An IT Architecture for Systems Medicine

Matthias Ganzinger, Matthias Gietzelt, Christian Karmen, Daniel Firnkorn, and Petra Knaup

Institute of Medical Biometry and Informatics
Department of Medical Informatics
Heidelberg University
CLIOMMICS

• „Clinically applicable, omics-based assessment of survival, side effects, and targets in multiple myeloma“

• Aims:
  – Integrate omics data with clinical data
  – Personalized treatment decisions
  – Enhance efficacy of therapy
  – Reduce side effects

Grant id: 01ZX1309A
Multiple Myeloma

- Malign disease of plasma cells in bone marrow
  - Incidence: 4-6 per 100,000 per year
  - Median age at diagnosis: 65-70 years
- Pathological production of monoclonal antibodies
Definition of Systems Medicine

“Systems medicine” is the application of systems biology approaches to medical research and medical practice.

Its objective is to integrate a variety of biological/medical data at all relevant levels of cellular organization using the power of computational and mathematical modelling, to enable understanding of the pathophysiological mechanisms, prognosis, diagnosis and treatment of disease.
Definition of Systems Medicine

“Systems medicine” is the application of systems biology approaches to medical research and medical practice. Its objective is to integrate a variety of biological/medical data at all relevant levels of cellular organization using the power of computational and mathematical modelling, to enable understanding of the pathophysiological mechanisms, prognosis, diagnosis and treatment of disease.
Requirements of Systems Medicine towards information technology

- Support medical research
  - understanding of pathophysiology

- Support medical practice
  - Diagnosis
  - Prognosis
  - Treatment

- Integrate data

- Modelling
Process model

- **Research Data Pool**
  - GWAS (SNP), RNA, FISH, images (MRT, CT), clinical data, etc.

- **Data Consolidation**
  - Data normalization, data selection, data compression

- **Data Correlation**
  - Combine all data sources into model

- **Model**
  - Disease specific representation of data relations

- **Data Visualization**
  - Display research data

- **Research Archive**
  - Data archive for research purposes

- **Individual Patient Data**
  - Omic-data, images, clinical data, etc.

- **Data Consolidation**
  - Data normalization, data selection, data compression

- **Data Correlation**
  - Apply model to patient data

- **Therapy**
  - Individual therapy decision

- **Data Visualization**
  - Display patient specific data

- **Clinical Archive**
  - Document diagnoses

---

**Data Privacy and Security**
- Patient related data, intellectual capital, pseudonymization, consent management, etc.

**Data Description and Data Quality**
- Audittrail, meta data
Data basis for Systems Medicine

• Omics data
  – DNA, RNA, proteome, metabolome, etc.

• Phenotype data
  – Clinical data, anamnesis, personality

• Environment
  – Lifestyle, nutrition, work conditions, etc.
Data integration example: Tumor classification

Data source A
T
22

Data source B
Data source C

T-Kat
2b

Harmonize data

Integrated data basis
KTKAT:T2B

T-Category

imbi
IT Architecture for Systems Medicine

<table>
<thead>
<tr>
<th>Research data warehouse</th>
<th>Omics data store</th>
<th>Layer 1: Data representation</th>
</tr>
</thead>
<tbody>
<tr>
<td>i2b2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generic case extractor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Research interface (case data export, e.g. R, SAS)</th>
<th>Parameter selection engine</th>
<th>Case-based reasoning engine</th>
<th>Classification and regression module</th>
<th>Omics pipeline</th>
<th>Layer 2: Decision support</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Parameter selection engine</td>
<td>Case-based reasoning engine</td>
<td>Classification and regression module</td>
<td>Omics pipeline</td>
<td>Layer 2: Decision support</td>
</tr>
<tr>
<td></td>
<td></td>
<td>jColibri/cbr:works</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical user interface / reports engine (portal, GEP-R, etc.)</th>
<th>Layer 3: User interface</th>
</tr>
</thead>
</table>

Research user

Clinical user

Heidelberg University Hospital

IMBI
Layer 1: Data representation

- Data are harmonized and organized
- Primary data base system: research data warehouse (RDW)
- Case-oriented export of patient data for research and decision support
- Separate handling of omics data
Layer 2: Decision support

- Modelling based on data layer
- Analysis of data sets for parameters associated with endpoints like
  - overall survival
  - progression free survival
- Feature selection
- Omics pipeline

<table>
<thead>
<tr>
<th>research data warehouse l2b2</th>
<th>omics data store</th>
<th>layer 1: data representation</th>
</tr>
</thead>
<tbody>
<tr>
<td>generic case extractor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>research interface (case data export, e.g. R, SAS)</td>
<td>parameter selection engine</td>
<td>layer 2: decision support</td>
</tr>
<tr>
<td></td>
<td>case-based reasoning engine</td>
<td>classification and regression module</td>
</tr>
<tr>
<td></td>
<td>jColibri/cb:works</td>
<td>omics pipeline</td>
</tr>
<tr>
<td></td>
<td>clinical user interface / reports engine (portal, GEP-R, etc.)</td>
<td>layer 3: user interface</td>
</tr>
</tbody>
</table>

- Different approaches
  - case-based reasoning
  - Semantic networks
- Systems biology models
  - SBML engine
- Inclusion of external knowledge
Layer 3: User interface

- Suitable visualization for clinical use
- Comprehensible display of dependencies
- Generation of reports
- Consideration of clinical time constraints

**Research Interface**
- Analysis of cohorts
- Export for statistical software (R, SAS, etc.)
Discussion: Existing data

• Collected for a specific purpose
  – Diagnosis
  – Therapy control
  – Clinical trials

• Can these data be used for systems medicine?
• Do we have the right data?
Discussion

• Complex IT requirements

• Flexible architecture
  – Data sources
  – Models
  – External knowledge

• Components are replaceable