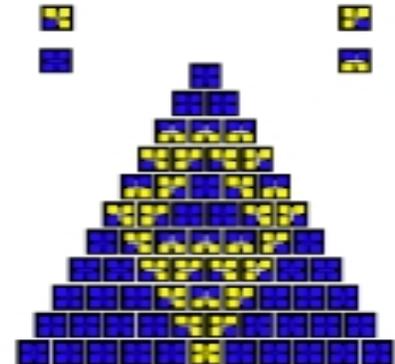
Programmable Nano-structures



Demonstrate techniques for producing a broad class of Self-assembled, computationally driven DNA Structures

2-D, 3-D

- **Application Demonstrations: Examples**
 - Cages for Crystallography
 - Layout for Molecular Electronics/ Q-dots
 - Precision features: 10s of nm





AREA 1: Topic 4

Synthetic Bio-Circuits



- Implementing computational elements and circuits that use in-vitro transcription and/or translation, and application demonstrations
 - Traditional manipulation repertoire: ligation, restriction, hybridization
 - Expand repertoire to include transcription and/or translation
 - **Implementation**
 - **Controllable switches**
 - **Logic Elements: Boolean, Sequential (Flip-Flops)**
 - **Interconnection**
 - **Demonstrate for use in:**
 - **Realizing algorithms**
 - Genetic, Neural Network Programs
 - **In-Vivo Control**
 - **Other applications**



AREA 1: Topic 5

Other Related Topics



- **Other related topics with significant impact.**

Note: Explore working with
Long DNA Strands > 200+ bases

Separately identify:

**Cost/Base
Lengths
Concentrations**



Teaming for Area 1



- Inter-disciplinary
 - Bio-Chemists
 - Chemists
 - Computer Science
 - Engineering
 - Other Relevant



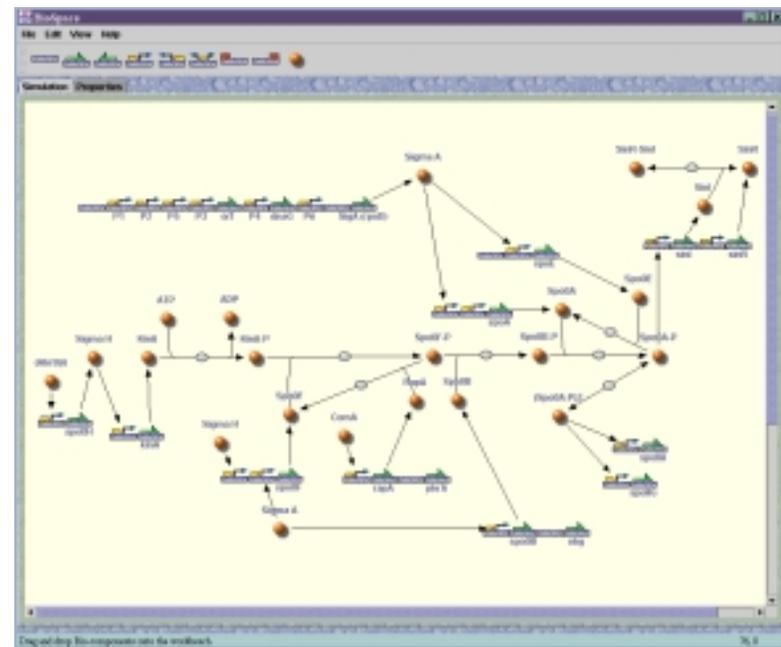
Technical Area 2: Computational Models of Intra-Cell Processes, and Systems



Develop Bio-SPICE

SIMULATION PROGRAM FOR INTRA-CELL EVALUATION

- Tool: In Silico Analysis
- SPATIO-TEMPORAL Models
- Capturing interactions in the network of Gene-protein interactions





Computational Models: Research Goals



- **Develop BIO-SPICE**
 - Open Source Framework
 - Iterative development with ongoing experiments

- **Experimental Validation**
 - **Realm: Conserved Mechanisms**
 - Characterize, Predict, Control
 - **Demonstrate effectiveness of BIO-SPICE**
 - **Demonstrate Impact to DOD**
 - Pathogenic Processes
 - War fighter effectiveness in stressed conditions
 - Bio-sensors
 - Enhanced DNA Computing



Area 2: Research Topics



- 1. Model Kernel**
- 2. Experimental Validation**
- 3. Simulation Environment**
- 4. Software Integration**



Area 2: Topic 1

Model Kernel



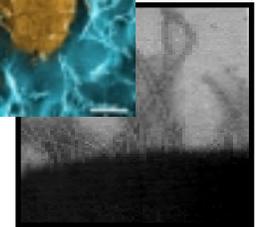
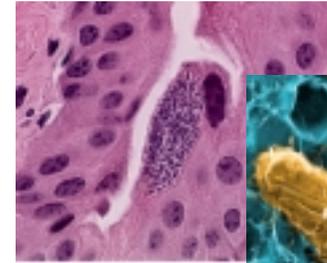
- Spatio-Temporal Models
 - Reaction/Diffusion
 - Deterministic, Stochastic
 - Analog, Discrete, Asynchronous
 - Transport, Compartmental
- Multi-Scale, Multi-resolution Models
 - Time (msecs to hours)
 - Size (few to large – gene/proteins)
- Analytical Tools
 - Stability, Bifurcation
 - Phenomenological models
 - Model fitting from uncertain data

Area 2: Topic 2

Experimental Validation

EXAMPLES, not LIMITED TO:

- DNA Editing In-Vivo
- Circadian Rhythms
- Piliation
- Sporulation
- Secretion
- Asymmetric Division
- Cell Cycle
-

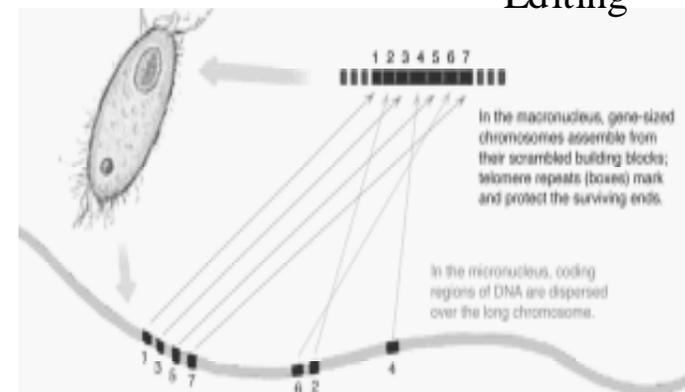


Piliation



B.subtilis

Editing





Area 2: Topic 3

Simulation Environment



- Parallel Simulation to gain speed
- Biologist Friendly
 - GUI
 - Data Visualization
- Easily programmable
 - High Level Language and compilation
- Data basing tools:
 - access, query
 - Local, remote, distributed environment
- Operating environment
 - Efficiently manage all components
 - Platform independence



Area 2: Topic 4

Software Integration



- **Issues**
 - **Develop open architecture, working with the community**
 - **Controlling Revisions and Repository**
 - **Expert panel**
 - **Revision (1-2 times per yr)**
 - **Software Integration and Revisions**
 - **Version Control, Model evaluations**
 - **Team for software integration**
 - **Committed to open source development**
 - **Strong technical expertise, all-aspects**



Area 2: Teaming Desirability



- Teams for Topic 1 and 2
 - Modeling + Experimentation
 - Biologists, Biochemists, CS, Engineering..
- Teams addressing all aspects of Topic 3
 - Sufficient domain knowledge
- Teams addressing all aspects of Topic 4
 - Sufficient domain knowledge
 - Commitment to open source



Bio-Spice Components and Roadmap

