Research Interests:

Statistical signal processing, Predictive modeling
High Performance and Embedded Computing

Multidisciplinary Applications:
  Computational & Systems Biology
  Environmental modeling and monitoring
Recent Projects

**Computational Biology**

- Machine learning methods for high throughput proteomics image analysis [*Proteomics 2009*]
- Improving sequence similarity search for protein homology inference using structural information and Bayesian methods

**Systems Biology**

- Efficient architectures for the stochastic simulation of large biochemical reaction networks
Efficient algorithms and architectures for protein 3-D structure comparison

Collaborators

**Elias Manolakos (PI),** Assoc. Professor, Dept. of Informatics and Telecommunications, University of Athens

**Ioannis Emiris,** Professor, Dept. of Informatics and Telecommunications, University of Athens

**Georgios Panagiotou,** Director, Institute of Molecular Oncology, B.S.R.C. “Alexander Fleming”

PhD Candidate: Anuj Sharma

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Introduction - Motivation

In Protein Structure Comparison (PSC) methods, complexity is introduced along three orthogonal dimensions:

- size of structure databases,
- need to support multiple comparison algorithms,
- complexity of the pair-wise comparison (PWC) algorithms used.

In order to develop fast and efficient PSC methods, all these factors must be addressed.
Introduction - Motivation

- The modern trend, in the field, is to harness computing capabilities of distributed computing systems (clusters and grids) for the task.
- This tackles only the first two of the three dimensions.
- Many-core CPU architectures provide a means for exploiting high level of parallelism
  - Intel Single-Cloud Computer (SCC) is an example of a many-core processor with 48 cores organized as a Network on Chip (NoC)
  - Can be used to tackle the first two of the three dimensions in a single CPU
- Field Programmable Gate Arrays (FPAGs) provide the means for exploiting the low level parallelism (PWC)
  - Recently methods using GPUs have also emerged for this task
Research Tasks – Intel SCC Related

- Port popular PSC methods to the SCC NoC architecture.
  - A limited number of third party libraries are available on the SCC
  - RCCE, a Message Passing library, must be used to exploit parallelism on the SCC
- Investigate the impact of using multiple cores on speed up of PSC methods using the Master-Slaves paradigm
  - Data-parallel strategy requires load balancing to hide latency and efficiently utilize computing resources
Implement hybrid strategies, distributed/parallel computing, using the SCC for the PSC problem

- Many-core architectures provide a flexible means for combining distributed and parallel computing

Implement multi-criteria consensus based PSC using the SCC and factor out common operations

- PSC methods share common aspects such as extracting protein structure fragments, fragment alignment etc.
- The cores on the SCC are connected with a high speed network
Research Tasks - FPGA Related

- Develop co-processors based implementation for the TM-align PSC method to provide fine-grained parallelism.
  - The initial alignments performed are independent of each other and could be performed in parallel.
  - Alignment of protein structures, based on pair-wise residue alignment, performed in order to fill a score matrix could be parallelized.

- Develop fast and accurate data compression hardware for Universal Similarity Metric PSC method.
  - USM relies on the calculation of complexities of protein structures by compressing them
Research Tasks – FPGA Related

- Develop parallel Dynamic Programming (DP) implementation for the Combinatorial Extension PSC method.
  - Dynamic Programming alignment of the protein structures is the most time consuming step

- Develop fragment alignment co-processor for multi-criteria PSC
  - Fragment alignment with different metrics, used by different methods, can be performed in parallel
  - Fast hardware implementation of fragment alignment can provide significant speedup to PSC methods
Research Tasks - Large Scale Validation

- Datasets
  - Chew-Kedem Dataset
  - Rost-Sander Dataset
  - SCOP Astral

- Alignments generated by ported algorithms will be compared with those of the baseline algorithms.
- Performance testing will be performed comparing the time for all-vs-all comparison using the ported and baseline algorithms.
Scalable Reconfigurable SoCs for the Stochastic Simulation of large-scale Biochemical Reaction Networks

Research Team:

Prof. Elias S. Manolakos, PI

PhD Candidate: Evangelos Logaras
MSc Students: Orsalia G. Hazapis, Eleftherios Ouzounoglou
Introduction

**Objective:**
Perform State prediction of biochemical reaction networks in reasonable amount of time.

**Approach:**
Using Gillespie’s Stochastic Simulation Algorithms which attempt to simulate the process of solving the General Chemical Master equation

**Our Solution:**
Application Specific architectures implemented with FPGAs for high performance, as the problem scales to networks with thousands of reactions
Reactions Networks

MAP-Kinase Reaction Network
State of the art

ReCSiP2 is a dedicated FPGA board level design that can be used as a PC accelerator.

ReCSiP2 was mapped on the Xilinx Virtex XC2VP70-5 FPGA, achieves operating frequency of 107 MHz and has been shown to outperform a Xeon 2.80 GHz CPU by approximately 80 times when simulating up to $M=1024$ reactions.

University of Washington researchers designed circuits that implement a reaction model’s operation directly in model-specific circuitry which consists of a large system of distributed logic and random number generator blocks.
Researchers from the University of Pisa Italy have implemented the FRM SSA on GPUs and accomplished a ~2x in accelerating a single FRM-SSA simulation run, using Nvidia’s GEForce 8600M GS GPU to simulate an E-coli bacterial biomodel with only 28 species and 61 reactions.

STOCHSIMGPU is a software tool using Nvidia GPUs to accelerate the SSA implementation in Matlab’s System Biology Toolbox 2. The average speedup factor achieved is 85x for simulating a biomodel of 30 reactions.
Our solution – SoC for the FRM-SSA

- Designed a SoC for the FRM-SSA using up to $N = 8$ cores (PEs)
- The SoC can simulate networks with up to 4096 reactions using a moderate size FPGA
- It is synthesized based on a fully parameterized VHDL IP core
  - Parameters: number of processors ($N$), number of species ($S$) in the model, number of reactions ($M$), maximal reactions order ($q$).
- Supports two modes of operation (using $N$ PEs):
  - one simulation running in parallel using $N$ PEs
    - (each PE runs $M/N$ reactions)
  - $N$ different simulation runs executed in parallel
    - (each PE runs $M$ reactions)
- Achieves the highest throughput reported in the literature
  - (2.6 Mega Reactions cycles/sec)
- Demonstrated speedup factor 342x compared to i7 Intel CPU (6 GB Ram, 2.66 GHz) for a benchmark biomodel with 512 Reactions
SoC Architecture

Virtex 5 FPGA

Biomodel Information

FRM SoC implementation with 4 PE cores.
Simulation and Performance Results

<table>
<thead>
<tr>
<th>Xilinx (Virtex 5 XC5VLX110T-1ff1136 – Virtex 7 XC7VX855T-3ffg1157)</th>
<th>FRM1X</th>
<th>FRM2X</th>
<th>FRM4X</th>
<th>FRM8X</th>
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<tbody>
<tr>
<td>Reactions</td>
<td>512</td>
<td>1024</td>
<td>2048</td>
<td>4096</td>
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<tr>
<td>Frequency (MHz)</td>
<td>200-320</td>
<td>200-320</td>
<td>200-320</td>
<td>200-320</td>
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<tr>
<td>Latency (cycles)</td>
<td>Q (44-70)+9</td>
<td>Q (44-70)+11</td>
<td>Q (44-70)+13</td>
<td>Q (44-70)+15</td>
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<tr>
<td>Performance (Mreactions/sec)</td>
<td>173-181*</td>
<td>303-525*</td>
<td>485-776*</td>
<td>687-1099*</td>
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<td>292-302**</td>
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<td>RAM-BLOCKS</td>
<td>53</td>
<td>118</td>
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<td>141</td>
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</table>

* Worst case of 3rd reaction order biomodels where the reactions are identical. Performance results respectively for Virtex5 -7
**Biomodels of first or second order (most usual case). Performance results respectively for Virtex5 -7

P.P.R synthesis results for the scalable FRMNX SoC implementations (N=1, 2, 4, 8 PEs and up to 3rd order reactions) for Xilinx Virtex 5 and 7 FPGAs

Clock cycles for simulating a reactions cycle with m=512,1K,2K, 4K reactions using FRM SoCs with increasing number of PEs.
Work in progress

Design a Multiple Operation SoC to implement different SSA algorithms FRM, NRM, wNRM etc.

Create an on-line platform with FPGAs allowing Biologists to directly connect and simulate any biomodel of large complexity

Extend the SSA capabilities to fully describe bimolecular processes such as diffusion processes, analysis of molecular interactions in 3D space and time.

Thank you for your attention!

Questions?
References


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[11] Xu and Cai: "Weighted next reaction method and parameter selection for efficient simulation of rare events in
biochemical reaction systems ". EURASIP Journal on Bioinformatics and Systems Biology 2011 2011 :4

[12] ORSALIA-GEORGINA HAZAPIS, ELIAS S MANOLAKOS, Scalable FRM-SSA SoC Design for the simulation of Networks with thousands
of biochemical reactions in real time " IEEE FPL pp 459-463 2011.
BACKUP SLIDES
The FRM-SSA

Algorithm 1. First Reaction method

Initialize $X_0(t) = x_0$
While $(t < t_{\text{max}})$
    { For every $j$ do  % start a new reactions cycle
        { Evaluate propensity function $a_j(x)$, generate a random number $r_j$:
            Determine the time $\tau_j$ until the next $R_j$ reaction
            \[ \tau_j = \frac{1}{a_j} \ln \left( \frac{1}{r_j} \right) \]
        } end for;
    If $\tau_\mu = \min(\tau_j)$ then
        { Let $R_\mu$ be the “winning” reaction resulting the smallest $\tau_j$
            Determine the new state after reaction $R_\mu$ occurs:
            $t' = t + \tau_\mu$ and $X(t)' = x + v_\mu$:
        } end if;
    End While;