

Harish Chandran

CONTACT INFORMATION

D 330 Levine Science Research Center
Department of Computer Science
Duke University
Durham, NC 27708 USA

Voice: (919) 724-8205
Fax: (919) 660-6519
email: harish@cs.duke.edu
URL: www.cs.duke.edu/~harish

RESEARCH

Algorithms, Mathematical Modeling, Stochastic Analysis, Self-assembly, DNA Nanoscience

EDUCATION

Doctor of Philosophy in Computer Science

Duke University, Durham, North Carolina, USA (*expected May 2012*) GPA: **3.902/4.000**

Certificate in Nanoscience

Duke University, Durham, North Carolina, USA (*expected May 2012*) GPA: **4.000/4.000**

Master of Science in Computer Science

Duke University, Durham, North Carolina, USA (May 2010) GPA: **3.902/4.000**

Bachelor of Engineering in Computer Science and Engineering

Anna University, Chennai, Tamil Nadu, India (May 2007) GPA: **77.650/100.00**

HONORS AND AWARDS

Faculty of 1000, Associate Faculty Member (Jan 2010 - Present)

Nanoscience Fellowship, Duke University (Aug 2007 - May 2008, Jan - May 2009)

Graduated First Class with Distinction, Anna University (May 2007)

WORK EXPERIENCE

Microsoft Research, Biological Computation Group, Cambridge, United Kingdom

Research Intern (May 2011 - Aug 2011)

Worked with Dr. Andrew Phillips to program and model-check various localized hybridization networks using Microsoft Research's Visual DSD and PRISM tools. Worked with other team members in extensions to the syntax and semantics of DSD and suggested vital performance improvements. Published our preliminary findings in DNA 17, a premier conference in DNA computing.

AIMS Education, Chennai, Tamil Nadu, India

Associate, Marketing and Content Development (May 2004 - May 2005)

Spearheaded a marketing campaign aimed at high school students by organizing a city wide science Olympiad, attended by sixteen thousand students. Used data collected from the Olympiad to run a targeted phone advisement campaign. Created educational content for grades eleven and twelve in forms of quizzes, examinations.

PROGRAMMING LANGUAGES

1. **Experience:** C++
2. **Exposure:** C, Java, C#, HTML, CSS, SQL, MATLAB

SELECTED PROGRAMMING PROJECTS

1. **MMINiDASS**(C++, Jul 2005- Jul 2007, WARFT India): Was part of a team that developed a framework for event-driven simulations of large scale biological neural networks over a cluster. Developed efficient distributed data structures and synchronization mechanisms to store and manipulate the structure of the neural network. Developed thread level speculative execution policies so that processor idle time is kept low, especially since our switch was sub-gigabit. Implemented an extensible framework for multiparameter simulated annealing algorithm.
2. **BENSIM**(C++, Jul 2006- Jul 2007, WARFT India): Was part of a team that created a framework for the synthesis of custom benchmarks to evaluate supercomputing architectures. Implemented a wide library of scientifically important algorithms, such as matrix decompositions, convex hull etc. and created a system for parametric specification of benchmarks.
3. **IDE:DNAN**(C++ & C#, Aug 2011- Present, Duke): Part of a team trying to develop an integrated development environment for the specification, simulation and visualization of complex DNA hybridization networks. Currently we are looking at data structures for the efficient storage and manipulation of DNA nanostructures and the syntax and semantics of DNA hybridization based systems.

RESEARCH
EXPERIENCE

Department of Computer Science, Duke University, Durham, North Carolina USA

Research Assistant to Prof. John Reif (Aug 2007 - Present)

Tiling Theory, Algorithmic Self-assembly, DNA Nanorobotics, Complexity Theory, Probabilistic Analysis, Structural DNA Nanotechnology, Modeling DNA Systems, Synthetic Biology

LaBean-Reif Lab, Duke University, Durham, North Carolina USA

Research Assistant (Apr - Aug 2008, Apr - Aug 2009, Apr - Aug 2010)

DNA Purification, Analytical PAGE, Fluorespectrometry, DNA-AuNP experiments, AFM, Data Analysis

Waran Research Foundation, Chennai, Tamil Nadu India

Research Assistant (Jul 2005 - Jul 2007)

Microprocessor Design Automation, Brain Modeling, High Performance Computing, Benchmarking

BOOK CHAPTERS

1. **Self-assembled DNA Nanostructures and DNA Devices**, Nanofabrication Handbook, Taylor and Francis Group 2012, with Nikhil Gopalkrishnan, Thom LaBean and John Reif
2. **DNA Nanorobotics**, Nanorobotics, Springer 2012, with Nikhil Gopalkrishnan and John Reif
3. **Biomolecular Computing Systems**, Molecular and Supramolecular Information Processing: From Molecular Switches to Logic Systems, , Wiley 2012, with Sudhanshu Garg, Nikhil Gopalkrishnan and John Reif

JOURNAL AND
CONFERENCE
PAPERS

1. **Tile Complexity of Approximate Squares**, *to appear in* Algorithmica, with Nikhil Gopalkrishnan, and John Reif
2. **Meta-DNA: Synthetic Biology via DNA Nanostructures and Hybridization Reactions**, JRSI 2012, with Nikhil Gopalkrishnan, Bernard Yurke and John Reif
3. **Localized Hybridization Circuits**, DNA 17, with Nikhil Gopalkrishnan, Andrew Phillips and John Reif
4. **High-Fidelity DNA Hybridization using Programmable Molecular DNA Devices**, DNA 16, with Nikhil Gopalkrishnan and John Reif
5. **The Tile Complexity of Linear Assemblies**, ICALP 09, with Nikhil Gopalkrishnan and John Reif
6. **DNA Based Evolutionary Approach for Microprocessor Design Automation**, ICAN-NGA 07, with Arjun Kumeresh and Venkateswaran Nagarajan

CONFERENCE
POSTERS

1. **Speeding up DNA Circuits using Localized Hybridization**, FNANO 11, with Nikhil Gopalkrishnan, Sudhanshu Garg and John Reif
2. **Design for Experimental Demonstration of Linear Activatable Assemblies**, DNA 15, with Nikhil Gopalkrishnan, Thom LaBean and John Reif
3. **Meta-DNA: Synthetic Biology via DNA Nanostructures and Hybridization Reactions**, FNANO 10, with Nikhil Gopalkrishnan, Bernard Yurke and John Reif
4. **Target DNA Detection by Strand Displacement and Deoxyribozymogen Amplification**, FNANO 09, with Thom LaBean, John Reif, Erik Schultes, Geetha Shetty and Hao Yan
5. **A Dendritic DNA Nanostructure for Target DNA Detection**, FNANO 09, with Thom LaBean, John Reif, Erik Schultes, Geetha Shetty and Peng Yin
6. **Structural Optimization of Dendritic DNA Self-Assembly**, FNANO 09, with Morgan Bishop, John Reif, Thomas Renz, Eric Schultes and Clare Thiem
7. **MMINI-DASS - Large-scale Brain Circuit Construction and Simulation for Interconnectivity Prediction**, Neuroinformatics 08, with Vijay Daniel, Vignesh Jaganathan, Ashutosh Mohan, Venkateswaran Nagarajan, Vijay R and Karthik Srinivasan
8. **Microprocessor Design Automation: A DNA Based Evolutionary Approach**, BICS 06, with Arjun Kumeresh, Venkateswaran Nagarajan, Vasanth Pachai Perumal and Deephan Venkatesh

TEACHING
ACTIVITIES

1. Teaching Assistant, CPS 130 - Design and Analysis of Algorithms, Duke University, Fall 08
2. Teaching Assistant, CPS 130 - Design and Analysis of Algorithms, Duke University, Fall 09
3. Teaching Assistant, CPS 296.3 - Algorithms in the Real World, Duke University, Spring 11
4. Teaching Assistant, CPS 210 - Operating Systems, Duke University, Spring 11
5. Teaching Assistant, CPS 130 - Design and Analysis of Algorithms, Duke University, Fall 11

PROFESSIONAL
SERVICES

Memberships

Board Member R & D Executive Committee, SSNCE Alumni Association, USA Chapter, Mar 2011-Present

Organizing Committee

1. Assisant Organizer, FNANO 11, Foundations of Nanoscience, Snowbird, Utah, Apr 2011
2. Assisant Organizer, FNANO 10, Foundations of Nanoscience, Snowbird, Utah, Apr 2010
3. Assisant Organizer, FNANO 09, Foundations of Nanoscience, Snowbird, Utah, Apr 2009
4. Assisant Organizer, Dhi Yantra 07, Workshop on Brain Modeling and Supercomputing, Chennai, Jul 2007
5. Organizer, Biomolecular Computation Journal Club, Duke University, Jan 09 - Present

Peer Reviewing

1. Primary Reviewer for ToCS, DNA 16, DNA 17, SODA 2012 and Faculty of 1000 Biology
2. Secondary Reviewer for Science, STOC 2010, Natural Computing Journal, SIAM Journal on Computing, ICALP 2010, SODA 2011

Grant Writing

Assisted in writing grant NSF SHF 10572: Meta-DNA, Synthetic Biology via DNA Nanostructures & Hybridization Reactions, NSF SHF 10572: Integrated Design Environment for Dynamic DNA Nanosystems, DARPA-BAA-11-42: GeneGuards for Microorganisms via Engineered Suicide Circuits

INVITED
TALKS

1. Localized Hybridization Circuits, Microsoft Research Lectures, Microsoft Research Cambridge, Aug 2011
2. State of the Art of DNA Nanoscience, Invited Talk, Waran Research Foundation, Dec 2010
3. Tile Complexity of Linear Assemblies, Algorithm Seminar, Duke University, Nov 2010
4. Introduction to DNA Computing, Invited Talk, SSN College of Engineering, Anna University, Aug 2009
5. Introduction to DNA Nanoscience, Invited Talk, Waran Research Foundation, Aug 2008
6. Microprocessor Design Automation, Dhi Yantra, Worskshop on Brain Modeling and Super Computing, June 2007

RELEVANT
COURSEWORK

Graduate

Advanced Algorithms, Randomized Algorithms, Linear & Integer Programming, Sequential Decision Theory, Complexity Theory, Alternate Model of Computation, Computational Microeconomics, Artificial Intelligence, Advanced Computer Architecture, Mathematical Methods in System Analysis, Bio Nanotechnology, Foundations of Nanoscience.

Undergraduate

Algebra, Calculus, Probability and Queuing Theory, Numerical Methods, Discrete Mathematics, Theory of Computing, Compilers, Algorithms, Data Structures, Software Engineering, Object Oriented Analysis and Design, System Software, Computer Graphics, Artificial Intelligence, Operating Systems, Networks, Databases, Computer Architecture, Microprocessors, Digital Electronics, Electronic Circuits, Signal Processing, Physics, Semiconductors and Optoelectronics, Chemistry, Engineering Mechanics and relevant lab work for these.

SELECTED
PROJECTS

I have been an academic researcher for the past six years in various fields of computer science and natural science at three major research institutions: WARFT, India, Duke University, USA and Microsoft Research Cambridge, UK. I have worked with large and small teams in various projects in computer architecture, supercomputing, benchmarking, computational neuroscience, algorithms, algorithmic self-assembly, DNA self-assembly and DNA nanoscience. Listed below are a few sample projects I have worked on:

ALGORITHMS &
THEORY

Stochastic Online Bipartite Matching

The problem of stochastic online bipartite matching, which has applications in adword matching, was studied under the *iid* model where we assume that each impression type arrives with a certain fixed probability that is independent of the sequence seen so far. Best known algorithms achieve a competitive ratio of 0.67 using the idea of *two suggested matching*. We developed a *refined suggested matching* algorithm which can be proved to achieve a

competitive ratio of at least 0.67 and believe that a more sophisticated analysis of our algorithm will yield a much better competitive ratio.

Probabilistic Tile Assembly Model

The fundamental observation was that Winfree's Tile Assembly Model does not allow for multiple tile types to bind at a given position. This unnatural restriction leads to higher tile complexity for even simple linear assemblies. We were able to lower the tile complexity for linear structures of expected length n from $\mathcal{O}(n)$ to $\mathcal{O}(\log n)$. We also showed a matching lower bound of $\mathcal{O}(\log n)$ for each $n \in \mathbb{N}$, which is stronger than the usual Kolmogorov based lower bounds which only hold almost always. We also developed notions of multi-pad systems and achieved linear assembly of expected length n using $\mathcal{O}(\frac{\log n}{\log \log n})$ 2-pad tile types and proved a matching lower bound. All our probabilistic constructions were free from co-operative tile binding errors and could be modified to produce assemblies whose probability distribution of lengths have arbitrarily small tail bounds dropping exponentially with a given multiplicative factor increase in number of tile types. Thus, for linear assembly systems, we showed that randomization can be exploited to get large improvements in tile complexity at a small expense of precision in length.

Approximate Squares

We considered the problem of building approximate squares in the Tile Assembly Model. Given any $\epsilon \in (0, \frac{1}{4}]$ we showed how to construct squares whose sides are within $(1 \pm \epsilon)N$ of any given positive integer N using $\mathcal{O}\left(\frac{\log \frac{1}{\epsilon}}{\log \log \frac{1}{\epsilon}} + \frac{\log \log \epsilon N}{\log \log \log \epsilon N}\right)$ tile types. We proved a matching lower bound by showing that $\Omega\left(\frac{\log \frac{1}{\epsilon}}{\log \log \frac{1}{\epsilon}} + \frac{\log \log \epsilon N}{\log \log \log \epsilon N}\right)$ tile types are necessary almost always to build squares of required approximate dimensions. In comparison, the optimal construction for a square of side exactly N in TAM uses $\mathcal{O}\left(\frac{\log N}{\log \log N}\right)$ tile types. Our constructions could get highly accurate squares using a very few number of tile types and are feasible starting from values of N that are orders of magnitude smaller than the best comparable constructions previously suggested. If the concentrations of the tile types are carefully chosen, we proved that our construction assembles an $L \times L$ square in optimal assembly time $\mathcal{O}(L)$ where $(1 - \epsilon)N \leq L \leq (1 + \epsilon)N$.

Circuit Constructing Turing Machines

In this project we explored the power of Turing machines that could construct Boolean circuits and query these circuits later like a sub-routine. A practical implementation of this idea would be a microprocessor with an FPGA co-processor. The microprocessor would configure the FPGA co-processor to form circuits that implement most commonly used subroutines, which can then be queried to obtain considerable speedups. Various programs can use a part of the FPGA to implement their own common subroutines. We formalized these notions as a circuit constructing Turing machines. Various complexity classes on these machines were defined and their relations with the classical complexity classes were studied.

Geometric Duality and Linear Programming

We used geometric duality to convert a set of constraints C to a point set S in the dual space and then apply the idea of approximate point set of S . In particular we studied the following problem: let $L(C, obj)$ represent the maximal value of some objective function obj constrained by a set of constraints C . Then, for given set of constraints C with a non null feasible region, a parameter $\epsilon \in (0, 1)$ and any objective function obj , is there a sparse set of constraints C' such that $L(C, obj) \leq L(C', obj) \leq (1 + \epsilon)L(C, obj)$?

COMPUTER
ARCHITECTURE

Dynamic Heterogeneous Core Scheduling

We investigated the benefits of a multicore processor design with cores of varied pipeline depth and frequency. Through intelligent speculative context swapping between cores, concurrent threads could be optimally allocated among the various heterogeneous cores based on their respective likelihood of branch misprediction. To test this, we considered a dynamic analysis method by which we heuristically determined when such swaps should occur. In order to evaluate our design, we compared our simulation results with those achieved by both an equivalent homogeneous multi-core processor and an idealized heterogeneous design using an oracle to make optimal swapping decisions.

Supercomputer Benchmark Simulator: BENSIM

BENSIM is an effort to create a synthetic benchmark for use on supercomputing clusters. Key metrics determining the goodness of a system: power, performance and scalability, are determined when the cluster runs a synthetic mixture of algorithms created based on inputs from the user from a pre-existing bank of algorithms. A kernel extracts performance and power figures from the cluster-specific, simulator based inputs and also calculates scalability by varying cluster size for the same benchmark.

DNA Evo Based Design Microprocessor Automation

This project aimed at developing a methodology to automate the design process of a microprocessor by using a DNA based evolutionary approach. Parameters that define a microprocessor are encoded onto DNA sequences which then undergo recombinations with other sequences along with mutations. These offsprings are then decoded into microprocessors and evaluated. Over a period of time a Gene-pool is built up from which processors according to user specifications can be evolved.

Localized Hybridization Circuits

Molecular computing executed via local interactions of spatially contiguous sets of molecules has potential advantages of speed due to increased local concentration of reacting species, sharper switching behavior and higher precision due to single molecule interactions, parallelism since each circuit operates independently of another and modularity and scalability due to the ability to reuse DNA sequences in spatially separated regions. We proposed detailed designs for local molecular computations that involve spatially contiguous molecules arranged on addressable substrates. The circuit acts via enzyme-free DNA hybridization reaction cascades. Our designs included composable OR, AND, propagation Boolean gates and techniques to achieve higher degree fan-in and fan-out. A biophysical model of localized hybridization reactions was used to estimate the effect of locality on reaction rates. We also used Microsoft Research's Visual DSD simulation software in conjunction with these localized reaction rates to simulate a localized circuit for computing the square root of a four bit number.

Hybridization Chain Reaction for DNA Analyte Detection

The goal of the project was to develop an autocatalytic hybridization chain reaction that is triggered by the presence of an analyte. The analyte of interest is a DNA strand and the autocatalytic system is an equimolar mixture of two hairpin structures that can repeatedly open up each other via strand displacement. The analyte serves as the trigger which opens up the first of these loops which leads to an exponential signal amplification via a dendritic tree. We also demonstrated coupling of the detection system to AuNP based plasmonic detection scheme which in theory could lead to naked eye readout and tested the detection of the HIV and Chlamydia viruses.

Biomolecular Detection using DNA Based Nanoparticle Arrays

Disease diagnosis often requires multiple time-consuming, labor-intensive methods. A quick and simple detection system for multiplexed analysis, using self-assembly of nanoparticle functionalized DNA tiles, was proposed. Two potential approaches to biomolecular detection were examined: Surface Enhanced Raman Spectroscopy assays and a computational DNA tiling system. Spectra of the different systems and enhancements of nanoparticle arrays were determined analytically. It was found that both detection schemes exhibit promise, and further experimental exploration was recommended.

Synthetic Biology: Meta-DNA

The approach taken here was to develop a biochemical system which we called meta-DNA (abbreviated as mDNA), based entirely on strands of DNA as the only component molecules. Each base of a mDNA was a DNA nanostructure. Our mDNA bases were paired similar to pairing in DNA bases, but had a much larger alphabet of bases, thereby providing increased power of base addressability. Our mDNA bases could be assembled to form flexible linear assemblies (single stranded mDNA) analogous to single stranded DNA, and could be hybridized to form stiff helical structures (duplex mDNA) analogous to double stranded DNA, and could also be denatured back to single stranded mDNA. We described various isothermal hybridization reactions that manipulate our mDNA in powerful ways analogous to DNA-DNA reactions and the action of various enzymes on DNA. We provided a formal model to describe the required properties and operations of our mDNA, and showed that our proposed DNA nanostructures and hybridization reactions provide these properties and functionality.

High-fidelity DNA Hybridization

This project developed techniques for ensuring specific high-fidelity DNA hybridization reactions for target strands of arbitrary length. We are given an in-vitro solution which contains various DNA strands with differing sequences, among them a particular known target DNA sequence s of relatively long length (say at least 60 to hundreds of bases). Our goal was to bind to each subsequence segment of s with high specificity and exact complementarity for a significant fraction of strands s in the solution. To do this, we developed a protocol that relies only on hybridization reactions between relatively short length (of at most 15 bases) DNA sequence segments. Our basic approach was to design DNA devices that essentially scan over strands in solution, subsegment by subsegment, and determine if one is indeed an instance of the given target strand s . Our high-fidelity DNA hybridization protocol was driven by a series of conversions of single stranded DNA into duplex DNA that help overcome kinetic energy traps, similar to DNA walkers.

Computational Neuroscience: MMINiDASS

The MMINi-DASS aims at predicting the neuronal interconnectivity of various cortices of the human brain. We start out with a random interconnectivity of a cortex and then refine it iteratively based on actual fMRI imaging. In each iteration, input stimuli are injected as spike trains into few neurons and the overall activity of the cortex is recorded based on the hemodynamics of the neurons. This simulated fMRI is then compared with the actual fMRI obtained for the same input. The difference between the two is reduced by altering the structure using Simulated Annealing.

REFERENCES

Prof. John Reif (reif@cs.duke.edu)

Prof. John Reif is a Distinguished Professor of Computer Science at Duke University with over 35 years of academic research resulting in around 250 publications. A well known academic leader credited with many seminal results in various areas of computer science, he my primary advisor for my doctoral work at Duke.

Prof. Venkateswaran Nagarajan (waran@warftindia.org)

Prof. Nagarajan is the Director of WARFT India, a research institute for computational neuroscience and supercomputing. With over 35 years of academic research at various universities, Prof. Nagarajan is a well known Indian scientist and was my advisor when I was a researcher at WARFT India, supervising my research work there.

Prof. Thom LaBean (thlabean@ncsu.edu)

Prof. Thom LaBean recently took appointment as an Associate Professor of Materials Science & Engineering at NCSU. Before that he was at Duke university for over 15 years in various capacities culminating in an Associate Research Professorship in Computer Science for the past 6 years. I have worked with Prof. LaBean closely for the past 4 years.