

The pre-history of kinetic modelling and simulation

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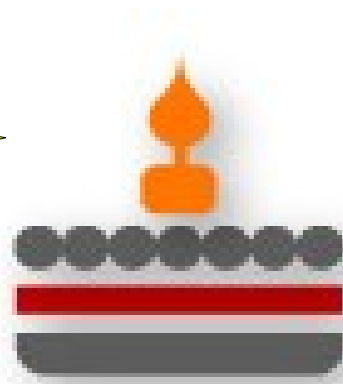
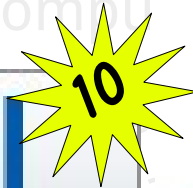
Virginia Bioinformatics Institute, Virginia Tech

Happy Birthday SBML!

Pedro Mendes

School of Compu

Man

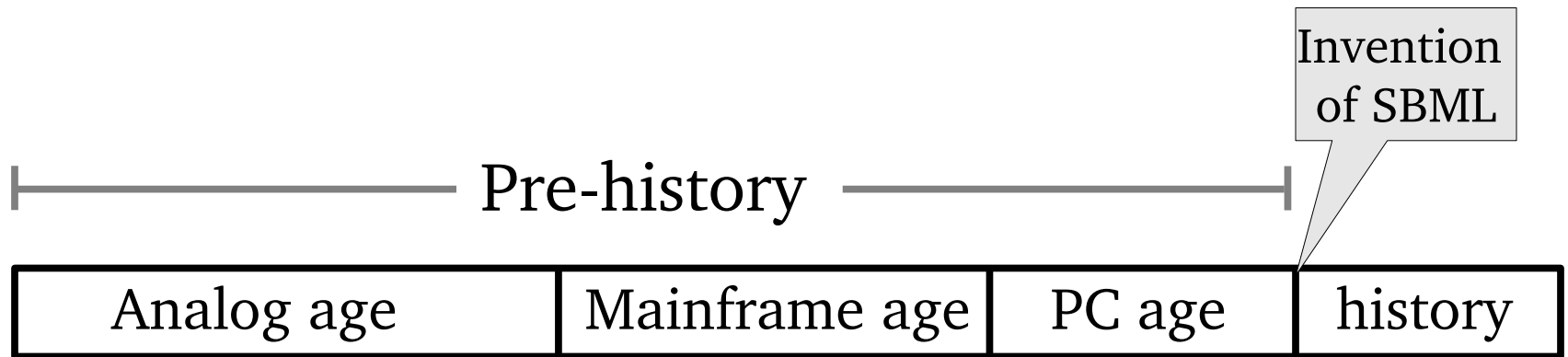
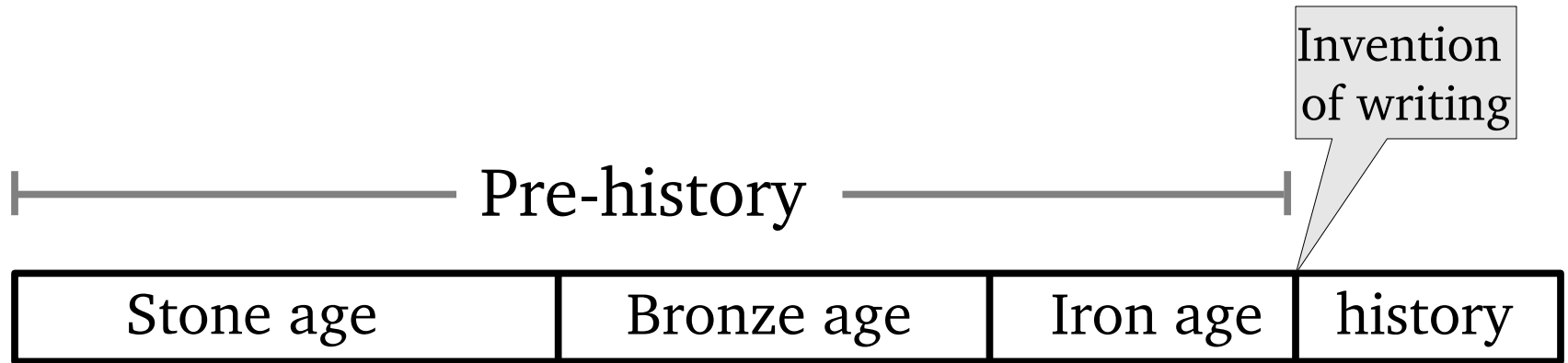


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Timelines



Obligatory quote

Those who cannot remember the past are condemned to repeat it.

George Santayana (1905)

The Life of Reason: or, the Phases of
Human Progress

Experiment + simulation in 1943

J. Biol. Chem. 1943 151: 553-577

THE KINETICS OF THE ENZYME-SUBSTRATE COMPOUND OF PEROXIDASE

By BRITTON CHANCE

*(From the Johnson Research Foundation, University of Pennsylvania, Philadelphia,
and the Physiological Laboratory, University of Cambridge, Cambridge, England)*

(Received for publication, May 26, 1943)

Studies on the over-all kinetics of enzyme action revealed in the majority of cases and over certain concentration ranges that the enzymatic activity was related linearly to the enzyme concentration and hyperbolically to the substrate concentration. On the basis of such evidence Michaelis and Menten (13) showed that such relationships were explained on the assumption that an intermediate compound of enzyme and substrate was formed: $E + S \rightarrow ES \rightarrow E + P$. As the rate of formation of such a compound was assumed to be quite rapid, the rate of breakdown was the rate-determining step. This theory was extended by Briggs and Haldane (2) who pointed out that the rate of formation of the intermediate compound could in certain cases be limited by the number of collisions of enzyme and substrate, and modified the Michaelis theory accordingly. The resulting

Experiment + simulation in 1943

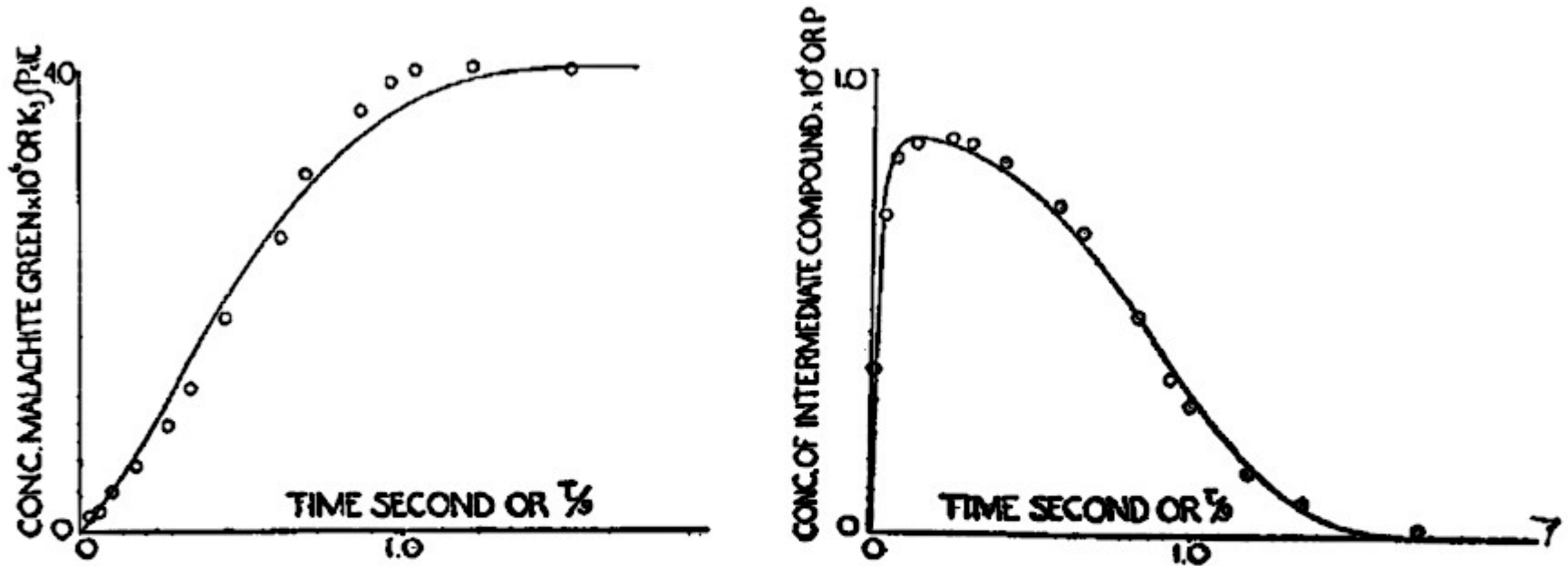


FIG. 10. A comparison of experimental enzyme-substrate and "over-all" kinetics (circles) with a mathematical solution of the Michaelis theory for experimentally determined reaction velocity constants and concentrations (solid lines).

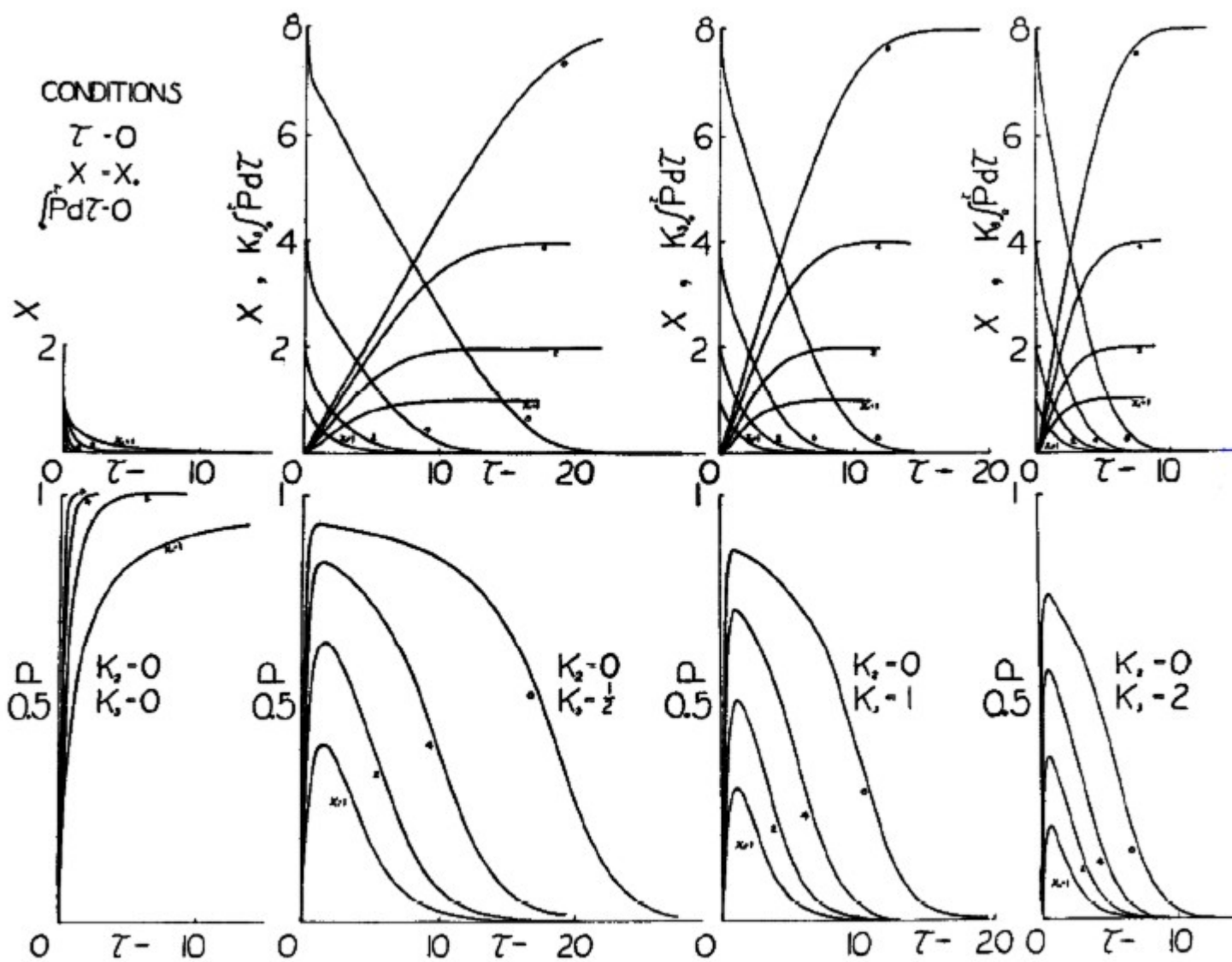
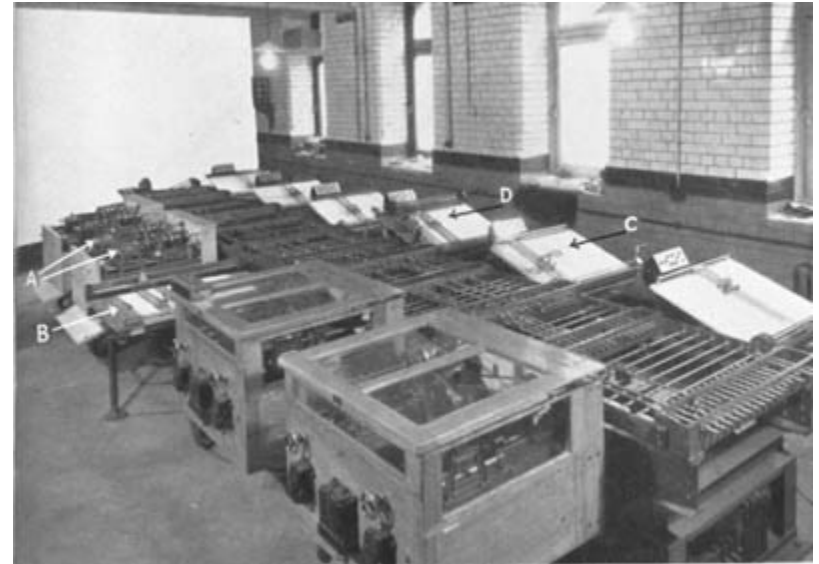
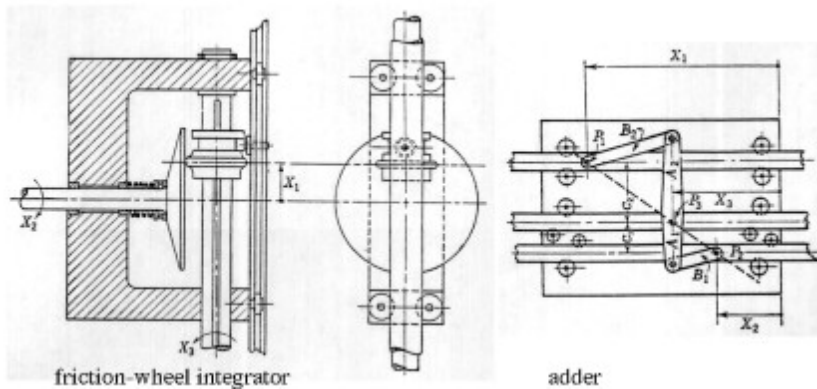


FIG. 12. Differential analyzer solutions of the Michaelis theory for the over-all reaction (upper group) and the kinetics of the enzyme-substrate compound (lower group).

Differential analyser



Metropolitan Vickers differential analyzer at Manchester University.

Electric analog computer model of catalase

Arch. Biochem. Biophys. 1952 37: 322-339

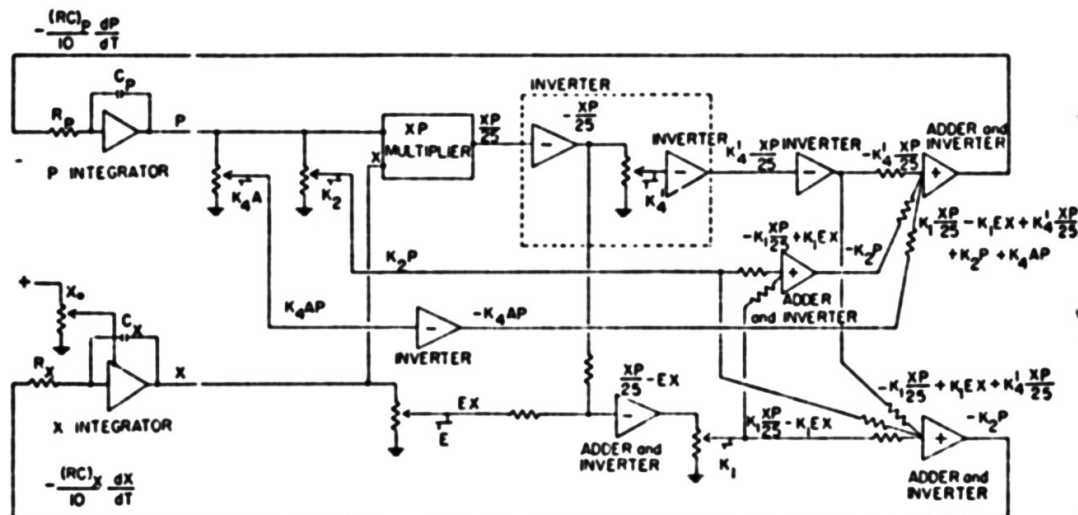
The Mechanism of Catalase Action. ¹

II. Electric Analog Computer Studies

Britton Chance, David S. Greenstein, Joseph Higgins and C. C. Yang

*From the Johnson Research Foundation, University of Pennsylvania,
Philadelphia, Pennsylvania*

Received October 26, 1951



Digital computer model of glycolysis - 1960!

THE JOURNAL OF BIOLOGICAL CHEMISTRY
Vol. 235, No. 8, August 1960
Printed in U.S.A.

Metabolic Control Mechanisms

V. A SOLUTION FOR THE EQUATIONS REPRESENTING INTERACTION BETWEEN
GLYCOLYSIS AND RESPIRATION IN ASCITES TUMOR CELLS*†

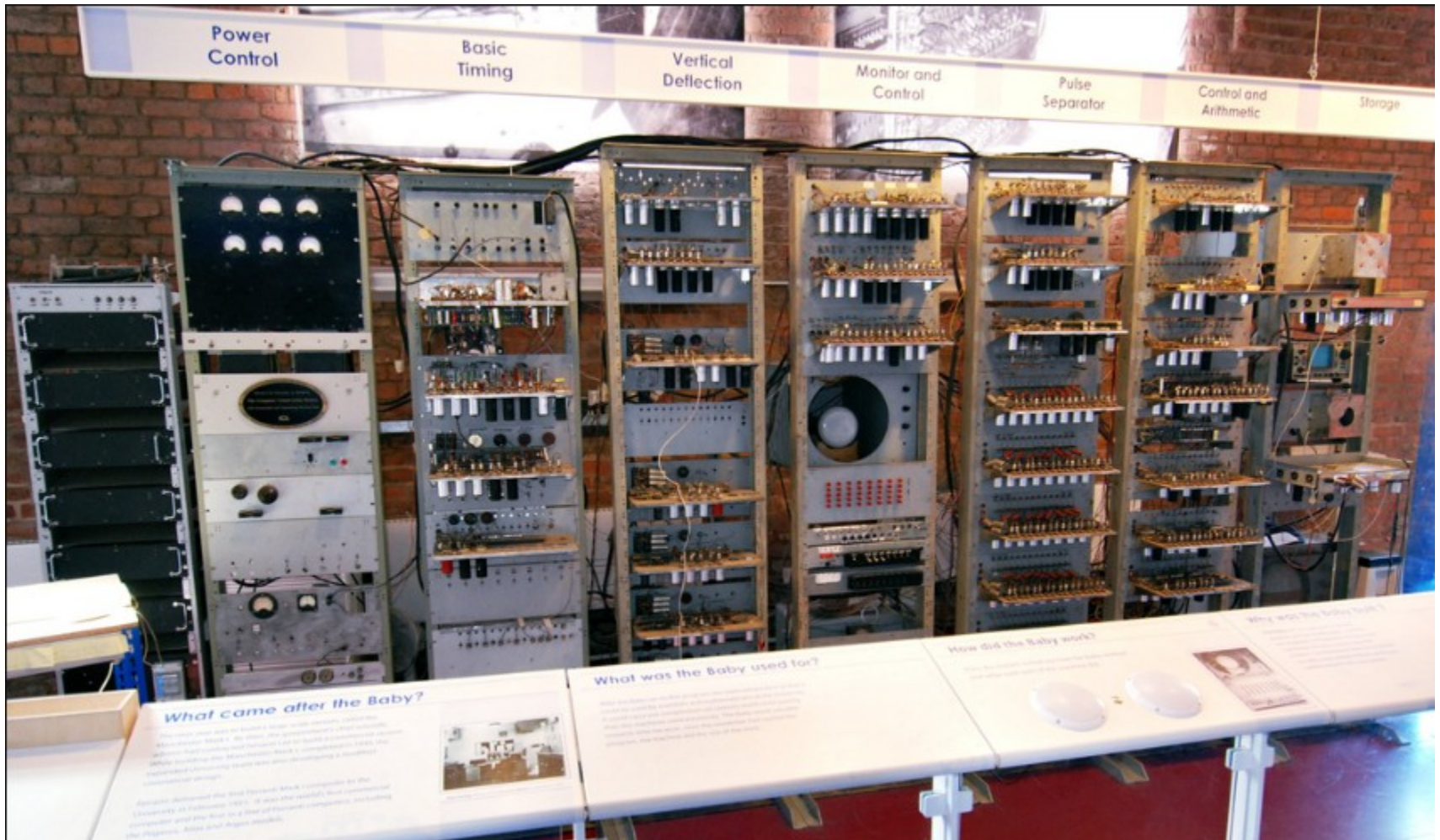
BRITTON CHANCE, DAVID GARFINKEL,‡ JOSEPH HIGGINS,§ AND BENNO HESS¶

- Analog computers could not cope with large networks
- 500 hours of UNIVAC I time
- Euler method for integration, 12-digit numbers
- Many failures of model against experiment but an exemplary application of model-based reasoning

UNIVAC I at U. Penn.



The Manchester "Baby"



First generic simulator – BIOSSIM

COMPUTERS AND BIOMEDICAL RESEARCH **2**, 31–44 (1968)

A Machine-Independent Language for the Simulation of Complex Chemical and Biochemical Systems*

DAVID GARFINKEL

Johnson Research Foundation, University of Pennsylvania, Philadelphia, Pennsylvania 19104

Received April 6, 1968

Stiff ODEs in 1970s

Ann. Rev. Biophys. Bioeng. 1977. 6:525-42

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STIFF DIFFERENTIAL EQUATIONS¹

David Garfinkel and Carl B. Marbach

Moore School of Electrical Engineering, University of Pennsylvania,
Philadelphia, Pennsylvania 19174

Norman Z. Shapiro

The Rand Corporation, Santa Monica, California 90406

1980s: microcomputers → “user-friendliness”



METAMOD - 1986

CABIOS

Vol 2 no 4 1986
Pages 243 - 249

METAMOD: software for steady-state modelling and control analysis of metabolic pathways on the BBC microcomputer

J.H.S.Hofmeyr and K.J.van der Merwe*

METAMOD

- 1) Read in metabolic path
- 2) Catalogue disc
- 3) View path
- 4) Change concentrations/status
- 5) Calculate steady state
- 6) Control analysis
- 7) Tune algorithms
- 8) EXIT from program

Please enter option _

PMB: Portable MetaBolic standard format - 1999

- Preliminary efforts for a common file format, last revision September 1999
- Franco Bignone, Athel Cornish-Bowden, David Fell, Igor Goryanin, Jannie Hofmeyr, Pedro Mendes, Brett Olivier, Mark Poolman, Johann Rohwer, Herbert Sauro, Alex Selkov
- *We really need good abstract model. Which language may be used for describing it (BNF, SGML or XML DTD, relational - you name it) much less significant.* Igor Goryanin

Specification for a Portable Metabolic Binary Format (pmb file)

Copyright © 1999 MMFF List Committee

Public version 1.0
Last revised 10 September 1999

Intended audience

This specification is intended for use by implementors of software to interconvert specific storage schemes for metabolic simulation data into a portable common format.

The text of the specification assumes a basic background in programming at the level of bits and other primitive data representations.

Introduction

This document describes the first pmb (Portable Metabolic Binary) specification, an extensible and portable binary file format for the storage and trans-



- ODE and stochastic simulation
- MCA, stability analysis, parameter
- Optimisation, fitting
- Sensitivity

Latest release: **Build 33**
 Now under OSI approved
 license: **Artistic License 2.0**

The image displays three screenshots from the COPASI 4.0 Build 33 software interface:

- Left Screenshot:** Shows the 'Model' tree structure with categories like Biochemical, Compartments, Reactions, and Mathematical. The 'Differential Equations' section is expanded, showing a system of equations for species concentrations over time.
- Middle Screenshot:** Shows a table of model components with columns for ID, Name, Type, and Description. The table lists various parameters and modifiers.
- Right Screenshot:** Shows a 'Plot' window with a graph of species concentrations over time. The x-axis is labeled 'A' and ranges from 0 to 40. The y-axis ranges from 0 to 3. Multiple colored lines (red, green, blue) represent different species, showing oscillatory behavior.

<http://www.copasi.org>