Medical Informatics & Artificial Intelligence in Human Immunodeficiency Virus (HIV)

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What is Medical Informatics?

- **Simplistic definition:** Computer applications in medical care.

- **Complex definition:**
  - Emerging Discipline
  - Defined as: study, invention & implementation of structures & algorithms
  - Improve communication, understanding & management of clinical information
  - Coalescing of data, knowledge & tools
  - Decision-making process

*The focus on the structures and algorithms necessary to manipulate the information separates Medical Informatics from other medical disciplines where information content is the focus.*
What is Artificial Intelligence (AI)?

- **Simplistic definition:** “Thinking Machines”.

- **Complex definition:**
  - A device performs functions associated with human intelligence processes.
  - Processes = Acquisition of information + Rules for using it (learning) + Rules to reach conclusions (reasoning) & self-correcting.

- **In a few words:** AI approximates human reasoning by organizing & manipulating factual & heuristic knowledge.
A global view of HIV infection
38.6 million people [33.4–46.0 million] living with HIV, 2005
Figure 2. Occurrence of AIDS-Indicating Conditions in the Natural History of HIV Infection, According to CD4+ Cell Count.
LABORATORY MARKERS OF HIV INFECTION

Used for:

- Disease staging
- AIDS definition
- Prognosis
- Treatment initiation
- Monitoring
- Design clinical trials
Relating Disease Progression to Plasma HIV RNA Level and CD4 Cell Count

Treatment needs are evolving

• Nearly one-third of patients are third-line or beyond in their therapy

• As patients live longer, their treatment needs evolve as resistance to older ARVs develop

source TK
An efficient means to predict HIV therapeutic outcomes is critically needed.

Conventional statistical models based on regression analysis cannot longitudinally follow patient therapeutic profiles.

We had developed neural networks to predict HIV morbidity and mortality. (JAMIA 2001, 2002; ACL 2002)
What is a Neural Network?

An information technology based on the way neurons in the brain collectively process information

- The human brain: a Biological Neural network.
What is a Neural Network?

- Brief description [1]:
  - a parallel multiprocessor system
  - simple processing elements
  - a high degree of interconnection
  - simple scalar messages
  - adaptive interaction between elements
What is a Neural Network?

- Some applications examples:
  - **Static:**
    - Car driving (ALVINN project)
    - Face recognition
  - **Temporal:**
    - Speech recognition/synthesis
    - Voice recognition
    - Music synthesis
NEURAL NETWORK DESIGN

Input Layer: $v_{ij}$

Hidden Layer

Output Layer: $w_{ij}$

Morbidity

Mortality
Receiver Operating Characteristics (ROC) Curve

ROC Analysis performed on morbidity prediction from HIV+ to AIDS. Neural Network performance compared to Cox Regression modeling. Neural Network outscored Cox Regression in predictability with an area under the curve 0.888 vs 0.760 respectively.
NEURAL NETWORK DESIGN

Baseline

Input Layer

Hidden Layer

Output Layer

Ist Time Point

CD3+
CD4+
CD8+
CD28+
CD38+

Input Layer

Hidden Layer

Output Layer
Fuzzy Set Theory a.k.a. Fuzzy Logic:

An information technology based on the use of approximate information and uncertainty to generate decisions in a manner similar to human reasoning.
Structure of ANN models

- **Feed Forward Back Propagation (FFBP) ANN** (structure used in our previously published work)

- **Elman ANN** (used in the present work)

  Elman ANN is a time-dependent structure based on Feed Forward Back-Propagation. The major difference is the context layer (marked) which processes patients' history and "remembers" individual patients' patterns of responses. Follow-up of progression is thus facilitated.

Adapted from Neuro Solutions Demo
Training of the Time-Dependent ANN while following the over-time progression of immune markers (CD4%, CD8%, etc). Training is achieved at a minimal number of iterations where training and cross-validation curves meet. Even when computation of weights is perturbed, the ANN reaches optimum training conditions shortly afterwards.

During Training, the predicted values of immune variables approximate the "known" inputs i.e. the cohort’s immune variables whose progression over time is followed. An example of good approximation for selected variables is provided.

Training and Cross-Validation curves. Training of the ANN stops where and when the two curves intersect.

Adapted from Neuro Solutions Demo
Objective

To develop a neural network prediction model by incorporating time-dependent neural network structures to improve the accuracy of prediction of antiretroviral drug failure following an initial period of treatment success.
**EARTH Cohort**
The master database hosting the Electronic Anti-Retroviral THerapy cohort (EARTH) is still being updated. Participating clinics are from Canada (4), Greece (1), Cyprus (1), India (2) and Congo (1).

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients registered in cohort</strong></td>
<td>2565</td>
<td>2308</td>
<td>257</td>
</tr>
<tr>
<td><strong>Patients’ age (Range)</strong></td>
<td>14-85</td>
<td>16-85</td>
<td>14-75</td>
</tr>
<tr>
<td><strong>Number of deaths as of the establishment of the individual patient population groups</strong></td>
<td>728</td>
<td>662</td>
<td>66</td>
</tr>
<tr>
<td><strong>Number of patients on Anti-Retrovirals today</strong></td>
<td>935</td>
<td>813</td>
<td>122</td>
</tr>
<tr>
<td><strong>Length of treatment (first to most recent visit - Range only)</strong></td>
<td>6 mos - 16 yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Number of co-infected patients (HBV/HCV)</strong></td>
<td>6%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
EARTH Cohort

- Participating
- To be initiated
The Libyan AIDS crisis and a miscarriage of justice
Electronic Anti-Retroviral Treatment History Cohort

Dr. George Fanes
1st IKA Hospital
Internal Medicine Clinic
Greece

Earth Database User's Guide
Version 1.2
Earth Database Important Information

The CD enclosed in your binder contains the folder entitled: “Earth Database Panos”. The CD and its contents is read-only protected. You must first make a copy of the folder on your computer and then modify the attributes of each file.

1. How to modify the file attributes

Once the copy is done, open the folder “Earth Database Panos”. You will find the following 2 files:

EarthCohort2.mdb
This is the database containing your data in Access 2000 version. A version in Access 97 is also available upon request.

Earth2.mdw
This is the working group information file. The database is linked to this working group. If you are not joined to this working group you will not be able to have access to the database.

Right-click on each file and select ‘Properties’, uncheck the Read-only attributes and click ‘Apply’.
2. How to connect to the working group information file (cont)... 

If you are using Microsoft Office 2002, 2003 or XP

1. Open Microsoft Access 
2. The Workgroup Administrator is accessible through Tools/Security/Workgroup Administrator 
3. In the Workgroup Administrator dialog box, click Join.

4. Type the path and the name of the workgroup information file (ex: D:\Earth2.mdw) and then click OK or click Browse and then use the “Select Workgroup Information File” dialog box to locate the workgroup information file.

5. The following message confirms the connection.

This operation must be done on every computer that will have access to the database.

A logon name is provided with this working group information file. 
You are the owner of the database and you are a member of the admin group.

- **logon name:** gpanes
- **logon password:** 12345678
- **permission:** all

For security purposes you should change this password:

Tools Menu / Security / User and group accounts / Change Logon Password
Main menu of the Earth database

Two keys are very important to ensure relationships in your database

1. **Patient unique identification as “Patient No”**

   The first number represents the site (total 6 digit number)
   
   2 = Greece / Dr. George Pappas

![Diagram of patient information system]
Earth Database Important Information

2. **Sample unique identification as “Sample ID”**
   The first number represents the site (total 8 digit number)

   ![Sample ID Register](image)

   **Examples:**
   Sample ID: “20000000”
   “20000001”
   “20000002”

   These two numbers, “Patient No” and “Sample ID”, will be critical to the use of the database. It is important to be familiar with their use.

   **Do not remove these two default values:** Patient No “410000” and Sample ID “40000000”

3. **View of the relationship of the Earth Cohort Database**

   You can view the relationships using Access toolbar
   Tools: => Relationship...
1.0 Create a new “Patient No”

Patient unique identification as “Patient No”

Start from the Main Menu:

Select “Demographics” option and open the form using the open form button.

The “Patient References” form will open. Use the “Patient Name” combo box to verify if the patient already exists in the database.

If the patient does not exist, click “New Patient” and a table showing a complete list of patients will open.

The record selector allows you to navigate in the table.
### Summary Report

#### Biochemistry

<table>
<thead>
<tr>
<th>Date</th>
<th>BUN</th>
<th>Cr</th>
<th>Etc</th>
<th>Amul</th>
<th>Cr</th>
<th>LDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>01-Feb-07</td>
<td>3</td>
<td>60</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>01-Jan-07</td>
<td>3</td>
<td>60</td>
<td></td>
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<td></td>
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</table>

#### Liver Function

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<tr>
<th>Date</th>
<th>DBIL</th>
<th>AST</th>
<th>ALT</th>
<th>GGT</th>
<th>BUN</th>
<th>ALB</th>
<th>Albumen</th>
<th>INR</th>
<th>Fibrinogen</th>
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<tbody>
<tr>
<td>01-Feb-07</td>
<td></td>
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</table>

#### Metabolic

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<thead>
<tr>
<th>Date</th>
<th>TProt</th>
<th>Albumen</th>
<th>Chol</th>
<th>Trig</th>
<th>HDL</th>
<th>LDL</th>
<th>Glucose</th>
<th>HbA1c</th>
<th>Cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>01-Feb-07</td>
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</table>

#### Hematology

<table>
<thead>
<tr>
<th>Date</th>
<th>WBC</th>
<th>RBC</th>
<th>Hgb</th>
<th>Hct</th>
<th>MCV</th>
<th>PLT</th>
<th>Lymph</th>
<th>Neutro</th>
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</thead>
<tbody>
<tr>
<td>01-Feb-07</td>
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</tr>
</tbody>
</table>

*Wednesday May 15, 2007*
Institute of Medical Education and Research
Department of Internal Medicine
Chandigarh
India
Phone: 91 172 2704 528

Rash History

<table>
<thead>
<tr>
<th>MRN</th>
<th>Simple ID</th>
<th>Rash Reaction</th>
<th>Date Start</th>
<th>Date Stop</th>
<th>Duration</th>
<th>Time to onset</th>
<th>Description</th>
<th>Intensity</th>
<th>Med Causing Rash</th>
</tr>
</thead>
</table>

Chat:
Mr. Singh: Hello Dr. Tsoukas. Good morning.
Chris Tsoukas: Please point to where you have your rash on your face.
The Postgraduate Institute of Medical Education and Research
Chandigarh
EARTH Cohort

- G. Hatzakis, PhD
  - Los Angeles, USA
- M. Mathur, D. Cutler
  - Montreal, Canada
- J. Gill, MD
  - Calgary, Canada
- C. Kovacs, MD
  - Toronto, Canada
- H. Loemba, MD
  - Moncton, Canada
- G. Panos, MD
  - Athens, Greece
- I. Demetriades, MD
  - Nicosia, Cyprus
- A. Wanchu, MD
  - Chandigahr, India
- J. K. Maniar
  - Mumbai, India
- R. Taty-Taty
  - Brazzaville, Congo
- A. K. Patel
  - Ahmedabad, India
- R. Caesar
  - Fort de France, Martinique
- M. El Turki
  - Benghazi, Libya