BERKELEY MADONNA IMPLEMENTATION of IKEDA's MODEL

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INTRODUCTION

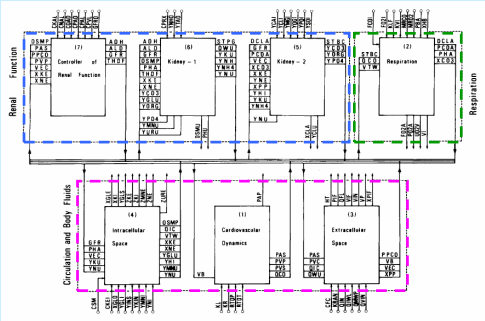
- ✓ Development of ever more **sophisticated models** at many scales
- ✓ But non-existence of a comprehensive, organism-level environment available for inspection, modification and extension
- ✓ **SAPHIR** project (involved in the IUPS Physiome project effort) = development of a comprehensive, modular, interactive modeling environment
  - centred on overall regulation of blood pressure and body fluids
  - and based on 2 models: the **Guyton's** (overall regulation of blood pressure) and the **Ikeda's** (fluid regulation)

A.C. Guyton, T.G. Coleman & H.J. Granger, "Circulation: overall regulation", *Annual Review of Physiology*, vol: 34, 1972, pp. 13-46.
N. Ikeda, F. Marumo, M. Shirataka & T. Sato, "A model of overall regulation of body fluids", *Annals of Biomedical Engineering*, vol: 7, 1979, pp. 135-166.

Our aim here: **Showing the possibility of transposing the existing Ikeda's model under Berkeley-Madonna software**

IKEDA's: an integrated biological system model

- ✓ Model of body-fluid regulation
- ✓ Comprehensive with subsystems
- ✓ Study of body fluid disturbances and fluid therapy
- ✓ Nice complement to Guyton-type model



7 blocks (each described by one scheme) **classified in 3 categories:**

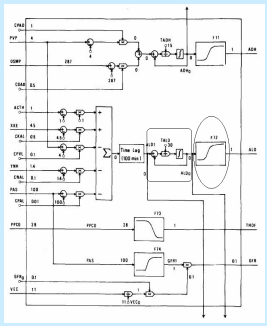
- **Circulation and body fluids**
- **Respiration**
- **Renal function**

IMPLEMENTATION

More than **200 parameters and variables**

130 differential and algebraic equations
Explicitly or tacitly described from the blocks

$$ALD = \frac{10}{1+\exp(-0.4394(ALD0-5))} \qquad \frac{d(ALD0)}{dt} = \frac{ALD1 - ALD0}{TALD}$$



Implemented with **Berkeley-Madonna**: Software for Modeling and Analysis of dynamic systems (Differential equation solver)

Definitions of constant parameters
MRO2=0.259

Differential equations
d/dt(UO2V)=(QCO*(UO2A-UO2V) -MRO2)/VTW
init (UO2V)=0.1515

Algebraic equations
UO2A=3.168*10^-5*PO2A+UHBO
VTW=VEC+VIC
Etc…

- ✓ Fast computation
- ✓ Easy to use
- ✓ User-friendly interface

Linear programming
Integration method: RK 4

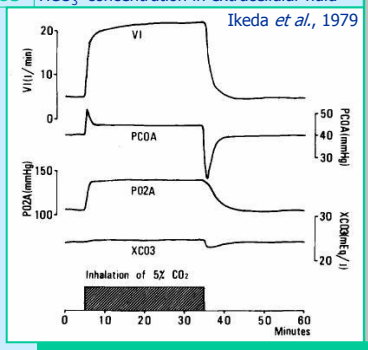
SIMULATIONS under BERKELEY-MADONNA

- ✓ Responses to various inputs
- ✓ Same simulations as in the original paper

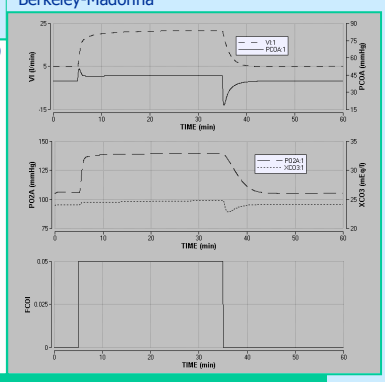
=> Original responses recovered

FCOI	Volume fraction of CO_2 in dry inspired gas
PCOA	CO_2 pressure in alveoli
PO2A	O_2 pressure in alveoli
VI	Ventilation
XCO3	HCO_3^- concentration in extracellular fluid

Ikeda *et al.*, 1979



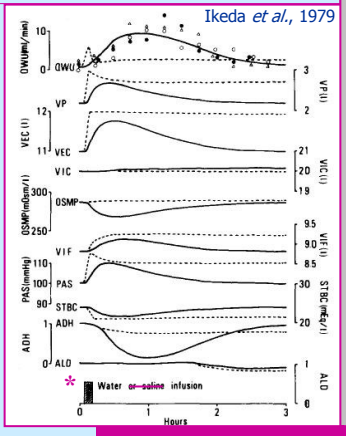
Berkeley-Madonna



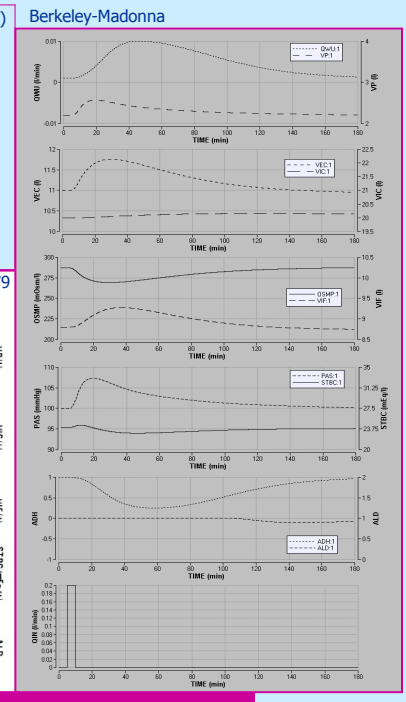
System response to the inhalation of 5% CO2

ADH	Effect of antidiuretic hormone (ratio to normal)
ALD	Effect of aldosterone (ratio to normal)
OSMP	Plasma osmolality
PAS	Systemic arterial pressure
QIN	Rate of drinking
QWU	Urine output
STBC	Standard bicarbonate at pH=7.4
VEC	Extracellular fluid volume
VIC	Intracellular fluid volume
VIF	Interstitial fluid volume
VP	Plasma volume

Ikeda *et al.*, 1979



Berkeley-Madonna



System response to water loading

* Observe black thick lines for water infusion simulated responses *

DISCUSSION

- ✓ Model's behavior correctly simulated
- ✓ New simulations: easy test of new conditions
  - => Application to clinical problems in the diagnosis and therapy of body fluid balance
  - => Possibilities for simulating some pathological states
- ✓ Incomplete description of the overall regulation of blood pressure and body fluids: additional and missing elements in relation to Guyton's
  - => Comparison between the 2 models to define the basis model of the SAPHIR project

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