

ND-A176 359

COMPUTATIONAL APPROACHES TO PROTEIN STRUCTURE DESIGN:
BETA-BELLIN(U) MASSACHUSETTS GENERAL HOSPITAL BOSTON
J NOVOTNY 26 JAN 87 N00014-86-K-0116

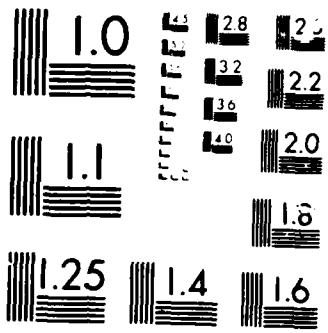
1/1

UNCLASSIFIED

F/G 6/1

NL





AD-A176 359

REPORT DOCUMENTATION PAGE

1a REPORT SECURITY CLASSIFICATION (U)			1b RESTRICTIVE MARKINGS NA			
2a SECURITY CLASSIFICATION AUTHORITY NA			3 DISTRIBUTION / AVAILABILITY OF REPORT Distribution unlimited			
2b DECLASSIFICATION / DOWNGRADING SCHEDULE NA						
4 PERFORMING ORGANIZATION REPORT NUMBER(S) Massachusetts General Hospital/Harvard Med.Sch.			5. MONITORING ORGANIZATION REPORT NUMBER(S) NA			
6a NAME OF PERFORMING ORGANIZATION Massachusetts General Hospital		6b OFFICE SYMBOL (If applicable) NA	7a NAME OF MONITORING ORGANIZATION Office of Naval Research			
6c ADDRESS (City, State, and ZIP Code) Massachusetts General Hospital Jackson 13, Boston MA 02114			7b ADDRESS (City, State, and ZIP Code) 800 N. Quincy Street Arlington VA 22217-5000			
8a. NAME OF FUNDING / SPONSORING ORGANIZATION Office of Naval Research		8b OFFICE SYMBOL (If applicable) ONR	9 PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER N00014-86-K-0116			
8c. ADDRESS (City, State, and ZIP Code) 800 N. Quincy Street Arlington VA 22217-5000			10 SOURCE OF FUNDING NUMBERS			
			PROGRAM ELEMENT NO 61153N	PROJECT NO RR04106	TASK NO	WORK UNIT ACCESSION NO
11 TITLE (Include Security Classification) (U) Computational Approaches to Protein Structure Design: beta-Bellin						
12 PERSONAL AUTHOR(S) Novotny, Jiri						
13a TYPE OF REPORT Annual		13b TIME COVERED FROM 2/1/86 TO 1/30/87		14. DATE OF REPORT (Year, Month, Day) 1/26/1987	15 PAGE COUNT 6	
16 SUPPLEMENTARY NOTATION						
17 COSATI CODES			18 SUBJECT TERMS (Continue on reverse if necessary and identify by block number) Protein engineering, 3D structure, Molecular dynamics			
FIELD 08	GROUP	SUB-GROUP				
19 ABSTRACT (Continue on reverse if necessary and identify by block number) Computer analysis of protein models is used to aid design of new protein structures. Using atomic coordinates of beta-bellin, an antiparallel beta-sheeted protein model designed by Jane & David Richardson, characteristics such as solvent-accessible surface, polypeptide backbone twist, beta-barrel geometry, empirical potential energy etc. were computed and compared with values obtained from atomic coordinates of native proteins. This approach involves computer analysis of native proteins as well. In addition to static molecular properties, dynamical behavior of native proteins and protein models is compared using molecular dynamics calculations.						
20 DISTRIBUTION / AVAILABILITY OF ABSTRACT <input type="checkbox"/> UNCLASSIFIED/UNLIMITED <input type="checkbox"/> SAME AS RPT <input type="checkbox"/> DTIC USERS			21 ABSTRACT SECURITY CLASSIFICATION (U)			
22a NAME OF RESPONSIBLE INDIVIDUAL M. Marron			22b TELEPHONE (Include Area Code) 617-726-1858		22c OFFICE SYMBOL ONR	

DTIC
 SELECTED
 FEB 04 1987
 D
 D

DTIC FILE 0000

Annual report on "Computational Approaches to Protein Structure Design: β -Bellin.

The goals of this project are to aid design of new protein structures by computer analysis of protein models. Using atomic coordinates of β -bellin, an anti-parallel β -sheeted protein model designed by Drs. Jane & David Richardson, characteristics such as solvent-accessible surface, polypeptide backbone twist, b-barrel geometry (semiaxes of hyperboloidal cross-sections), empirical potential energy etc. were computed and compared with values obtained from atomic coordinates of native proteins. This approach involves computer analysis of native proteins as well. In addition to static molecular properties, dynamical behavior of native proteins and protein models is compared using molecular dynamics calculations.

In the first year of the project, computer analysis of native proteins concentrated on backbone twist of β -sheets and solvent- or large probe-accessible surfaces of selected proteins. Analysis of backbone twists showed large deviations from the average β -strand twist value of $+20^\circ$. The deviations correlate with anisotropy of non-covalent atomic force distribution throughout the structure. Large probe-accessible surfaces of enzymes were shown to coincide with sites of limited autolysis/proteolysis.

Backbone twist and solvent accessible surface of the β -bellin model were computed and compared to those of native proteins of similar molecular weight and architecture. Quenched molecular dynamics (i.e., a molecular dynamics simulation at $800^\circ K$ followed by a gradual cooling of the structure) over 10 ps resulted in partial unfolding of the model. More detailed dynamical investigation, at various temperatures (including $300^\circ K$) and on improved models, is currently under way.

One paper has been published as a result of this work. Reprints will be sent under separate cover.

Accession For	
NTIS CRA&I	<input checked="" type="checkbox"/>
DTIC TAB	<input type="checkbox"/>
Unannounced	<input type="checkbox"/>
Justification	
By	
Distribution /	
Availability Codes	
Dist	Avail and/or Special
A-1	

DISTRIBUTION LIST MOLECULAR BIOLOGY PROGRAM

ANNUAL, FINAL, AND TECHNICAL REPORTS (One copy each except as noted)

Dr. Lewis F. Affronti
George Washington University
Department of Microbiology
2300 I ST NW
Washington, DC 20037

Dr. J. Thomas August
The Johns Hopkins University
School of Medicine
720 Rutland Avenue
Baltimore, MD 21205

Dr. Myron L. Bender
Chemistry Department
Northwestern University
Evanston, IL 60201

Dr. R. P. Blakemore
University of New Hampshire
Department of Microbiology
Durham, New Hampshire 03824

Dr. Ronald Breslow
Columbia University
Department of Chemistry
New York, NY 10027

Dr. James P. Collman
Department of Chemistry
Stanford University
Stanford, California 94305

Dr. Alvin Crumbliss
North Carolina Biotechnology Center
Post Office Box 12235
Research Triangle Park, NC 27709

Dr. Marlene Deluca
University of California, San Diego
Department of Chemistry
La Jolla, CA 92093

Dr. Bruce Erickson
Chemistry Department
University of North Carolina
Chapel Hill, NC 27514

Dr. Richard B. Frankel
Massachusetts Institute of Technology
Francis Bitter National Laboratory
Cambridge, MA 02139

Dr. Hans Frauenfelder
Department of Physics
University of Illinois
Urbana, IL 61801

Dr. Bruce Gaber
Naval Research Laboratory
Code 6190
Washington, DC 20375

Dr. R. W. Giese
Northeastern Univ
Section of Medicinal Chemistry
360 Huntington Ave
Boston, MA 02115

Dr. Barry Honig
Columbia University
Dept of Biochemistry and Molecular Biophysics
630 West 168th St.
New York, NY 10032

Dr. Alex Karu
Department of Plant Pathology
College of Natural Resources
University of California
Berkeley, CA 94720

Dr. Robert G. Kemp
University of Health Sciences
Chicago Medical School
Department of Biochemical Chemistry
3333 Green Bay Road
North Chicago, IL 60064

Dr. Ghobind H. Khorana
Massachusetts Institute of Technology
77 Massachusetts Avenue
Cambridge, MA 02139

Dr. Richard Laursen
Chemistry Department
Boston University
590 Commonwealth Avenue
Boston, MA 02215

Dr. Robert W. Lenz
Chemical Engineering Department
University of Massachusetts
Amherst, MA 01003

Dr. Harden M. McConnell
Stanford University
Department of Chemistry
Stanford, CA 94305

Dr. Kristin Bowman Mertes
University of Kansas
Department of Chemistry
Lawrence, Kansas 66045

Dr. Edgard F. Meyer
Texas A&M University
Department of Biochemistry and Biophysics
Box 3578
College Station, TX 77843

Dr. Jiri Novotny
Laboratory of Cellular and Molecular Research
Massachusetts General Hospital
Boston, MA 02114

Dr. Carl O. Pabo
Johns Hopkins Medical School
Department of Biophysics
Baltimore, MD 21205

Dr. Franklyn Prendergast
Mayo Foundation
200 First St. SW
Rochester, MN 55905

Dr. Naftali Primor
New York Zoological Society
New York Aquarium
Osborne Laboratory of Marine Science
Brooklyn, NY 11224

Dr. K. S. Rajan
Illinois Institute of Technology
Research Institute
10 W. 35th St.
Chicago, IL 60616

Dr. C. Patrick Reynolds
Naval Medical Research Institute
Transplantation Research Program Center
Bethesda, MD 20814

Dr. Alexander Rich
Department of Biology
Massachusetts Institute of Technology
Cambridge, MA 02139

Dr. J. H. Richards
California Institute of Technology
Division of Chemistry and Chemical Engineering
Pasadena, CA 91125

Dr. J. S. Richardson
Duke University School of Medicine
Department of Anatomy
Durham, NC 27910

Dr. Richard Roblin
Genex Corporation
16020 Industrial Drive
Gaithersburg, MD 20877

Dr. Peter G. Schultz
Department of Chemistry
University of California
Berkeley, CA 94720

Dr. Michael E. Selsted
Department of Medicine
UCLA School of Medicine
37-055 CHS
Los Angeles, CA 90024

Dr. Michael Shuler
School of Chemical Engineering
Cornell University
Ithaca, New York 14853

Dr. David S. Sigman
UCLA School of Medicine
Department of Biological Chemistry
Los Angeles, CA 90024

Dr. John M. Stewart
University of Colorado Health Science Center
Department of Biochemistry
Denver, CO 80262

Dr. Dan W. Urry
Laboratory of Molecular Biophysics
University of Alabama
P. O. Box 311
Birmingham, AL 35294

Dr. J. Herbert Waite
College of Marine Studies
University of Delaware
Lewes, DE 19958

Dr. Gerald D. Watt
Battelle-C. F. Kettering Research Laboratory
150 East South College Street
P. O. Box 268
Yellow Springs, Ohio 45387

Dr. Jon I Williams
Allied Corporation
Columbia Rd and Park Ave.
Morristown, NJ 07960

Dr. Eli D. Schwell, Code 1141MB
Office of Naval Research
800 North Quincy Street
Arlington, VA 22217-5000

Dr. Michael T. Marron, Code 1141MB
Office of Naval Research
800 North Quincy Street
Arlington, VA 22217-5000

Dr. Margo G. Haygood
Office of Naval Research
800 North Quincy Street
Arlington, VA 22217-5000

Adminstrator (2 copies, Enclose DTIC Form 50)
Defense Technical Information Center
Building 5, Cameron Station
Alexandria, VA 22314

ANNUAL AND FINAL REPORTS ONLY (One copy each)

Commander
Chemical and Biological Sciences Division
Army Research Office
P. O. Box 12211
Research Triangle Park, NC 27709

Directorate of Life Sciences
Air Force Office of Scientific Research
Bolling Air Force Base
Washington, DC 20332

Chemistry and Atmospheric Sciences Directorate
Air Force Office of Scientific Research
Bolling Air Force Base
Washington, DC 20332

Director
Biotechnology Division
CRDEC
Aberdeen Proving Grounds, MD 21010-5423

Administrative Contracting Officer
ONR Resident Representative
(Address varies - obtain from your business office)

Director, Code 12
Applied Research and Technology Directorate
Office of Naval Research
800 North Quincy Street
Arlington, VA 22217-5000

Director, Code 22
Support Technology Directorate
Office of Naval Technology
800 North Quincy Street
Arlington, VA 22217-5000

Director, Code 112
Environmental Sciences Directorate
Office of Naval Research
800 North Quincy Street
Arlington, VA 22217-5000

Director, Code 113
Chemistry Division
Office of Naval Research
800 North Quincy Street
Arlington, VA 22217-5000

FINAL AND TECHNICAL REPORTS ONLY

Director (6 copies)
Naval Research Laboratory
Attn: Technical Information Division, Code 2627
Washington, DC 20375

END

3-87

DTIC