

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Brutlag, Douglas L.		POSITION TITLE Professor of Biochemistry, Medical Informatics, & Computer Science (by courtesy)	
eRA COMMONS USER NAME brutlag.douglas			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Calif. Institute of Technology, Pasadena, CA	B.S.	1968	Biology
Stanford University, Stanford, CA	Ph.D.	1972	Biochemistry

**A. Positions and Honors.****Positions and Honors:**

6/72 - 6/74 Research Scientist at the CSIRO, Canberra Australia.  
 9/74 - 1980 Assistant Professor of Biochemistry, Stanford University.  
 9/80 - 9/97 Associate Professor of Biochemistry, Stanford University.  
 9/97 - present Professor of Biochemistry, Stanford University  
 9/96 - present Professor of Medicine (by courtesy) Stanford University  
 9/2001-present Honorary Professor of Bioinformatics, Keio University  
 1975 Elected to Federation of American Societies for Experimental Biology  
 1976 Member, American Society of Biological Chemists  
 1981 Guggenheim Fellowship, (declined).  
 1981 - 82 NIH Senior Fogarty International Fellow  
 1986 Elected Fellow of the American Assoc. for the Advancement of Science  
 1992 Computerworld-Smithsonian Award for Best Computer Application in Science

**Public Service:**

5/1978 National Institutes of Health, Cell Biology Study Section  
 5/1979 National Institutes of Health, Molecular Cytology Section  
 1982 - 1986 National Institutes of Health, Genetics Study Section  
 1985 - 1986 National Library of Medicine, Long-range Planning Committee  
 1989 - 1993 National Library of Medicine, Board of Scientific Counselors  
 1985 - 1989 BIONET National Computer Resource for Molecular Biology, Investigator  
 1987 - 1992 Consultant to NIH GenBank Database  
 1989 - 1992 Course organizer, Computer Applications in Molecular Biology, UNIDO  
 1993 - 1995 Course organizer, Computer Applications in Molecular Biology, ANGIS  
 1993 Editorial Board, Journal of Computational Biology  
 6/96 - pres. Cofounder *International Society for Computational Molecular Biology*  
 9/97 - pres. Chairman Scientific Advisory Board of TimeLogic Inc.  
 3/03 - 6/06 Scientific Advisory board, Pathwork Informatics  
 6/03 - 6/09 Presidential Scientific Advisory Board, Max Planck Institutes

**B. Selected peer-reviewed publications (in reverse chronological order).**

Huang, X., & Brutlag, D. L. (2007). Dynamic use of multiple parameter sets in sequence alignment. *Nuc. Acids Res*, 35, 678-687  
 Chiang, T. H., Apaydin, M. S., Brutlag, D. L., Hsu, D., & Latombe, J. C. (2007). Using stochastic roadmap simulation to predict experimental quantities in protein folding kinetics: folding rates and phi-values. *J Comput Biol*, 14(5), 578-593.  
 Tellez, A. B., Crowder, S., Spagnolo, J. F., Thompson, A. A., Peersen, O. B., Brutlag, D. L., et al. (2006). Nucleotide channel of RNA-dependent RNA polymerase used for intermolecular uridylylation of protein primer. *J Mol Biol*, 357(2), 665-675.  
 Saxonov, S., Berg, P., & Brutlag, D. L. (2006). A genome-wide analysis of CpG dinucleotides in the human genome distinguishes

- two distinct classes of promoters. *Proc Natl Acad Sci U S A*, 103(5), 1412-1417.
- Rhee, S. Y., Taylor, J., Wadhera, G., Ben-Hur, A., Brutlag, D. L., & Shafer, R. W. (2006). Genotypic predictors of human immunodeficiency virus type 1 drug resistance. *Proc Natl Acad Sci U S A*, 17355-17360.
- Naughton, B. T., Fratkin, E., Batzoglou, S., & Brutlag, D. L. (2006). A graph-based motif detection algorithm models complex nucleotide dependencies in transcription factor binding sites. *Nucleic Acids Res*, 34(20), 5730-5739.
- Fratkin, E., Naughton, B. T., Brutlag, D. L., & Batzoglou, S. (2006). MotifCut: regulatory motifs finding with maximum density subgraphs. *Bioinformatics*, 22(14), e150-157.
- Ebert, J., & Brutlag, D. L. (2006). Development and Validation of a Consistency Based Multiple Structure Alignment Algorithm Running title: Consistency Based Multiple Alignment. *Bioinformatics*, 22, 1080-1087.
- Ebert, J., & Brutlag, D. (2006). Development and validation of a consistency based multiple structure alignment algorithm. *Bioinformatics*, 22(9), 1080-1087.
- Su, Q. J., Lu, L., Saxonov, S., & Brutlag, D. L. (2005). eBLOCKs: enumerating conserved protein blocks to achieve maximal sensitivity and specificity. *Nucleic Acids Res*, 33(Database issue), D178-182.
- Bertaccini, E. J., Shapiro, J., Brutlag, D. L., & Trudell, J. R. (2005). Homology modeling of a human glycine alpha 1 receptor reveals a plausible anesthetic binding site. *J Chem Inf Model*, 45(1), 128-135.
- Wang, H., Segal, E., Ben-Hur, A., Koller, D., & Brutlag, D. (2004). *Identifying protein-protein interaction sites on a genome-wide scale*. Paper presented at the Neural Information Processing Systems (NIPS), Vancouver, British Columbia, Canada.
- Shapiro, J., & Brutlag, D. (2004). FoldMiner: structural motif discovery using an improved algorithm. *Protein Sci*, 13, 278-294.
- Shapiro, J., & Brutlag, D. (2004). FoldMiner and LOCK 2: protein structure comparison and motif discovery on the web. *Nucleic Acids Res*, 32(Web Server issue), W536-541.
- Liu, Y., Wei, L., Batzoglou, S., Brutlag, D. L., Liu, J. S., & Liu, X. S. (2004). A suite of web-based programs to search for transcriptional regulatory motifs. *Nucleic Acids Res*, 32(Web Server issue), W204-207.
- Liang, M. P., Troyanskaya, O. G., Laederach, A., Brutlag, D. L., & Altman, R. B. (2004). Computational Functional Genomics. *IEEE Signal Processing*(November), 62-69.
- Ben-hur, A., & Brutlag, D. L. (2004). *Protein Sequence motifs: highly predictive features of protein function*. Paper presented at the Neural Information Processing Systems, Vancouver British Columbia.
- Liang, M. P., Banatao, D. R., Klein, T. E., Brutlag, D. L., & Altman, R. B. (2003). WebFEATURE: An interactive web tool for identifying and visualizing functional sites on macromolecular structures. *Nucleic Acids Res*, 31(13), 3324-3327.
- Bennett, S. P., Nevill-Manning, C. G., & Brutlag, D. L. (2003). 3MOTIF: visualizing conserved protein sequence motifs in the protein structure database. *Bioinformatics*, 19(4), 541-542.
- Bennett, S. P., Lu, L., & Brutlag, D. L. (2003). 3MATRIX and 3MOTIF: a protein structure visualization system for conserved sequence motifs. *Nucleic Acids Res*, 31(13), 3328-3332.
- Ben-Hur, A., & Brutlag, D. (2003). Remote homology detection: a motif based approach. *Bioinformatics*, 19 Suppl 1, i26-33.
- Apaydin, M. S., Brutlag, D. L., Guestrin, C., Hsu, D., Latombe, J. C., & Varma, C. (2003). Stochastic roadmap simulation: an efficient representation and algorithm for analyzing molecular motion. *J Comput Biol*, 10(3-4), 257-281.
- Liu, X. S., Brutlag, D. L., & Liu, J. S. (2002). An algorithm for finding protein-DNA binding sites with applications to chromatin-immunoprecipitation microarray experiments. *Nat Biotechnol*, 20(8), 835-839.
- Brutlag, D., Apaydin, S., Guestrin, C., Hsu, D., Varma, C., Singh, A., et al. (2002). Using robotics to fold proteins and dock ligand. *Bioinformatics*, 18 Suppl 2, S74.
- Apaydin, M. S., Guestrin, C., Varma, C., Brutlag, D. L., & Latombe, J.-C. (2002). Stochastic Roadmap Simulation for the Study of Ligand-Protein Interactions. *Bioinformatics*, 18, S18-S26.
- Apaydin, M. S., Brutlag, D. L., Guestrin, C., Hsu, D., & Latombe, J.-C. (2002). Stochastic Roadmap Simulation: An Efficient Representation and Algorithm for Analyzing Molecular Motion. *Recomb 2002*, 9, 12-21.
- Liu, X., Brutlag, D. L., & Liu, J. S. (2001). BioProspector: discovering conserved DNA motifs in upstream regulatory regions of expressed genes. *Pac Symp Biocomput*, 127-138.
- Huang, J. Y., & Brutlag, D. L. (2001). The EMOTIF database. *Nucleic Acids Res*, 29(1), 202-204.
- Wu, T. D., Nevill-Manning, C. G., & Brutlag, D. L. (2000). Fast probabilistic analysis of sequence function using scoring matrices. *Bioinformatics*, 16(3), 233-244.
- Schmidler, S. C., Liu, J. S., & Brutlag, D. L. (2000). Bayesian segmentation of protein secondary structure. *J Comput Biol*, 7(1), 233-248.
- Wu, T. D., Nevill-Manning, C. G., & Brutlag, D. L. (1999). Minimal-risk scoring matrices for sequence analysis. *J Comput Biol*, 6(3), 219-235.
- Wu, T. D., Schmidler, S. C., Hastie, T., & Brutlag, D. L. (1998). Regression analysis of multiple protein structures. *J Comput Biol*, 5(3), 585-595.
- Rindfleisch, T. C., & Brutlag, D. L. (1998). Directions for clinical research and genomic research into the next decade: implications for informatics. *J Am Med Inform Assoc*, 5(5), 404-411.
- Nevill-Manning, C. G., Wu, T. D., & Brutlag, D. L. (1998). Highly specific protein sequence motifs for genome analysis. *Proc Natl Acad Sci U S A*, 95(11), 5865-5871.

- Brutlag, D. L. (1998). Genomics and computational molecular biology. *Curr Opin Microbiol*, 1(3), 340-345.
- Tomita, M., Shimizu, N., & Brutlag, D. L. (1996). Introns and reading frames: correlation between splicing sites and their codon positions. *Mol Biol Evol*, 13(9), 1219-1223.
- Brutlag, D. L., & Sternberg, M. J. (1996). Sequences and topology challenges for algorithms and experts. *Curr Opin Struct Biol* 6(3), 343-345.
- Naor, D., & Brutlag, D. L. (1994). On near-optimal alignments of biological sequences. *J Comput Biol*, 1(4), 349-366.
- Klingler, T. M., & Brutlag, D. L. (1994). Discovering structural correlations in alpha-helices. *Protein Sci*, 3(10), 1847-1857.
- Brutlag, D. L. (1994). Understanding the Human Genome. In P. Leder, D. A. Clayton & E. Rubenstein (Eds.), *Scientific American: Introduction to Molecular Medicine* (pp. 153-168). New York NY: Scientific American Inc.
- Brutlag, D. L., Dautricourt, J. P., Diaz, R., Fier, J., Moxon, B., & Stamm, R. (1993). BLAZE: An implementation of the Smith-Waterman Comparison Algorithm on a Massively Parallel Computer. *Computers and Chemistry*, 17, 203-207.
- Brutlag, D. L., Galper, A. R., & Millis, D. H. (1991). Knowledge-based simulation of DNA metabolism: prediction of enzyme activity. *Comput Appl Biosci*, 7(1), 9-19.
- Barsalou, T., & Brutlag, D. L. (1991). Searching gene and protein sequence databases. *MD Comput*, 8(3), 144-149.
- Brutlag, D. L., Dautricourt, J. P., Maulik, S., & Relph, J. (1990). Improved sensitivity of biological sequence database searches. *Comput Appl Biosci*, 6(3), 237-245.
- Hipeau-Jacquotte, R., Brutlag, D. L., & Bregegere, F. (1989). Conversion and reciprocal exchange between tandem repeats in *Drosophila melanogaster*. *Mol Gen Genet*, 220(1), 140-146.
- Goldstein, A., & Brutlag, D. L. (1989). Is there a relationship between DNA sequences encoding peptide ligands and their receptors? *Proc Natl Acad Sci U S A*, 86(1), 42-45.
- Fairman, R., & Brutlag, D. L. (1988). Expression of the *Drosophila* type II topoisomerase is developmentally regulated. *Biochemistry*, 27(2), 560-565.
- Lohe, A. R., & Brutlag, D. L. (1987). Identical satellite DNA sequences in species of *Drosophila*. *J Mol Biol*, 194(2), 161-170.
- Lohe, A. R., & Brutlag, D. L. (1987). Adjacent satellite DNA segments in *Drosophila* structure of junctions. *J Mol Biol*, 194(2), 179.
- Heller, R., Philip, M., & Brutlag, D. (1987). Structure of the Embryonic Transcript encoding the *Drosophila* DNA topoisomerase II. *Nucleic Acids Res*, 14(1), 17-20.
- Lohe, A. R., & Brutlag, D. L. (1986). Multiplicity of satellite DNA sequences in *Drosophila melanogaster*. *Proc Natl Acad Sci U S A*, 83(3), 696-700.
- Kornher, J. S., & Brutlag, D. (1986). Proximity-dependent enhancement of Sgs-4 gene expression in *D. melanogaster*. *Cell*, 44, 879-883.
- Heller, R. A., Shelton, E. R., Dietrich, V., Elgin, S. C., & Brutlag, D. L. (1986). Multiple forms and cellular localization of *Drosophila* DNA topoisomerase II. *J Biol Chem*, 261(17), 8063-8069.
- Altenberg, L., & Brutlag, D. (1986). Selection for modularity in the genome: Reading Frame Evidence for Exon Shuffling.
- Gilson, E., Clement, J. M., Brutlag, D., & Hofnung, M. (1984). A family of dispersed repetitive extragenic palindromic DNA sequences in *E. coli*. *Embo J*, 3(6), 1417-1421.
- Dahmus, G. K., Glover, C. V., Brutlag, D. L., & Dahmus, M. E. (1984). Similarities in structure and function of calf thymus and *Drosophila* casein kinase II. *J Biol Chem*, 259(14), 9001-9006.
- Abarbanel, R. M., Wieneke, P. R., Mansfield, E., Jaffe, D. A., & Brutlag, D. L. (1984). Rapid searches for complex patterns in biological molecules. *Nucleic Acids Res*, 12(1 Pt 1), 263-280.
- Shelton, E. R., Osheroff, N., & Brutlag, D. L. (1983). DNA topoisomerase II from *Drosophila melanogaster*. Purification and physical characterization. *J Biol Chem*, 258(15), 9530-9535.
- Osheroff, N., Shelton, E. R., & Brutlag, D. L. (1983). DNA topoisomerase II from *Drosophila melanogaster*. Relaxation of supercoiled DNA. *J Biol Chem*, 258(15), 9536-9543.
- Glover, C. V., Shelton, E. R., & Brutlag, D. L. (1983). Purification and characterization of a type II casein kinase from *Drosophila melanogaster*. *J Biol Chem*, 258(5), 3258-3265.
- Friedland, P., Kedes, L., Brutlag, D., Iwasaki, Y., & Bach, R. (1982). GENESIS, a knowledge-based genetic engineering simulation system for representation of genetic data and experiment planning. *Nucleic Acids Res*, 10(1), 323-340.
- Brutlag, D. L., Clayton, J., Friedland, P., & Kedes, L. H. (1982). SEQ: a nucleotide sequence analysis and recombination system. *Nucleic Acids Res*, 10(1), 279-294.
- Bach, R., Friedland, P., Brutlag, D. L., & Kedes, L. (1982). MAXIMIZE. A DNA sequencing strategy advisor. *Nucleic Acids Res*, 10(1), 295-304.
- Wiegand, R. C., & Brutlag, D. L. (1981). Histone acetylase from *Drosophila melanogaster* specific for H4. *J Biol Chem*, 256(9), 4578-4583.
- Nelson, T., Wiegand, R., & Brutlag, D. (1981). Ribonucleic acid and other polyanions facilitate chromatin assembly in vitro. *Biochemistry*, 20(9), 2594-2601.
- Hsieh, T., & Brutlag, D. (1980). ATP-dependent DNA topoisomerase from *D. melanogaster* reversibly catenates duplex DNA

- rings. *Cell*, 21(1), 115-125.
- Brutlag, D. L. (1980). Molecular arrangement and evolution of heterochromatic DNA. *Annu Rev Genet*, 14, 121-144.
- Nelson, T., Hsieh, T. S., & Brutlag, D. (1979). Extracts of *Drosophila* embryos mediate chromatin assembly in vitro. *Proc Natl Acad Sci U S A*, 76(11), 5510-5514.
- Nelson, T., & Brutlag, D. (1979). Addition of homopolymers to the 3'-ends of duplex DNA with terminal transferase. *Methods Enzymol*, 68, 41-50.
- Hsieh, T., & Brutlag, D. L. (1979). A protein that preferentially binds *Drosophila* satellite DNA. *Proc Natl Acad Sci U S A*, 76(2), 726-730.
- Hsieh, T., & Brutlag, D. (1979). Sequence and sequence variation within the 1.688 g/cm<sup>3</sup> satellite DNA of *Drosophila melanogaster*. *J Mol Biol*, 135(2), 465-481.
- Germond, J. E., Rouviere-Yaniv, J., Yaniv, M., & Brutlag, D. (1979). Nicking-closing enzyme assembles nucleosome-like structures in vitro. *Proc Natl Acad Sci U S A*, 76(8), 3779-3783.
- Fry, K., & Brutlag, D. (1979). Detection and resolution of closely related satellite DNA sequences by molecular cloning. *J Mol Biol*, 135(3), 581-593.
- Carlson, M., & Brutlag, D. (1979). Different regions of a complex satellite DNA vary in size and sequence of the repeating unit. *Mol Biol*, 135(2), 483-500.
- Brutlag, D., & Peacock, W. J. (1979). Sequences of the 1.672 g/cm<sup>3</sup> satellite DNA of *Drosophila melanogaster*. *J Mol Biol*, 135, 565-580.
- Carlson, M., & Brutlag, D. (1978). One of the copia genes is adjacent to satellite DNA in *Drosophila melanogaster*. *Cell*, 15(3), 733-742.
- Carlson, M., & Brutlag, D. (1978). A gene adjacent to satellite DNA in *Drosophila melanogaster*. *Proc Natl Acad Sci U S A*, 75(18), 5898-5902.
- Brutlag, D., Carlson, M., Fry, K., & Hsieh, T. S. (1978). DNA sequence organization in *Drosophila* heterochromatin. *Cold Spring Harbor Symp Quant Biol*, 42 Pt 2, 1137-1146.
- Rubenstein, J. L., Brutlag, D., & Clayton, D. A. (1977). The mitochondrial DNA of *Drosophila melanogaster* exists in two distinct and stable superhelical forms. *Cell*, 12(2), 471-482.
- Carlson, M., & Brutlag, D. (1977). Cloning and characterization of a complex satellite DNA from *Drosophila melanogaster*. *Cell*, 11(2), 371-381.
- Westergaard, O., Brutlag, D., & Kornberg, A. (1973). Initiation of Deoxyribonucleic Acid Synthesis. IV. INCORPORATION OF 1 RIBONUCLEIC ACID PRIMER INTO THE PHAGE REPLICATIVE FORM. *J. Biol. Chem.*, 248(4), 1361-1364.
- Wickner, W., Brutlag, D., Schekman, R., & Kornberg, A. (1972). RNA Synthesis Initiates in vitro Conversion of M13 DNA to Its Replicative Form. *PNAS*, 69(4), 965-969.
- Setlow, P., Brutlag, D., & Kornberg, A. (1972). Deoxyribonucleic acid polymerase: two distinct enzymes in one polypeptide. I. A proteolytic fragment containing the polymerase and 3' leads to 5' exonuclease functions. *J Biol Chem*, 247(1), 224-231
- Setlow, P., Brutlag, D., & Kornberg, A. (1972). Deoxyribonucleic Acid Polymerase: Two Distinct Enzymes in One Polypeptide. I. PROTEOLYTIC FRAGMENT CONTAINING THE POLYMERASE AND 3' LEADS TO 5' EXONUCLEASE FUNCTIONS. *J. Bio Chem.*, 247(1), 224-231.
- Schekman, R., Wickner, W., Westergaard, O., Brutlag, D., Geider, K., Bertsch, L. L., et al. (1972). Initiation of DNA Synthesis: Synthesis of phi X174 Replicative Form Requires RNA Synthesis Resistant to Rifampicin. *PNAS*, 69(9), 2691-2695.
- Brutlag, D., & Kornberg, A. (1972). Enzymatic synthesis of deoxyribonucleic acid. 36. A proofreading function for the 3' leads to exonuclease activity in deoxyribonucleic acid polymerases. *J Biol Chem*, 247(1), 241-248.
- Brutlag, D., & Kornberg, A. (1972). Enzymatic Synthesis of Deoxyribonucleic Acid. XXXVI. A PROOFREADING FUNCTION FOR THE 3' -> 5' EXONUCLEASE ACTIVITY IN DEOXYRIBONUCLEIC ACID POLYMERASES. *J. Biol. Chem.*, 247(1), 241-248.
- Brutlag, D. (1972). *Enzymatic mechanisms in DNA replication*. Ph.D. Thesis Stanford University. Dept. of Biochemistry., Stanford University.
- Brutlag, D., Schekman, R., & Kornberg, A. (1971). A Possible Role for RNA Polymerase in the Initiation of M13 DNA Synthesis. *PNAS*, 68(11), 2826-2829.
- Brutlag, D., Schlehuber, C., & Bonner, J. (1969). Properties of formaldehyde-treated nucleohistone. *Biochemistry*, 8(8), 3214-3218.
- Brutlag, D., Atkinson, M. R., Setlow, P., & Kornberg, A. (1969). An active fragment of DNA polymerase produced by proteolytic cleavage. *Biochem Biophys Res Commun*, 37(6), 982-989.
- Marushige, K., Brutlag, D., & Bonner, J. (1968). Properties of chromosomal histone protein of rat liver. *Biochemistry*, 7(9), 3149-3155.