

BIOMEDICAL SIMULATIONS RESOURCE
UNIVERSITY OF SOUTHERN CALIFORNIA

Workshop On

**ADVANCED METHODS OF
PHARMACOKINETIC AND PHARMACODYNAMIC
SYSTEMS ANALYSIS**

May 18-19, 1990

Marina International Hotel
4200 Admiralty Way
Marina del Rey, California

Sponsored by

**BIOMEDICAL RESEARCH TECHNOLOGY PROGRAM
NATIONAL CENTER FOR RESEARCH RESOURCES
NATIONAL INSTITUTES OF HEALTH**

With special thanks to

**ABBOTT LABORATORIES
ADRIA LABORATORIES
GENENTECH, INC.**

Chairman and Organizer:

David Z. D'Argenio

Associate Director, Biomedical Simulations Resource

Friday, May 18, 1990

8:30	Introductory Remarks	David Z. D'Argenio University of Southern California
8:45	Predicting Drug Absorption in Humans	Gordon L. Amidon University of Michigan
9:15	Pharmacokinetics of Reversible Metabolic Systems	Haiyung Cheng Merrell Dow Pharmaceuticals, Inc.
9:45	Genetic Polymorphisms of Drug Metabolism	Mary V. Relling Saint Jude Children's Research Hospital
10:15	Discussion	
10:30	Break	
10:45	The Significance of Marked Universal Dependence of Drug Concentration on Blood Sampling Site in Pharmacokinetics and Pharmacodynamics	Win L. Chiou University of Illinois at Chicago
11:15	Pharmacokinetic Models for Anticancer and Antiviral Drugs Following Administration as Novel Drug Delivery Systems	James M. Gallo University of Georgia
11:45	Discussion	
12:00	Lunch Break	
1:30	Residence Time Distributions in Pharmacokinetics: Behavioral and Structural Models	Michael Weiss Martin-Luther-Universität, Halle-Wittenberg
2:00	Relationships Between Intra or Interindividual Variability and Biological Covariates: Application to AZT Pharmacokinetics	France Mentre INSERM U194, Paris
2:30	On the Single-Point, Single-Dose Problem	George D. Swanson University of Colorado Medical Center
3:00	Discussion	
3:15	Break	
3:30	Application of Stochastic Control Theory to Optimal Design of Dosage Regimens	Alan Schumitzky University of Southern California
4:00	Incorporating Model Uncertainty in Pharmacokinetic Parameter Estimation	David Z. D'Argenio University of Southern California
4:30	Discussion	
5:00	Reception	

Saturday, May 19, 1990

8:30	Algebraic and Differential Relations for Membranes in Series: Permeabilities, Lag Times, Mean Residence Times, and Solute Consumption	Ronald A. Siegel University of California at San Francisco
9:00	Physiological Alternatives to the Effect Compartment Model	Nicholas H.G. Holford University of Auckland
9:30	Pharmacokinetics/Dynamics of Corticosteroids	William J. Jusko State University of New York at Buffalo
10:00	Discussion	
10:15	Break	
10:30	Impact of Age and Disease on Intra- and Inter-individual Variability in Human Cardiovascular Pharmacodynamics	Darrell R. Abernethy Brown University
11:00	Pharmacodynamic Modeling of Thiopental Depth of Anesthesia	Donald R. Stanski Stanford University
11:30	Discussion	
11:45	Lunch Break	
1:30	A Bayesian Kinetic Control Strategy for Cyclosporin in Renal Transplantation	Brian Whiting University of Glasgow
2:00	Targeted Systemic Exposure for Pediatric Cancer Therapy	John H. Rodman University of Tennessee at Memphis
2:30	Targeting the Effect Site with a Computer Controlled Infusion	Steven L. Shafer Stanford University
3:00	Discussion	
3:15	Break	
3:30	Pharmacokinetic-Dynamic Models for Feedback Controlled Drug Administration in Anaesthesia: The Use as Therapeutic System and Research Tool	Helmut Schwilden Rheinische Friedrich-Wilhelms Universität, Bonn
4:00	Development of a Fiber Optic Biosensor for Measurement of General Anesthetics	Paul Yager University of Washington
4:30	Closing Remarks	David Z. D'Argenio University of Southern California
5:00	Reception	

BIOMEDICAL SIMULATIONS RESOURCE
UNIVERSITY OF SOUTHERN CALIFORNIA

Workshop on

ADVANCED METHODS OF
PHARMACOKINETIC AND PHARMACODYNAMIC
SYSTEMS ANALYSIS

May 18-19, 1990
Marina del Rey, California

DIRECTORY OF PARTICIPANTS

Peter H. Abbrecht
Department of Medicine and Physiology
Uniformed Services University
of the Health Sciences
F. Edward Hebert School of Medicine
4301 Jones Bridge Road
Bethesda, MD 20814-4799

Darrell R. Abernethy
Division of Clinical Pharmacology
Brown University
Roger Williams General Hospital
825 Chalkstone Avenue
Providence, RI 02908

Andrew A. Acheampong
Allergan Inc.
2525 Dupont Drive
Irvine, CA 92715

Gordon L. Amidon
College of Pharmacy
The University of Michigan
Ann Arbor, MI 48109-1065

Mordechai Ben Porat
Department of Chemistry
Israel Governmental Research Laboratories
5 Maklis
Petach - Tikva 49558
Israel

Stefano Biasioli
Divisione Nefrologia, Emodialisi
Ospedale Lognago
37145 Legnago (VR)
Italy

Sven Björkman
Anesthesia (112 A)
V.A. Medical Center
Palo Alto, CA 94304

Clive E. Bowman
PROCESS
11 Fielding Road
Maidenhead
Berks, SL6 5DE
United Kingdom

David C. Bradley
Department of Physics & Biophysics
University of Southern California
2025 Zonal Avenue
Los Angeles, CA 90033

Kenneth Brouwer
School of Pharmacy CB #7360
University of North Carolina
Chapel Hill, NC 27599

Kim L.R. Brouwer
School of Pharmacy CB #7360
University of North Carolina
Chapel Hill, NC 27599

Ann Chang
Department of Pharmacology
23-384 BRI
University of California
Los Angeles, CA 90024

Benjamin C. Chen
1 Moonmist Drive
Rancho Palos Verdes, CA 90274

Haiyung Cheng
Merrell Dow Pharmaceuticals, Inc.
Dept. of Pharmacokinetics
& Drug Metabolism
9550 N. Zionsville Road
Indianapolis, IN 46268

Mary H. Cheng
Clinical Laboratory - Chemistry
Children's Hospital of Los Angeles
4650 Sunset Blvd.
Los Angeles, CA 90027

Du-Shieng Chien
Allergan Pharmaceuticals
2525 Dupont Drive
Irvine, CA 92715

Win L. Chiou
Department of Pharmacodynamics
College of Pharmacy
P.O. Box 6998
University of Illinois at Chicago
Chicago, IL 60680

Arthur K. Cho
Department of Pharmacology
23-384 BRI
University of California
Los Angeles, CA 90024

Teresa Chu
1544 Armacost Avenue #E
Los Angeles, CA 90025

Thomas G. Coleman
Department of Physiology & Biophysics
University of Mississippi, Medical Center
2500 North State Street
Jackson, MS 39216-4505

Kenneth Courtney
Palo Alto Medical Foundation
860 Bryant Street
Palo Alto, CA 94301

Pamela G. Coxson
Research Medicine 55-121
Lawrence Berkeley Lab.
Berkeley, CA 94720

Fran Cunningham
Department of Pharmacy Practice
University of Illinois
Chicago, IL 60612

David Z. D'Argenio
Department of Biomedical Engineering
University of Southern California
Los Angeles, CA 90089-1451

Carlo De Angeles
Sunnybrook Health Science Centre
Department of Pharmacy
2075 Bayview Avenue
North York, Ontario
Canada M4N 3M5

Charles Denaro
Division of Clinical Pharmacology
Room 3220, Building 30
San Francisco General Hospital
1001 Potrero Avenue
San Francisco, CA 94110

Barry Dick
Anesthesia Service [112-A]
Palo Alto Veterans Medical Center
3801 Miranda Drive
Palo Alto, CA 94304

Joseph J. DiStefano, III
Computer Science Department
University of California, L.A.
4731 Boelter Hall
Los Angeles, CA 90024-1596

Wael Doukmak
Department of Pharmaceutics
College of Pharmacy/UGA
Athens, GA 30602

Michael Dudley
Anti-Infective Pharmacology Research Unit
Brown University
Roger Williams General Hospital
825 Chalkstone Blvd.
Providence, RI 02908

William F. Ebling
Anesthesia Service [112-A]
Palo Alto Veterans Medical Center
3801 Miranda Drive
Palo Alto, CA 94304

James H. Fischer
47 Eureka Avenue
Lemont, IL 60439

John S. Fitzpatrick
Department of Biomedical Engineering
University of Southern California
Los Angeles, CA 90089-1451

Carolyn M. Fleming
Division of Clinical Pharmacology
556 MRB, 23rd at Pierce
Vanderbilt University
Nashville, TN 37122

Roberto Foroni
Divisione Fisica Sanitaria
Plaza Stefani 3
USLL 25
37122 Verona
Italy

Alan Forrest
University of Maryland Cancer Center
(BRB 9-023)
655 W. Baltimore Street
Baltimore, MD 21201

James M. Gallo
Department of Pharmaceutics
College of Pharmacy
University of Georgia
Athens, GA 30602

Douglas Geraets
College of Pharmacy, Quad 2262
The University of Iowa
Iowa City, IA 52242

Thomas Gilman
University of Southern California
School of Medicine
1985 Zonal Avenue
Los Angeles, CA 90033

Li-Min Haung
Computer Science Department
University of California, L.A.
4731 Boelter Hall, Biocybernetics Lab
Los Angeles, CA 90024-1596

Pilar Gomis
School of Medicine
University of Southern California
2011 Zonal Avenue HMR 805
Los Angeles, CA 90033

Thomas K. Henthorn
Northwestern University
303 E. Chicago Avenue
Ward 12-189
Chicago, IL 60611

Jess Gornbein
Biomathematics Department
CVS-Room 617
University of California, L.A.
Los Angeles, CA 90024-1766

Kenneth J. Himmelstein
Allergan
2525 Dupont Drive
Irvine, CA 92715

Mark Gumbleton
Department of Pharmacy
University of California, San Francisco
San Francisco, CA 94143

Nicholas Holford
Department of Pharmacology
University of Auckland
Auckland
New Zealand

Suneel K. Gupta
ALZA Corporation
950 Page Mill Road
Palo Alto, CA 94303-0802

Phillip Hong
School of Pharmacy, PSC 512
University of Southern California
1985 Zonal Avenue
Los Angeles, CA 90033

Victoria Hale
843 W. University Parkway
Baltimore, MD 21210

Agneta Hurst
School of Pharmacy (PSC 602)
University of Southern California
1985 Zonal Avenue
Los Angeles, CA 90033

Charles E. Halstenson
The Drug Evaluation Unit
Hennepin County Medical Center
701 Park Avenue
Minneapolis, MN 55415

George Jaresko
School of Pharmacy
University of Southern California
PSC Room 106
1985 Zonal Avenue
Los Angeles, CA 90033

Emadeldin Hassan
Department of Pharmaceutics
University of Georgia, College of Pharmacy
Athens, GA 30602

Roger W. Jelliffe
School of Medicine HMR 805
University of Southern California
2011 Zonal Avenue
Los Angeles, CA 90033

Masahiro Kurita
Division of Gastroenterology
Department of Medicine, T-013
University of California, San Diego
La Jolla, CA 92093-0813

Donald T. Jung
3401 Hillview Ave., A3-165
Palo Alto, CA 94304

Elliot M. Landaw
Department of Biomathematics
School of Medicine
University of California, L.A.
Los Angeles, CA 90024-1766

Robert E. Kates
Analytical Solutions, Inc.
568 Weddell Drive #5
Sunnyvale, CA 94089

David Lau
Pharmacy Department, Box 0446
University of California
San Francisco, CA 94143-0446

Darryl Katz
Department of Mathematics
California State University
Fullerton, CA 92634

Frank Lee
Glaxo Incorporated
5 Moore Drive
RTP, NC 27709

Toshihiro Kikkoji
Department of Pharmacy
University of California, San Francisco
San Francisco, CA 94143

Vahn A. Lewis
University of Texas
Health Sciences Center
Dental Branch
P.O. Box 20068, Room 403
Houston, TX 77225

Richard Ko
125 N. 2nd Street #C
Alhambra, CA 91801

Song W. Ko
30 Meadow View Drive
Pomona, CA 91766

Lena Y. Lin
801 Hilgard Avenue
Los Angeles, CA 90024

Thomas H. Kramer
Department of Pharmacology
College of Medicine
University of Arizona
Tucson, AZ 85724

Shu-Ching Lin
Department of Pharmacodynamics
College of Pharmacy, M/C 865
University of Illinois at Chicago
Chicago, IL 60612

Yoshito Kumagai
3780 Keystone Avenue #215
Los Angeles, CA 90034

Thomas Ludden
Department of Pharmacology
University of Texas Health Science Center
7703 Floyd Curl Drive
San Antonio, TX 78284

Jean-Michel I. Maarek
Department of Biomedical Engineering
University of Southern California
Los Angeles, CA 90089-1451

Joyce Mordenti
Genentech, Inc.
460 Point San Bruno Blvd.
South San Francisco, CA 94080

Kirk Mahoney
Department of Biomathematics
UCLA School of Medicine
Los Angeles, CA 90024

Maulik Nanavaty
Baxter Healthcare Corporation
One Baxter Parkway
Deerfield, IL 60015

Daniel C. Maneval
Genentech, Inc.
460 Point San Bruno Blvd.
South San Francisco, CA 94080

Chin K. Ng
Division of Nuclear Medicine
& Biophysics B2-086 CHS
UCLA School of Medicine
Los Angeles, CA 90024

Etan Markowitz
22925 Van Deene Avenue
Torrance, CA 90502

Thuvan T. Nguyen
Computer Science Department
University of California, L.A.
4731 Boelter Hall
Los Angeles, CA 90024-1596

Richard M. Matsumoto
Allergan Pharmaceuticals
2525 Dupont Drive
Irvine, CA 92715

Shigehiro Ohdo
2427 West Main St. #6
Alhambra, CA 91801

France Mentre
INSERM U194
Department de Biomathematiques
91, Bd de l'Hopital
F-75643 Paris Cedex 13
France

Joseph Ojingwa
Department of Pharmacy, Box 0446
University of California
San Francisco, CA 94143-0446

Gary Milavetz
College of Pharmacy, Quad 2262
The University of Iowa
Iowa City, IA 52242

Sasa Pajevic
Computer Science Department
3436 Boelter Hall
405 Hilgard Avenue
University of California, L.A.
Los Angeles, CA 90024

Malcolm J. Moore
Department of Medicine
Princess Margaret Hospital, Room 499
500 Sherbourne Street
Toronto, Ontario
Canada M4X 1K9

Nita Patel
121 Eula Drive
Montebello, CA 90640

Lorraine B. Peddada
Alpha Therapeutic Corporation
1213 John Reed Court
City of Industry, CA 91744

John G. Pierce
1024 18th Street #D
Santa Monica, CA 90403

Beatrice Perotti
Department of Pharmacy
University of California, San Francisco
San Francisco, CA 94143

Gary M. Pollack
School of Pharmacy CB #7360
University of North Carolina
Chapel Hill, NC 27599

J.H. Proost
Dept. of Pharmacology & Therapeutics
University Centre of Pharmacy
University of Groningen
A. Demsinglaan 2
9713 AW Groningen
The Netherlands

Thomayant Prueksaritanont
Department of Pharmacy, Box 0446
University of California
San Francisco, CA 94143-0446

David Raffell
Medical Science Center, Room 1530
University of Wisconsin
1300 University Avenue
Madison, WI 53706

Srinivas Ramamurthy
Department of Pharmacology
23-384 BRI
University of California
Los Angeles, CA 90024

Mary Relling
Pharmaceutical Division
St. Jude Children's Research Hospital
332 N. Lauderdale
P.O. Box 318
Memphis, TN 38101

Joseph Richman
Allergan Pharmaceuticals
2525 Dupont Drive
Irvine, CA 92715

Vincent C. Rideout
Electrical and Computer Engineering
Engineering Building
University of Wisconsin
Madison, WI 53706

John Rodman
Pharmacokinetics Laboratory
St. Jude Children's Research Hospital
332 N. Lauderdale
Memphis, TN 38105

Brian M. Sadler
Research Triangle Institute
P.O. Box 12194
Research Triangle Park, NC 27709

Ronald J. Sawchuk
College of Pharmacy
University of Minnesota
308 Harvard St. S.E.
Minneapolis, MN 55455

Olga Schmidlin
Department of Pharmacy, Box 0446
University of California
San Francisco, CA 94143-0446

Debra Schmitz
518 Susana Avenue
Redondo Beach, CA 90277

Roy W. Schubert
Department of Biomedical Engineering
Louisiana Tech University
Box 10348
Ruston, LA 71272

Ru-Liang Shih
School of Pharmacy
University of Southern California
1985 Zonal Avenue #702
Los Angeles, CA 90033

Alan Schumitzky
Department of Mathematics
University of Southern California
Los Angeles, CA 90089-1113

Ronald A. Siegel
School of Pharmacy
University of California
San Francisco, CA 94143-0446

Helmut Schwilden
Institut für Anästhesiologie
Universität Bonn
Sigmund-Freud-Strasse 25
D-5300 Bonn 1,
Federal Republic of Germany

John B. Slate
MiniMed Technologies
12744 San Fernando Rd.
Sylmar, CA 91342

Steven L. Shafer
Anesthesia Service 112A
Veterans Administration Medical Center
3801 Miranda Avenue
Palo Alto, CA 94304

N. Ty Smith
Department of Anesthesia
University of San Diego
VA Medical Center
San Diego, CA 92108

Jaymin Shah
Syntex A3-165
3401 Hillview Avenue
Palo Alto, CA 94303

Gisela Spieler
Department of Mathematics
California State University
P.O. Box 34080
Fullerton, CA 92634-9480

Xuesi Shao
c/o Dr. Meyer Jackson
University of California, L.A.
Los Angeles, CA 90024-1606

S.P. Srinivas
Department of Ophthalmology,
Room S030
Stanford University
Stanford, CA 94305

Lewis B. Sheiner
Department of Laboratory Medicine
and Medicine
School of Medicine & Pharmacology
University of California
San Francisco, CA 94143

Donald R. Stanski
Anesthesia Service 112A
Veterans Administration Medical Center
3801 Miranda Avenue
Palo Alto, CA 94304

J.H. Steinbach
Gastroenterology, V-111-D
Veterans Administration Medical Center
3350 La Jolla Village Drive
San Diego, CA 92161

John St. Peter
Hennepin County Medical Center,
RKDP
701 Park Avenue S.
Minneapolis, MN 55415

Helen Sun
Department of Pharmacy, Box 0446
University of California
San Francisco, CA 94143-0446

George D. Swanson
Department of Physical Education
California State University, Chico
Chico, CA 95929

Mary Teresi
College of Pharmacy, Quad 2262
The University of Iowa
Iowa City, IA 52242

Jake J. Thiessen
Faculty of Pharmacy
University of Toronto
19 Russell Street
Toronto, M5S 1A1
Canada

Hugo Vargas
Department of Pharmacology
CHS 23-231
UCLA School of Medicine
Los Angeles, CA 90024-1735

Jan Volhejn
MEDISOFT, Hájecká 10
100 00 Prague 10
Czechoslovakia

D. Russell Wada
Department of Anesthesia
University of California
CHS-BH511
Los Angeles, CA 90024

Parker Waechter
Computer Science Department
University of California, L.A.
4731 Boelter Hall - Biocybernetics Lab
Los Angeles, CA 90024-1596

Jonathan Wakefield
The Maths Department
University Park
Nottingham University
Nottingham NG72RD
United Kingdom

Jeffrey Wald
Department of Pharmaceutics
School of Pharmacy
State University of New York at Buffalo
Buffalo, NY 14260

Denham S. Ward
Department of Anesthesia
University of California
CHS-BH511
Los Angeles, CA 90024

Richard Watanabe
Department of Physiology & Biophysics
University of Southern California
School of Medicine
2025 Zonal Avenue
Los Angeles, CA 90033

Michael Weiss
Institut für Pharmakologie und Toxikologie
Martin Luther Universität Halle-Wittenberg
Leninallee 4
4020 Halle
German Democratic Republic

Brian Whiting
Department of Materia Medica
University of Glasgow
Stobhill General Hospital
Glasgow, G21 3UW
United Kingdom

Karen Wickham
1836 MacArthur Street
Rancho Palos Verde, CA 90732

Paul Yager
Center for Bioengineering, MS SL20
AERL 336
University of Washington
Seattle, WA 98195

Wan-Ching Yen
School of Pharmacy
University of Southern California
1985 Zonal Avenue #702
Los Angeles, CA 90033

Yi-Meng Yen
Computer Science Department
University of California, L.A.
4731 Boelter Hall
Los Angeles, CA 90024-1596

Roumei Zhang
Department of Biomedical Engineering
OHE 500, 1451
University of Southern California
Los Angeles, CA 90089-1451