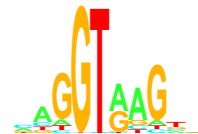


CURRICULUM VITAE

THOMAS D. SCHNEIDER, PH. D.

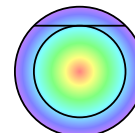
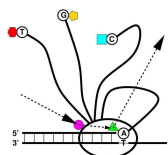


PERSONAL INFORMATION

Title: Research Scientist, Senior Investigator
Date of Birth: November 9, 1955
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schneidt@mail.nih.gov
toms@alum.mit.edu (permanent)
<http://alum.mit.edu/www/toms> (permanent)¹
<http://ccr.cancer.gov/Staff/staff.asp?profileid=5753>
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Gene Regulation and Chromosome Biology Laboratory
NCI-Frederick Bldg 539, Room 129A
P.O. Box B
Frederick, MD 21702-1201

MAJOR ACCOMPLISHMENTS

- **Invented the sequence logo**,
a widely used information-theory based graphic to display sequence alignments [12]
- **Invented the MedusaTM Sequencer**,
a DNA sequencing machine that is one molecule [81]
- **Discovered 70% molecular efficiency**,
which defines the exact relationship between information and energy in biological systems [77]



EDUCATION/TRAINING

- 1987 - Postdoctoral Fellowship (Molecular Biology), University of Colorado, Boulder, CO
- 1984 - Ph.D. (Molecular Biology), University of Colorado, Boulder, Colorado
- 1978 - B.S. (Biology), Massachusetts Institute of Technology, Cambridge, Massachusetts

¹Note: web links are active on the PDF.

PROFESSIONAL EXPERIENCE

- 2010 August - present: **Tenured** position as a Research Biologist, Gene Regulation and Chromosome Biology Laboratory, NIH, NCI, CCR

Work on **nanotechnology** projects [81] and **molecular efficiency** [77].

- 1999 June - 2010 August: **Tenured** position as a Research Biologist, Laboratory of Experimental and Computational Biology (renamed Center for Cancer Research Nanobiology Program in 2005 August), NIH, NCI, CCR

Work to **demonstrate the application of information theory to a wide variety of molecular systems**: DNA replication [21, 32, 53, 54], transcription factors [9, 41, 35, 58, 71, 72, 75], RNA polymerases [9, 11, 64, 67, 70], splice junctions [18], (also mutations in splice junctions causing human disease [26, 36, 37, 48], including the cancer xeroderma pigmentosum [40, 50, 56, 61, 73]), RNA folding [68], ribosome binding sites [9, ?, 13, 17, 23, 52], protein structure [47] and evolution and phylogeny [27, 39, 49, 64, 67].

- December 1987 - June 1999: **Senior Staff Fellow or Investigator** (starting 11/12/95), Laboratory of Mathematical Biology (Division Basic Sciences, National Cancer Institute, National Institutes of Health, Frederick Cancer Research and Development Center, Maryland)

Continuation of work on T7 described below and creation of a theory of molecular machines, based on Shannon's channel capacity formula [14, 15]. **Invention of the now widely used sequence logos, [12] individual information [33] and sequence walkers [34].**

- January 1987-November 1987: **Postdoctoral Research Associate** with Gary Stormo, Department of Molecular, Cellular and Developmental Biology, University of Colorado

Conclusion of the T7 promoter experiment [11].

- 1984-1986: **Postdoctoral Research Associate** with Larry Gold, Department of Molecular, Cellular and Developmental Biology, University of Colorado

Randomized synthetic DNA genetic engineering experiment to determine whether the excess information at bacteriophage T7 promoters is used by the polymerase [11]. The experiment was successful, and showed that the T7 polymerase does not use the excess sequence conservation. This supports the hypothesis that a second protein binds.

Served on the GenBank Advisory Committee as a graduate student and postdoc.

- 1978-1984: **Ph.D. candidate**, Department of Molecular, Cellular and Developmental Biology, University of Colorado

Designed and wrote a computer language called Delila for manipulating DNA sequences [2, 6], which we used to investigate the statistics of ribosome binding sites [1, 3]. We used this system to train a perceptron to identify ribosome binding sites, and so we were the first group to apply neural networks to the problem of finding nucleic acid binding sites [4]. I designed and built plasmids for studying the quantitative relationships between sequence and function of ribosome binding sites [7, ?, 23]. My thesis was on the information content of nucleic-acid binding sites [9]. It describes the excess information (excess sequence conservation) found

at bacteriophage T7 promoters. This purely mathematical calculation led me to predict the existence of a second binding protein.

- 1980: **Teaching Assistant**, Molecular Genetics, University of Colorado
Graded tests and helped students to understand the material.
- 1979: **Teaching Assistant**, Cell and Tissue Biology, University of Colorado
Taught two lab sections and graded tests.
- 1974-1978: **Undergraduate, Department of Biology, Massachusetts Institute of Technology**, Cambridge, Massachusetts
Worked at the Architecture Machine in the Department of Architecture on a computer system to recognize visual scenes by parallel processing. I did this on a serial processor since no parallel processors were available at that time. This work was funded for the summer of 1977 by the MIT Undergraduate Research Opportunities Program.
- 1975 and 1976: **Computer Aide**, Space Environment Laboratory, National Oceanic and Atmospheric Administration, Boulder, CO (summer)
I designed and wrote programs to display meteorological data gathered in real time on a NOAA airplane flying through storm systems such as hurricanes.

HONORS

- 2010: National Cancer Institute, Center for Cancer Research, Federal Technology Transfer Act award for the MedusaTM Sequencing project.
- 2006: Federal Laboratory Consortium For Technology Transfer (FLC) Technology Recognition Award for Nanoprobes for Detection or Modification of Molecules. The award recognizes “technologies not yet commercialized, but having great potential to be commercialized”. <http://alum.mit.edu/www/toms/patent/nanoprobe/>
- 2000: DBS Technology Transfer Award: for the Molecular Rotation Engine patent application: <http://alum.mit.edu/www/toms/patent/molecularrotationengine/>
- 1998: Federal Technology Transfer Act Cash Award (NCI): for “inventions, innovations, computer software, or other outstanding scientific or technological contributions of value to the United States due to commercial application or due to contributions to the missions of the NCI or the Federal government. Additionally, cash awards are provided for other exemplary activities that promote the domestic transfer of science and technology development.”
- 1998: On-the-Spot Award (DHHS, PHS): “for accomplishing the development of a program that has made a dramatic improvement on the work of his group”. This was for inventing the atchange program: <http://alum.mit.edu/www/toms/atchange.html>
- 1992: Frederick County Public School System’s Highest honor, a Board Pin for being a mentor in the National Cancer Institute Student Intern Program for 4 years.
- 1983: Graduate Student Research and Creative Work Award, University of Colorado.

- 1980-1981: National Institutes of Health Training Grant, NIH 5 T32 GM07385-04, at the University of Colorado
 - 1976: Robert A. Boit Writing Prize at MIT (2nd Place)
 - 1975: Ellen King Prize for Freshman Writing at MIT (3rd Place)
 - 1974: Westinghouse Science Talent Search (top 40)
-

INTRAMURAL NIH RESEARCH SUPPORT

- **Z01 BC 008396** Molecular Information Theory. This is my main project since 1987 and its funding covers the other projects.
<http://alum.mit.edu/www/toms/>
 - **Z01 BC 010771** MedusaTM Sequencer.
<http://alum.mit.edu/www/toms/patent/medusa/>
 - **Z01 BC 010772** Rod-Tether Nanoprobe.
<http://alum.mit.edu/www/toms/patent/nanoprobe/>
-

MEMBERSHIPS IN PROFESSIONAL ORGANIZATIONS

- Sigma XI, the Scientific Research Society
 - American Association for the Advancement of Science (AAAS)
 - Institute of Electrical and Electronics Engineers (IEEE): IEEE Information Theory Society and IEEE Communications Society
-

EDITORIAL BOARDS

- 1998 - 2006: member of the Editorial Board of Entropy, an International and Interdisciplinary Journal of Entropy and Information Studies ISSN 1099-4300. The first issue was published in March 1999. <http://www.mdpi.com/journal/entropy/>.
 - 2009 - : Editorial Board, Nucleic Acids Research
-

MEETINGS

- Third workshop on the national nucleic acid sequence data bank, National Institute of General Medical Sciences (NIGMS), Bethesda, Maryland, December 7, 1980
- Reviewer to evaluate the contract proposals for the establishment of a national nucleic acid sequence data bank, Bethesda, Maryland, March 30, 1982
- Advisor to NIGMS on GenBank, the national Genetic Sequence Data Bank. (Cambridge, Massachusetts, December 16, 1982; Los Alamos, New Mexico, January 13, 1984; Bethesda,

Maryland, October 31, 1985; Bethesda, Maryland, November 5-6, 1987; Los Alamos, New Mexico, April 11-12, 1988; Bethesda, Maryland, November 14-15, 1988)

- Advisor to the Protein Identification Resource (August 1992)
- Consultant to the Office of Naval Research, Biological Science and Technology Program on initiating projects on molecular computation, December 20, 1994
- Schneider, T. D. Invited by Tadashi Nakano (Assistant Adjunct Professor, Department of Computer Science, Donald Bren School of Information and Computer Sciences, University of California, Irvine, tnakano@ics.uci.edu) and Tatsuya Suda (Program Director, EMT Program, CCF/CISE/NSF, suda@ics.uci.edu) to chair Session 3: Coding Theory and Channel Capacity of Biological Communications Media at the NSF funded workshop on Molecular Communication: Biological Communications Technology, February 19-21, 2008, Arlington, Virginia. I invited 7 other attendees and organized the session. The final report is available from http://netresearch.ics.uci.edu/mc/nsfws08/NSFWS08_Report_080308final.pdf See section 2.3.
The slides are available at:
http://netresearch.ics.uci.edu/mc/nsfws08/slides/GC_finalized.pdf
We made these slides (pages 4-6):
 - Understanding Biology using Information and Coding Theory
 - Understanding Information and Coding Theory using Biology
 - Applying Information and Coding Theory to Bioinformatics and Bio/Nanotechnology
- Schneider, T. D. invited by Dr. John A. Niederhuber (Director, National Cancer Institute) and Anna D. Barker, Ph.D. (Deputy Director, National Cancer Institute) to attend and participate in a meeting: Integrating and Leveraging the Physical Sciences to Open a New Frontier in Oncology, sponsored by the National Cancer Institute, February 26-28, 2008, The Ritz-Carlton, Pentagon City Arlington, VA 22202.
- Dr. Niederhuber invited me again to participate in the October 2008 Think Tank “Physical Sciences-Based Frontiers in Oncology: The Coding, Decoding, Transfer, and Translation of Information in Cancer.”
- Invited to Co-chair a session and present my work at the NSF Workshop on Biologically-Enabled Wireless Networks Design and Modeling July 19-20, 2011 — Hilton Arlington, Arlington VA <http://madrid.ccs.neu.edu/nsfbw11/>.

PRESENTATIONS

For the most recent and confirmed upcoming events, see Forthcoming and Previous Presentations.

1. Second European Molecular Biology Conference on Computer Analysis of Nucleotide Sequence Information, Schonau, West Germany, May, 1981. “The Delila System”.
2. Maximum Entropy and Bayesian Methods in Applied Statistics, 6th Annual Workshop, Seattle, Washington, August 5-8, 1986. “Information Content of Binding Sites on Nucleotide Sequences”.

3. Macromolecules, Genes, and Computers, Waterville Valley, N. H., August 12-17, 1986. "Directions for Genetic Sequence Data Bases".
4. December 1988, Johns Hopkins, Baltimore, MD. Host: David Draper.
5. August 17, 1990 Johns Hopkins, Baltimore, MD.
6. Supercomputing Research Center, Bowie, MD. May 24, 1991, "Theory of Molecular Machines".
7. Partnerships in Education Workshop, The Regional Education Service Agency of Appalachian Maryland, Hagerstown, MD. January 31, 1992. "NCI-FCRDC Student Intern Program: Planning for our Scientific Future."
8. CREST Statewide Conference on Science and Engineering Partnerships. University of Maryland, College Park. April 7, 1992. "National Cancer Institute Student Intern Program: Planning for our Scientific Future."
9. Physics of Computation Workshop, Dallas, Texas, October 2-4, 1992, "Use of Information Theory in Molecular Biology".
10. Neils Bohr Institute in Copenhagen, Denmark, April 20, 1993: "Information Theory of Molecular Binding Sites: Bits and Sequence Logos"
11. Department of Physical Chemistry at the Technical University of Denmark, Lyngby, Denmark, April 22, 1993: "Theory of Molecular Machines: Gumballs and Hyperspace". (5 hours of lectures, in combination with previous lecture.)
12. Frederick Community College, May 10, 1993, "Use of Information Theory in Molecular Biology".
13. The Washington Evolutionary Systems Society (WESS) Washington, D.C., November 4, 1993, "Information Theory and Molecular Recognition".
14. Washington-Baltimore Section of the Society for Industrial and Applied Mathematics (SIAM) in conjunction with the American Mathematical Society and the Mathematical Association of America, Washington, D.C., April 26, 1994, "New Approaches in Mathematical Biology: Information Theory and Molecular Machines".
15. Biomolecular Databases: Current Status, June 13-14, 1994, Biophysical Society, Bethesda, MD. "Philosophy and Definition for a Universal Genetic Sequence Database".
16. Third International *E. coli* Genome meeting, Woods Hole, Massachusetts, November 4-8, 1994, "New approaches in mathematical biology: information theory and molecular machines".
17. New England Biolabs, Beverly Mass. February 9, 1995 "New Approaches in Mathematical Biology: Information Theory and Molecular Machines".
18. Ptashne Laboratory, Harvard, Mass. February 10, 1995 "New Approaches in Mathematical Biology: Information Theory and Molecular Machines".
19. Keynote speaker for the Informatics session of the Trieste Conference on Chemical Evolution, IV: Physics of the Origin and Evolution of Life, Cyril Ponnampuruma Memorial. Trieste, Italy, September 4-8, 1995. [29] "New Approaches in Mathematical Biology: Information Theory and Molecular Machines".

20. Department of Genetics of the North Carolina State University. February 26, 1996 “New Approaches in Mathematical Biology: Information Theory and Molecular Machines”.
21. Workshop on Gene Networks and Cellular Controls, Hotel duPont, Wilmington, Delaware 18-19 June 1996. Sponsored by the Office of Naval Research. “Information capacity and molecular recognition in gene control”.
22. Fourth Workshop on Physics and Computation: PhysComp96, Boston, Mass 22-24 November 1996, Boston University. “New approaches in mathematical biology: information theory and molecular machines”
23. Second Gordon Research Conference on “Modern Developments in Thermodynamics” February 16-21, 1997, Holiday Inn, Ventura, California. “Information theory and molecular recognition”.
24. National Library of Medicine, Bethesda, MD. Tue, Sep 30, 1997. “Logos and walkers: graphical analysis of splice junctions and other binding sites, with clinical application”
25. Johns Hopkins Department of Biophysics and Biophysical Chemistry, Johns Hopkins University School of Medicine, Baltimore, MD. October 1, 1997. “Logos and walkers: graphical analysis of splice junctions and other binding sites, with clinical application”
26. NIH Biotechnology Interest Group, 1997 October 14, “Logos and walkers: graphical analysis of splice junctions and other binding sites, with clinical application”
27. Organizer and speaker at the session Thermodynamics and Information Theory in Biology, 1998 American Association for the Advancement of Science (AAAS) Annual Meeting and Science Innovation Exposition Philadelphia, Pennsylvania. Monday, February 16, 1998, 3:00pm-6:00pm, Track: Emerging Science: Transforming the Next Generation Session number: 101.0. “Information Theory in Molecular Recognition: Efficiency of Molecular Machines”
28. Speaker at the meeting “After the Genome: Envisioning Biology in the Year 2010” conference IV, Jackson Hole, Wyoming, October 10-14, 1998.
29. Speaker in the Computational Sciences & Informatics Colloquium, George Mason University, “Molecular Information Theory: From Clinical Applications to Molecular Machine Efficiency” Dec. 3, 1998.
30. Invited to give a Science Innovation Topical Lecture at the AAAS Annual Meeting and Science Innovation Exposition (1999 January 23, 1:30pm-2:15pm, Anaheim, CA). “Molecular Information Theory: from Clinical Applications to Molecular Machine Efficiency”.
31. Molecular Information Theory, April 27, 1999 at the Transcription Factors Interest Group Conference, Holiday Inn Conference Center, Frederick, MD.
32. 2000 Feb 7: “Molecular Information Theory: from Clinical Applications to Molecular Machine Efficiency” at the Department of Biochemistry, University of Missouri-Columbia, Columbia MO.
33. 2000 May 20: “Evolution of Biological Information” at the Washington Evolutionary Systems Society Annual Symposium on General Evolutionary Systems, Georgetown University, Georgetown, MD.

34. “Molecular Information Theory” at the International Summer School on “DNA and Chromosomes: Physical and Biological Approaches” Institut d’Études Scientifiques de Cargèse, Cargèse, Corsica, France, July 31-August 12, 2000.
35. “Molecular Information Theory: from Clinical Applications to Molecular Machine Efficiency” in a symposium on “Macromolecular Machines” at the Burnham Institute, La Jolla, USA, April 5, 2001.
36. “Flippers, Flappers and Flip-Flops in DNA Binding”. George Mason University, School of Computational Sciences Bioinformatics Colloquium 2001 November 6. Host: Iosif Vaisman, <http://binf.gmu.edu/vaisman/>
37. “Flippers, Flappers and Flip-Flops in DNA Binding”. Frederick Faculty Seminar Series, December 12, 2001.
38. “Flippers, Flappers and Flip-Flops in DNA Binding”. 2002 January 17. Thursday, North Carolina State University in the Microbiology Department. 10:00-11:00 am, Stephens Room (Gardner 3533). Host: Eric Miller, <http://www.microbiology.ncsu.edu/people/faculty/Miller.html>
39. “Flippers, Flappers and Flip-Flops in DNA Binding”. 2002 February 7. Department of Mathematics. The Pennsylvania State University State College, Pennsylvania, Mathematics Colloquium. Host: Howard Weiss, <http://www.math.psu.edu/oldColloquium/020207.html>
40. “Twenty Years of Delila and Molecular Information Theory”. Altenberg-Austin Workshop in Theoretical Biology in Altenberg (Vienna), Austria, July 11-14, 2002. The 8th workshop, on BIOLOGICAL INFORMATION BEYOND METAPHOR: Causality, Explanation, and Unification.
41. Institute for Pure and Applied Mathematics (IPAM) Workshop I: Alternative Computing September 30 - October 3, 2002, UCLA Los Angeles CA. Molecular Information Theory: Molecular Efficiency and Flip-Flops. Wednesday October 2, 2002, 3:30 pm.
42. The Center for Advanced Research in Biotechnology CARB (9600 Gudelsky Drive, Rockville, Maryland 20850, contact: Dr. Harold Smith) by Tom Schneider. Flippers, Flappers and Flip-Flops in DNA Binding. 2002 December 2 Monday, 11:00 am.
43. The University of Richmond, Molecular Information Theory: from Clinical Applications to Molecular Machine Efficiency. 2003 January 27, Monday, 4:30 pm. Hosts: Karen Lewis and Peter Smallwood.
44. The Virginia Commonwealth University by Tom Schneider. Molecular Information Theory: from Clinical Applications to Binding Site Evolution. 2003 January 28, Tuesday, 1:00 pm. Host: Gail Christie
45. CANCUN Mexico 2003 17 - 21 September, 25th ANNUAL INTERNATIONAL CONFERENCE OF THE IEEE ENGINEERING IN MEDICINE AND BIOLOGY SOCIETY Special Session on Communication Theory, Coding Theory and Molecular Biology
46. “Genomes 2004: International Conference on the Analysis of Microbial and Other Genomes” (<http://www.tigr.org/conf/mg/>) held from April 14-17, 2004, The Wellcome Trust Conference Centre Hinxton, Cambridge, United Kingdom (This conference was originally

- to be held at the Institut Pasteur, France, April 14 - 17th, 2004 www.pasteur.fr/gmp but it was cancelled. It was then located to the UK.)
47. The Chemical Theatre of Biological Systems” 24th - 28th May, 2004 in Bozen, North Italy. Session: “Application of Information Theory to Chemical and Biological Systems” hosted by the Beilstein-Institut.
 48. Wesleyan Biology Department’s Seminar Series, Middletown, Connecticut, February 3, 2005. Molecular information theory: From clinical applications to molecular machine efficiency.
 49. FinBioNet 2005 Symposium, October 6-7, 2005. Ellivuori, Finland. Molecular information theory: From clinical applications to molecular machine efficiency.
 50. The University of Missouri - Kansas City Department of Computer Science and Electrical Engineering (CSEE) Seminar Series by Tom Schneider. Molecular Information Theory: from Clinical Applications to Binding Site Evolution, 2005 November 11.
 51. Mathematical Biosciences Institute (MBI) at the Ohio State University, Molecular Information Theory: from Clinical Applications to Binding Site Evolution, 2005 November 14-18. This is part of a workshop on Aspects of Self-Organization in Evolution organized by Chris Adami and Claus O. Wilke.
 52. Molecular Information Theory: from Clinical Applications to Molecular Machine Efficiency. Frederick Faculty Seminar Series, February 15, 2006.
 53. Department of Chemistry and Biochemistry, University of Maryland, Baltimore County, Baltimore, MD. 2006 Feb 22 4:00 pm, Molecular Information Theory: Flippers, Flappers and Flip-Flops in DNA Binding,
 54. School of Electrical and Computer Engineering – Cornell University Ithaca, NY 14853-6701. 2006 March 28 Molecular Information Theory: from Clinical Applications to Molecular Machine Efficiency, Host: Sergio Servetto of the Cornell Communication Networks Research Group.
 55. Graduate Group in Computational and Genomic Biology, University of California, Department of Molecular and Cell Biology, Berkeley, CA 94720, Sep 19, 2006. Molecular Information Theory: From Clinical Applications to Molecular Machine Efficiency,
 56. The Keck Graduate Institute, Claremont, CA, 91711, September 22, 2006. Molecular Information Theory: From Clinical Applications To Binding Site Evolution.
 57. Science Unrestricted (presentation for K-12 Students, Families and Teachers), Institute for Defense Analyses, Alexandria, VA, 22311-1882, April 2, 2008. Evolution in a Nutshell
 58. The Institute for Defense Analyses, Alexandria, VA, 22311-1882, May 29, 2008. Molecular Information Theory: From Clinical Applications To Binding Site Evolution.
 59. NCI at Frederick Frederick Faculty Seminar Series. More Molecular Information Theory. Jan 14, 2009.
 60. Plenary speaker at the Workshop on Biological and Bio-Inspired Information Theory held in conjunction with the 43rd Annual Conference on Information Sciences and Systems March 18-20, 2009 The Johns Hopkins University, Baltimore, Maryland, USA

61. Science Unrestricted (presentation for K-12 Students, Families and Teachers), Institute for Defense Analyses, Alexandria, VA, 22311-1882, March 31, 2009. Evolution in a Nutshell
62. Jena, Germany June 16-21, 2009, the Jena Life Science Forum 2009: The Molecular Language of Life
63. Information theory and molecular biology, September 24, 2009, National Heart, Lung, and Blood Institute (NHLBI), Rockville, MD. Host: Bernard Brooks.
64. Information theory and molecular biology, November 13, 2009, National Heart, Lung, and Blood Institute (NHLBI), Bethesda, Maryland. Host: Mark Knepper,
65. “Information theory and molecular biology”, December 10, 2009, National Library of Medicine, National Center for Biotechnology Information, Bethesda, Maryland. Host: Eugene Koonin.
66. Systems Biology Colloquium, Humboldt-Universität and Charitee University Berlin, Germany. 2010 Feb 12. Information theory and molecular biology, Host: Dr. Hanspeter Herzel of the Institute for Theoretical Biology
67. Plenary talk at the workshop Information Theory meets Biology, Feb 16 and 17 2010, Institute of Telecommunications and Applied Information Theory, Ulm University, Germany. Information theory and molecular biology, Information Theory meets Biology2010 (PDF). Host: Dr. Martin Bossert, Ulm University, Germany
68. Information theory and molecular biology, at the University of Maryland, Baltimore County Biological Sciences. 2010 April 1. BS 004, 4:00 pm, Host: Ivan Erill.
69. Science Unrestricted (presentation for K-12 Students, Families and Teachers), Institute for Defense Analyses, Alexandria, VA, 22311-1882, April 27, 2010. Evolution in a Nutshell
70. SIAM Conference on the Life Sciences (LS10 July 12-15, 2010, Pittsburgh, Pennsylvania, The David L. Lawrence Convention Center, MS69, Minisymposium: Information Theory for Bioinformatics 4:00 PM - 6:00 PM on July 15th, 4 pm. Efficiency of Molecular Machines. Organizers: Sarosh N. Fatakia (NIDDK, NIH) and Carosh Chow (NIDDK, NIH).
71. Perspectives in High Dimensions 2-6 August 2010 at Case Western Reserve University, Cleveland. 70% efficiency of bistate molecular machines explained by information theory, high dimensional geometry and evolutionary convergence, Host: Elizabeth Meckes. See: Embracing complexity: Theoretical math is the basis for facial recognition programs and modeling of intricate systems
72. “70% efficiency of bistate molecular machines explained by ‘information theory, high dimensional geometry and evolutionary ‘convergence’”, at the Rutgers Department of Electrical & Computer Engineering Colloquium Series February 23, 2011 Host: Dr. Athina Petropulu and Dr. Christopher Rose. Slides from the talk
73. Science Unrestricted (presentation for K-12 Students, Families and Teachers), Institute for Defense Analyses, Alexandria, VA, 22311-1882, May 4, 2011. Evolution in a Nutshell

POSTER SESSIONS

(partial list)

- NIH Research Festival '90, Bethesda, MD, September 10, 1990, T. D. Schneider “Sequence Logos: A New Way to Display Consensus Sequences”.
- NIH Research Festival '91, P. P. Papp, D. K. Chattoraj and T. D. Schneider Bethesda, MD, September 23, 1991, “Information analysis of a set of DNA sites that bind protein”.
- Second Foresight Conference on Molecular Nanotechnology, T. D. Schneider Palo Alto, CA, November 7-9, 1991, “Theory of Molecular Machines”.
- NIH Research Festival '92, T. D. Schneider Bethesda, MD, September 21, 1992, “Theory of Molecular Machines”.
- ACM Workshop on Information Retrieval and Genomics Bethesda, MD, USA, May 2-4, 1994, “A Philosophy and Definition for Genetic Sequence Databases”.
- NCI Division of Basic Sciences' Retreat, December 4-5, 1995, Marriott's Hunt Valley Inn, and Transcription Factor Interest Group, December 13, 1995, NIH Bethesda, “Consensus Sequences: Just Say No!”.
- NCI Division of Basic Sciences' Retreat, 1996, 1997
- NIH Research Festival October 6-9, 1998. S. G. Kahn, T. D. Schneider, K. H. Kraemer (NCI) “Splice Mutations in Xeroderma Pigmentosum Group C DNA: Intron Retention and Exon Skipping”
- Comparison of algorithms for computational identification of natural and mutant splice sites. Human Genome Organization, Mutation Database Meeting, Denver 1998 Oct. 27. Peter K. Rogan and Thomas D. Schneider.
- NCI Division of Basic Sciences' Retreat, January 7-8, 1999. “Splice Mutations In Xeroderma Pigmentosum Group C DNA : Intron Retention, Exon Skipping And Internal Neoplasms”, Sikandar G. Khan, Thomas D. Schneider, Kenneth H. Kraemer
- NIH Research Festival, October 3, 2001. “Influence of a single nucleotide polymorphism in an XPC splice acceptor site on alternative splicing”, S. G. Khan, T. Shahlavi, V. Muniz-Medina, H. Inui, T. Ueda, C. C. Baker, T. D. Schneider and K. H. Kraemer
- Poster: Modeling Splice Site and Transcription Factor Binding Site Variation by Information Theory. P. K. Rogan, S. R. Svojanovsky, I. Hurwitz, T. D. Schneider, J. S. Leder. American Society of Human Genetics Annual Meeting, 2002.
- NIH Research Festival, September 29, 2004, Lyakhov, Ilya G. (NCI) I.G. Lyakhov, Z. Chen, T.D. Schneider, “A Novel Bacteriophage Lambda Cro Responsive Element in the oop RNA Promoter”
- NIH Research Festival, September 29, 2004, Z. Chen and T.D. Schneider, “Comparative Analysis of T7-like Promoter Bearing Regions in Bacterial Genomes Reveals a Novel Group of Islands”
- NIH Research Festival, Oct. 19, 2005. “Take-over Pressure Explains Excess Information at T7-like Promoters,” Z. Chen and T.D. Schneider

REVIEWS

- Site Visit and Special Study Section to review an application by Dr. Charles Lawrence, Baylor University College of Medicine, Houston, TX. August 7-8, 1988.
- Reviewed papers for:
 - Acta Biotheoretica (Nov 2007, Sep 2009)
 - Bioinformatics (July 1999, December 2000, July 2001, September 2001, November 2011)
 - Biopoymers (February 2001)
 - BioMed Central (June 2002)
 - BMC Bioinformatics (Dec 2008)
 - CABIOS (January 1994, March 1994, March 1995)
 - Computational Statistics and Data Analysis (December 2001)
 - Developmental Biology (March 2012)
 - Gene (February 1992)
 - FASEB Journal (January 2001)
 - Entropy (March 2011)
 - Genomics (April 1996)
 - IEEE Transactions on Information Theory (March 2001)
 - IEEE IEEE/ACM Transactions on Computational Biology and Bioinformatics (December 2005)
 - Information (November 2011)
 - Journal of Bacteriology (May 1993, October 1993)
 - Journal of biotechnology (September 1988)
 - Journal of Biosciences (November 1997)
 - Journal of Molecular Biology (February 1990, April 2001)
 - Journal of Molecular Graphics and Modelling (March 2011)
 - Journal of Molecular Evolution (March 1997)
 - Journal of Theoretical Biology (December 1991, May 1994, April 1995, June 1996, October 1997, April 2001, July 2002, October 2002, Feb 2010)
 - Machine Learning (December 1993)
 - Molecular Carcinogenesis (May 1993)
 - Nanotechnology (November 1991, April 1995)
 - Nucleic Acids Research (December 1988, November 1989, June 1990, November 1990, September 1992, October 1992, January 1993, April 1993, July 1993, December 1994, August 1995, May 1996, March 1997, June 1997, December 1997, August 2000, November 2000, January 2001, July 2002, Aug-2002, Jan-2003, Feb-2003, May-2004, Feb-2006, Jan-2007, Jun-2007, May-2008, Jul-2008, Nov-2008, Jan-2009, Mar-2009, Sep-2009, Sep-2010, Apr-2011)

- Physical Review Letters (August 1990, Nov 2007)
- Physical Review E (Nov 2007, Dec 2007, Feb 2009, Aug 2010, Sep 2010)
- Pharmacogenetics (January 2001)
- Proc. Natl. Acad. Sci. USA (November 1998)
- Protein Sequences & Data Analysis (May 1988, January 1993)
- Science (February 1998)
- Receptors & Channels (May 1998)
- Theoretical Biology and Medical Modelling (October 2011)
- Reviewed Grants for:
 - National Science Foundation (March 1989, September 1989, October 1990, October 1992 [two])
 - National Institute of General Medical Sciences, NIH (September 1994)
 - NASA Life Sciences Review (July 1995)
- Reviewed a book proposal for Cambridge University Press (December 2010).

PATENTS

1. **U.S. Patent 4,276,570**, 1981, Method and Apparatus for Producing an Image of a Person's Face at a Different Age. Nancy Burson and Thomas D. Schneider This method is now being used to age the images of missing children to aid in their recovery. See the October 1995 *Smithsonian* (volume 26, number 7, p. 70-80).
<http://alum.mit.edu/www/toms/patent/face/>
2. **U.S. Patent 5,867,402**, 1999, Computational analysis of nucleic acid information defines binding sites, Thomas D. Schneider and Peter K. Rogan.
<http://alum.mit.edu/www/toms/patent/walker/>
3. **U.S. Patent 6,774,222**, 2004, Molecular Computing Elements: Gates and Flip-Flops, Thomas D. Schneider and Paul N. Hengen, European Patent No: 1057118.
<http://alum.mit.edu/www/toms/patent/molecularcomputing/>
4. **U.S. Patent 6,982,146**, 2006, High Speed Parallel Molecular Nucleic Acid Sequencing, Thomas D. Schneider and Denise Rubens,
<http://alum.mit.edu/www/toms/patent/dnasequencing/>
5. **U.S. Patent 7,349,834**, 2008. Australian Patent No. 784085, 2006. European Patent 1204680 (10 September 2008). Canadian Patent 2380611, June 8, 2010. U.S. Patent 8,086,432, 2011. Molecular Motor, Thomas D. Schneider and Ilya G. Lyakhov,
<http://alum.mit.edu/www/toms/patent/molecularrotationengine/>
6. **U.S. Patent 7,871,777**, 2011. Schneider, T. D., Lyakhov, I. G., and Needle, D.: Probe for nucleic acid sequencing and methods of use. European patent number 1960550 granted on 15 September 2010.
<http://alum.mit.edu/www/toms/patent/medusa/>

7. Lyakhov, I. G., Schneider, T. D., and Needle, D.: Nanoprobes for detection or modification of molecules. filed on December 12, 2005. Patent pending.
<http://alum.mit.edu/www/toms/patent/nanoprobe/>
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COMPUTER EXPERIENCE

- Since 1970 I have used the computer languages BASIC, FORTRAN, APL, LISP, Assembly, Algol, PL1, Pascal, PostScript, HTML, MatLab on many computer systems, mainly UNIX.
- I typeset my papers in \LaTeX and maintain a web page for biologists on LaTeX Style and BiBTeX Bibliography Formats for Biologists and TeX and LaTeX Resources.
- Generally I build tools such as the Delila language and system of programs for manipulating nucleic acid sequences [2, 6] and making sequence logos [12] and sequence walkers [34]
- Three especially useful general tools for scientists are:
 - atchange - instant automation of repeated tasks
 - nowhere - jump to any directory in your file structure
 - yvp - give the Year, Volume and Page of a paper and your browser will immediately jump to the corresponding PubMed entry.

These and other tools I have invented are available in my toolkit.

STUDENTS

I have brought Senior high school students into my lab by the National Cancer Institute's Werner H. Kirsten Student Intern Program (SIP) (<http://alum.mit.edu/www/toms/sipinfo.html>) since the beginning of the program. Publications are noted.

1. 1989-1990: R. Michael Stephens, a high school student supported by the NCI/FCRDC SIP and the NIH/FAES Mones Berman Memorial Fund [12, 18].
2. 1990-1991: Nathan D. Herman, SIP [16]
3. 1991-1992: Mark C. Shaner, SIP
4. 1991: Ian M. Blair, Montgomery Blair High School, Silver Spring, MD
5. 1992-1994: Stacy L. Bartram, SIP [35]
6. 1993-1994: Maria M. Alavanja, SIP
7. 1993-1994: Vishnu Jejjala, SIP, volunteer from University of Maryland
8. 1993-1995: Jaime A. Fenimore, SIP
9. 1994-1995: Leslie A. Strathern, SIP
10. 1994-1995: Paul A. Smith, High School student volunteer from Middletown High School
11. 1995-1996: R. Elaine Bucheimer, SIP [52]
12. 1996: Cheryl N. Johnston, SIP

13. 1995: Lisa E. Stewart, volunteer [35]
14. 1992-1997: Paul N. Hengen, Post doctoral student, Senior Staff Fellow [35, 54, 58, 60]
15. 1997-2003: Ryan K. Shultzaberger, SIP, college student, college graduate [41, 52, 70, 71, 72]
16. 1998-2002: Karen A. Lewis, SIP [51, 70, 72]
17. 1998-2009: Ilya G. Lyakhov, Postdoctoral fellow, Senior Staff Fellow [54, 58, 63, 71, 72, 74, 75, 82, 81]
18. 1999-2001: Shu Ouyang, Postdoctoral fellow, Senior Staff Fellow
19. 1999-2000: Nitasha G. Klar, SIP
20. 2000-2001: Brent M. Jewett, SIP
21. 2000-2002: Xiao (Sheldon) Ma, volunteer
22. 2001-2002: Brandon K. Cunningham, SIP, mentored by Ilya Lyakhov then TDS
23. 2001-2006: Zehua Chen, Postdoctoral fellow [64, 67, 72]
24. 2002-2009: Danielle Needle, Biologist [82, 81]
25. 2002-2003: Juliet Aiken, SIP
26. 2003-2005: Michael Y. Levashov, SIP Winner in the 2004 Spring Research Festival for his poster 'Computer Simulation of the Convergent Evolution of DNA Binding Sites as in the lambda cI/Cro Control System'. He was also a 63rd Annual Science Talent Search (STS) (2003-2004) Semifinalist.
27. 2004: Elizaveta Ershova, SIP
28. 2006-2009: Peyman Khalichi, Postdoctoral fellow
29. 2006-2009: Adam Diehl, SIP
30. 2009 Summer: David Wilson, High School Student
31. 2007 (summer) and 2008-2009: Blake Sweeney, postbac
32. 2011 (summer): Kevin Franco, Cancer Research Intern

SELECTED COLLABORATIONS

- 1990-1997: with Dhruba Chattoraj, Peter Papp (NIH, Bethesda, MD) experimental information analysis of repA protein binding sites [21, 32]
- 1991-: with Peter Rogan Department of Pediatrics, Milton S. Hershey Medical Center, Pennsylvania State University, Hershey Pa 17033; Application of sequence logos to PCR amplification for phylogenetic analysis [27]. Use of sequence logos for medical diagnosis [26, 36]
- 1991-: with Gaisela Storz (NIH, Bethesda, MD) Analysis of OxyR binding sites [25, 51]
- 1992-: Kenn Rudd (University of Miami, FL) [17, 52]
- 2002: Krishnamachari Annangarachari (Chari) a Fulbright visiting scholar from Jawaharlal Nehru University, New Delhi India visited my lab for 6 months. He is worked on the information analysis of p53 protein [75].

RESEARCH INTERESTS

There must be mathematical laws that describe nucleic acid sequences and molecular interactions; my goal is to find these laws. What aspects of nucleic acids can be approached, and what mathematics should one use? The fruitful answer for me has been to apply Shannon's information theory to nucleic acid binding sites. During my Ph.D. thesis work I discovered that in many genetic systems the information in the binding site sequences on DNA or RNA to which proteins bind is just enough for the sites to be found in the genome [9]. This result is surprising because the number of sites and size of the genome are determined by history and physiology, so the amount of information in the binding sites must evolve toward the amount predicted using genome size and the number of sites. I confirmed these ideas both experimentally [11] and by using a computer simulation [49]. (You can try this model on your own computer by going to <http://alum.mit.edu/www/toms/papers/ev.>) Thus my work has three major components: theory, computer analysis and genetic engineering experiments.

Whenever one has a strong theory, anomalies are interesting. We have investigated several major ones at the lab bench because they lead to new insights into biology. One is the excess information found at bacteriophage T7 promoters [9, 11]. These sequences conserve twice as much information as the T7 polymerase requires to locate them in the presence of the bacterial genome. One possible explanation is that a second protein binds to the DNA. Alternatively the bacteriophage may be set up to overwhelm the bacterial defenses. We have found evidence supporting the latter hypothesis. In a second case, we discovered that the *E. coli* F plasmid *incD* region, which is responsible for correct plasmid partitioning to the daughter cells, has a three-fold excess conservation. This implies that three proteins bind there and we were able to identify three candidate binding proteins [16]. Another anomaly I found is unusually conserved bases involved in DNA replication and RNA transcription [21, 32]. Such cases can be detected by inspecting the sequence information along a binding site since the major groove of DNA can carry up to 2 bits of information while the minor groove can only support 1 bit. When the minor groove has more than 1 bit of information the DNA must not be in B form. We tested this idea in the bacteriophage P1 RepA system. Our experimental evidence suggests that the proteins are flipping bases out of the DNA to start helix melting, thereby initiating replication and transcription [53, 54].

Shannon's measure of information has the form of an average, which raises the question: for binding sites, what are the individual components that make up this average? The obvious answer is to consider it to be the average of the information for individual sequences in the set of binding sites. This immediately allows one to write down an equation that defines the individual information and this solution was proven to be unique by Dr. John Spouge [33].

To help visualize these results, we invented methods for graphically displaying a set of binding sites for the average as sequence logos [12] and for individual sequences as sequence walkers [33, 34, 35, 36]. These graphics have revealed many interesting details of a variety of binding sites and are now being used by researchers around the world. They allow rapid and quantitative visualization of genetic regions, detection of database errors, analysis of single nucleotide polymorphisms (SNPs) to distinguish polymorphisms from mutations (<http://alum.mit.edu/www/toms/g863a.html>) and quantitative genetic engineering of sequences. We have found a correlation between information measures of splice junctions and the severity of genetic diseases [36], and obtained a patent on this method [42].

For convenience, I divide my theoretical work into several levels. Level 0 is the study of genetic sequences bound by proteins or other macromolecules, briefly described above. The success of this theory suggested that other work of Shannon should also apply to molecular biology. Level 1 theory introduces the more general concept of the molecular machine which dissipates energy to make choices. From this I was able to develop the concept of a machine capacity equivalent to Shannon's channel capacity [14]. In Level 2, the Second Law of Thermodynamics is connected to the capacity theorem [15], and the limits on the functioning of Maxwell's Demon become clear [24]. Levels 3, the efficiency of molecular machines, which is often 70%, and 4, explaining the observed efficiency, are in preparation, but a short version has been published [77] and a review [?]. My next major goal is to understand Level 5, the coding of molecular machines, by investigating the detailed structure and motions of molecules from the viewpoint of information and coding theory.

SPORTS

Skiing, Tai Chi Ch'uan, ultimate frisbee, scuba diving, mountain hiking, contra dancing, racket ball, bicycling

PUBLICATIONS

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 Thomas D. Schneider contributed 50 entries to the dictionary. The web links to Tom Schneider’s web site are incorrect but this has been handled on the server computer. See <http://alum.mit.edu/www/toms/toms/>. The entries in the book originated from the online page “A Glossary for Molecular Information Theory and the Delila System”,
<http://alum.mit.edu/www/toms/glossary.html>.
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