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VO 709.049 Medical Informatics  
14.10.2015 11:15-12:45

## Lecture 01 Introduction

### Computer Science meets Life Sciences: Challenges and Future Directions

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<http://hci-kdd.org/biomedical-informatics-big-data>

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### Reading on Paper or on any electronic device

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### Slide 0-1: Overview – Roadmap through this Course

- 01. Intro: Computer Science meets Life Sciences, challenges, future directions
- 02. Fundamentals of Data, Information and Knowledge
- 03. Structured Data: Coding, Classification (ICD, SNOMED, MeSH, UMLS)
- 04. Biomedical Databases: Acquisition, Storage, Information Retrieval and Use
- 05. Semi structured , weakly structured data and unstructured information
- 06. Multimedia Data Mining and Knowledge Discovery
- 07. Knowledge and Decision: Cognitive Science & Human-Computer Interaction
- 08. Biomedical Decision Making: Reasoning and Decision Support
- 09. Interactive Information Visualization and Visual Analytics
- 10. Biomedical Information Systems and Medical Knowledge Management
- 11. Biomedical Data: Privacy, Safety and Security
- 12. Methodology for Info Systems: System Design, Usability & Evaluation

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### Keywords of Lecture 01

- Big Data
- Life
- Proteins – DNA & RNA – Cell – Tissue – Organ – Cardiovascular Systems
- Medicine – Informatics – Computer
- Personalized Medicine
- Translational Informatics – Data Integration
- Open Medical Data
- Biomarker Discovery

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### Learning Goals

- At the end of this first lecture you will ...
- ... be fascinated to see our world in data;
- ... have a basic understanding of the building blocks of life;
- ... be familiar with some differences between Life Sciences and Computer Sciences;
- ... be aware of some possibilities and some limits of Biomedical Informatics;
- ... have some ideas of some future directions of Biomedical Informatics;

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### Advance Organizer (1/2)

- **Bioinformatics** = discipline, as part of biomedical informatics, at the interface between biology and information science and mathematics; processing of biological data;
- **Biomarker** = a characteristic (e.g. body-temperature (fever) as a biomarker for an infection, or protein measured in the urine) as an indicator for normal or pathogenic biological processes, or pharmacologic responses to a therapeutic intervention;
- **Biomedical data** = compared with general data, it is characterized by large volumes, complex structures, high dimensionality, evolving biological concepts, and insufficient data modeling practices;
- **Biomedical Informatics** = 2011-definition: similar to medical informatics but including the optimal use of biomedical data, e.g. from genomics, proteomics, metabolomics;
- **Classical Medicine** = is both the science and the art of healing and encompasses a variety of practices to maintain and restore health;
- **Genomics** = branch of molecular biology which is concerned with the structure, function, mapping & evolution of genomes;
- **Medical Informatics** = 1970-definition: "... scientific field that deals with the storage, retrieval, and optimal use of medical information, data, and knowledge for problem solving and decision making";
- **Metabolomics** = study of chemical processes involving metabolites (e.g. enzymes). A challenge is to integrate proteomic, transcriptomic, and metabolomic information to provide a more complete understanding of living organisms;
- **Molecular Medicine** = emphasizes cellular and molecular phenomena and interventions rather than the previous conceptual and observational focus on patients and their organs;

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**Advance Organizer (2/2)**

- **Omics data** = data from e.g. genomics, proteomics, metabolomics, etc.
- **Pervasive Computing** = similar to ubiquitous computing (Ubicomp), a post-desktop model of Human-Computer Interaction (HCI) in which information processing is integrated into every-day, miniaturized and embedded objects and activities; having some degree of "intelligence";
- **Pervasive Health** = all unobtrusive, analytical, diagnostic, supportive etc. information functions to improve health care, e.g. remote, automated patient monitoring, diagnosis, home care, self-care, independent living, etc.;
- **Proteome** = the entire complement of proteins that is expressed by a cell, tissue, or organism;
- **Proteomics** = field of molecular biology concerned with determining the proteome;
- **P-Health Model** = Preventive, Participatory, Pre-emptive, Personalized, Predictive, Pervasive (= available to anybody, anytime, anywhere);
- **Space** = a set with some added structure;
- **Technological Performance** = machine "capabilities", e.g. short response time, high throughput, high availability, etc.
- **Time** = a dimension in which events can be ordered along a time line from the past through the present into the future;
- **Translational Medicine** = based on interventional epidemiology; progress of Evidence-Based Medicine (EBM), integrates research from basic science for patient care and prevention;
- **Von-Neumann-Computer** = a 1945 architecture, which still is the predominant machine architecture of today (opp.: Non-Vons, incl. analogue, optical, quantum computers, cell processors, DNA and neural nets (*in silico*));

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**Acronyms/Abbreviations in Lecture 01**

- AI = Artificial Intelligence
- AL = Artificial Life
- CPG = Clinical Practice Guideline
- CPOE = Computerized physician order entry
- CMV = Controlled Medical Vocabulary
- DEC = Digital Equipment Corporation (1957-1998)
- DNA = Deoxyribonucleic Acid
- EBM = Evidence Based Medicine
- EPR = Electronic Patient Record
- GBM = Genome Based Medicine
- GC = Gas Chromatography
- GPM = Genetic Polymorphism
- HCI = Human-Computer Interaction
- LC = Liquid Chromatography
- LNCS = Lecture Notes in Computer Science
- MS = Mass Spectrometry
- mRNA = Messenger RNA
- NGC = New General Catalogue of Nebulae and Star clusters in Astronomy
- NGS = Next Generation Sequencing
- NMR = Nuclear Magnetic Resonance
- PDB = Protein Data Base
- PDP = Programmable Data Processor (mainframe)
- PPI = Protein-Protein Interaction
- RFID = Radio-frequency identification device
- RNA = Ribonucleic Acid
- SNP = Single Nucleotide Polymorphism
- TNF = Tumor Necrosis Factor
- TQM = Total Quality Management

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**Key Problems**

- **Zillions** of different biological species (humans, animals, bacteria, virus, plants, ...);
- Enormous **complexity** of the medical domain [1];
- **Complex**, heterogeneous, high-dimensional, big data in the life sciences [2];
- Limited **time**, e.g. a medical doctor in a public hospital has only 5 min. to make a decision [3];
- Limited **computational power** in comparison to the complexity of life (and the natural limitations of the Von-Neumann architecture, ...);

1. Patel VL, Kahol K, & Buchman T (2011) Biomedical Complexity and Error. *J. Biomed. Inform.*, 44(3):387-389.  
 2. Holzinger A, Dehmer M, & Jurisica I (2014) Knowledge Discovery and interactive Data Mining in Bioinformatics - State-of-the-Art, future challenges and research directions. *BMC Bioinformatics* 15(S6):1.  
 3. Gigerenzer G (2008) Gut Feelings: Short Cuts to Better Decision Making (Penguin, London).

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**Slide 1-1: Our World in Data (1/2) – Macroscopic Structures**

# What is the challenge ?

ESO, Atacama, Chile (2011)

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**Excursus: Two thematic mainstreams in dealing with data ...****Time**

e.g. Entropy

**Space**

e.g. Topology

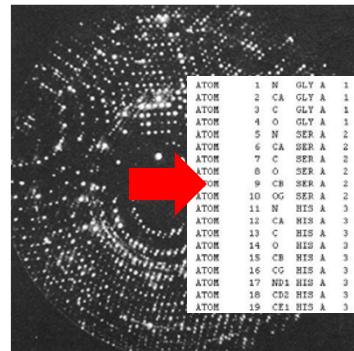


Dali, S. (1931) The persistence of memory

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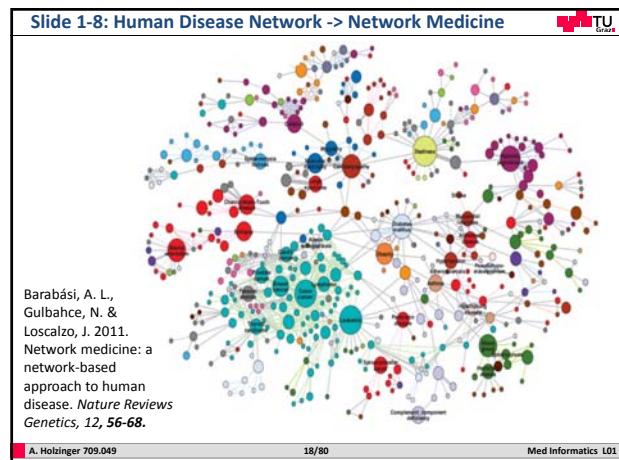
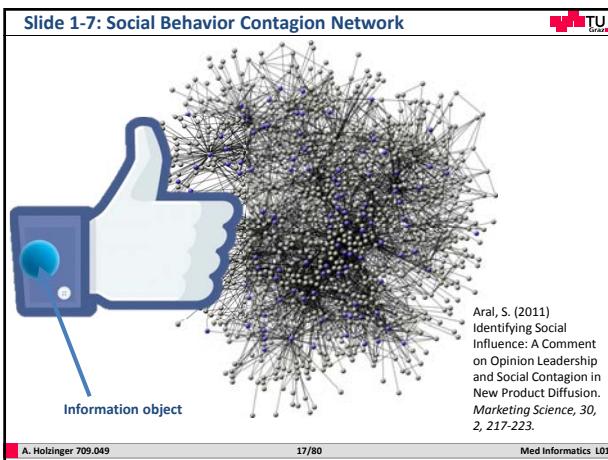
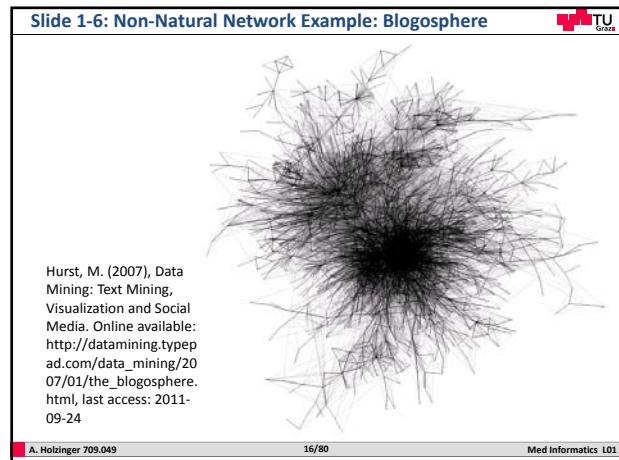
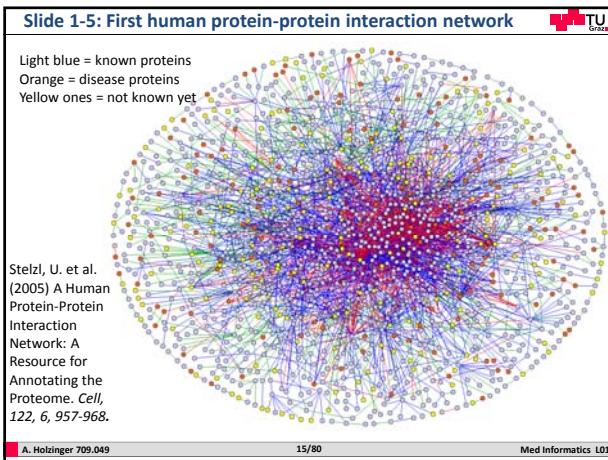
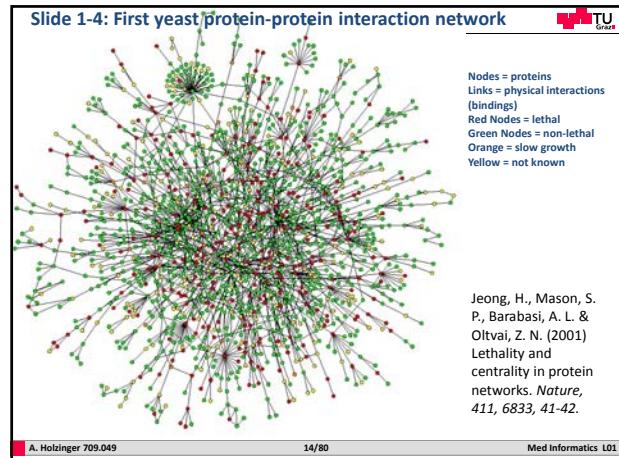
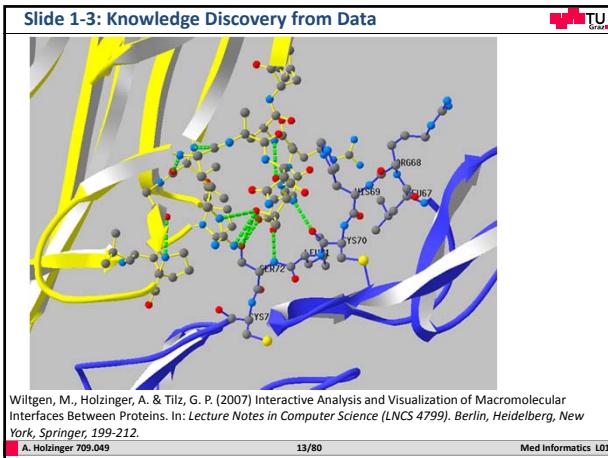
**Slide 1-2: Our World in Data (2/2) – Microscopic Structures**

Wiltgen, M. & Holzinger, A. (2005) Visualization in Bioinformatics: Protein Structures with Physicochemical and Biological Annotations. In: *Central European Multimedia and Virtual Reality Conference*. Prague, Czech Technical University (CTU), 69-74

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**Excusus: On the question of "what is information?"**

$$\left( -\frac{\hbar^2}{2m} \Delta + U(\vec{r}, t) \right) \psi(\vec{r}, t) = i\hbar \frac{\partial}{\partial t} \psi(\vec{r}, t)$$

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**Slide 1-9 Living things are able ...**

- to reproduce ...
- to grow ...
- to evolve ...
- to self-replicate ...
- to generate/utilize energy ...
- to process information ...

Schrödinger, E. (1944) *What Is Life? The Physical Aspect of the Living Cell*. Dublin Institute for Advanced Studies.

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**Slide 1-10: Life is complex information**

Lane, N. & Martin, W. (2010) The energetics of genome complexity. *Nature*, 467, 7318, 929-934.

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**Slide 1-11 Building Blocks of Life - Overview**

Level 4: The cell and its organelles	Level 3: Supramolecular complexes	Level 2: Macromolecules	Level 1: Monomeric units
Human eye	DNA	Nucleotides	Amino acids
Light microscope	Chromosome	Protein	Cellulose
Electron microscope	Plasma membrane	Sugars	Sugars
Special	Cell wall		

1m 1mm 1 μm 1nm 100 pm

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**Slide 1-12: The Dogma of Molecular Biology**

Crick, F. 1970. Central Dogma of Molecular Biology. *Nature*, 227, (5258), 561-563.

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**Slide 1-13 Amino-acid > Protein-chain > Protein-structure**

Primary structure:  $\text{H}_2\text{N}-\text{CH}(\text{R})-\text{COOH}$  (Amino group, Carboxyl group)

Secondary structure:  $\text{H}_2\text{N}-\overset{\text{R}_1}{\text{C}}(\text{O})-\text{NH}-\overset{\text{R}_2}{\text{C}}(\text{O})-\text{NH}-\text{CH}(\text{R})-\text{COOH}$  (Peptide bond)

Tertiary structure:  $\text{H}_2\text{N}-\overset{\text{R}_1}{\text{C}}(\text{O})-\text{NH}-\overset{\text{R}_2}{\text{C}}(\text{O})-\text{NH}-\text{CH}(\text{R})-\text{COOH}$  (Polypeptide chain)

Quaternary structure: Assembled subunits

Gromiha, M. 2010. *Protein Bioinformatics*, Amsterdam, Elsevier.

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**Slide 1-14 Tertiary Structure of a Protein**

The diagram shows a complex protein structure composed of multiple domains. It highlights various secondary structural elements: alpha helices (represented by coiled yellow lines) and beta sheets (represented by parallel red and blue lines). Some regions are labeled as 'Antiparallel beta sheet'. The overall arrangement is described as the 'Tertiary structure'.

Shehu, A. & Kavraki, L. E. 2012. Modeling structures and motions of loops in protein molecules. *Entropy*, 14, (2), 252-290.

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**Slide 1-15 Protein Analytics**

(a) Schematic of X-ray crystallography: An X-ray source emits X-rays onto a protein crystal, which diffracts them. These diffracted beams are detected by a detector (e.g., a CCD camera). (b) Two-dimensional gel electrophoresis (2D PAGE) image showing protein bands. (c) Denaturing high-performance liquid chromatography (HPLC) chromatograms showing peaks corresponding to different protein species.

Rabilloud, et al. 2010. Two-dimensional gel electrophoresis in proteomics: past, present and future. *Journal of proteomics*, 73, (11), 2064-2077.

Xiao, W. Z. & Oefner, P. J. 2001. Denaturing high-performance liquid chromatography: A review. *Human Mutation*, 17, (6), 439-474.

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**Slide 1-16: Comparison of some current Methods**

Technology	Sensitivity	Subcellular resolution	Cellular resolution	Minimally invasive?	Live cells?	Real time?
Genetically encoded transensors	Nanomolar to millimolar	Nanometer to millimeter	Yes	Yes	Yes	Yes
MRI	Mid-micromolar to millimolar (213)	No	Yes	Yes	Yes	Yes
PET	1–40 Bq mm <sup>-2</sup> (18)	No	No	No	Yes	Yes
X-ray synchrotron	<1 mg kg <sup>-1</sup> tissue (transit metals) (204)	No	Yes	No	No	No
SIMS	<1 fmol (67)	Yes	Yes	No	No	No
MALDI or TOF imaging	<1 ppm	Yes	50–300 μm (MALDI) 1–2 μm (TOF)	No	No	No
NIMS imaging	Yoctomolar (85)	No	50–300 μm	No	No	No
Mass spectrometry	Yoctomolar	No <sup>2</sup>	Yes	No	No	No
Raman	50 μM (70)	Yes	Yes	Yes	Yes	Yes

Okumoto, S., Jones, A. & Frommer, W. B. 2012. Quantitative imaging with fluorescent biosensors. *Annual review of plant biology*, 63, 663–706.

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**Slide 1-17 Enzymes**

Klibanov, A. M. 2001. Improving enzymes by using them in organic solvents. *Nature*, 409, (6817), 241-246.

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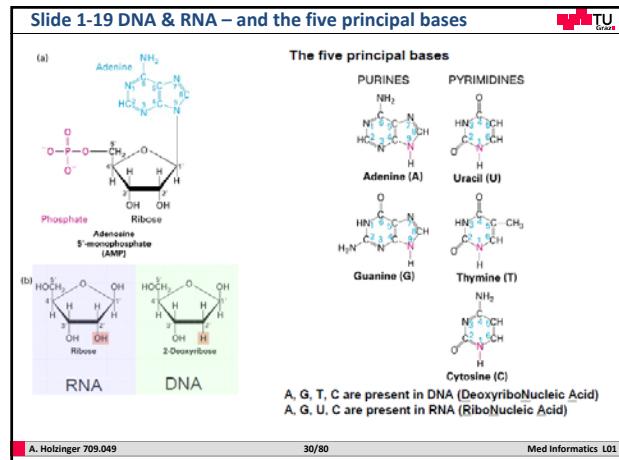
**Slide 1-18 DNA-RNA-Proteins**

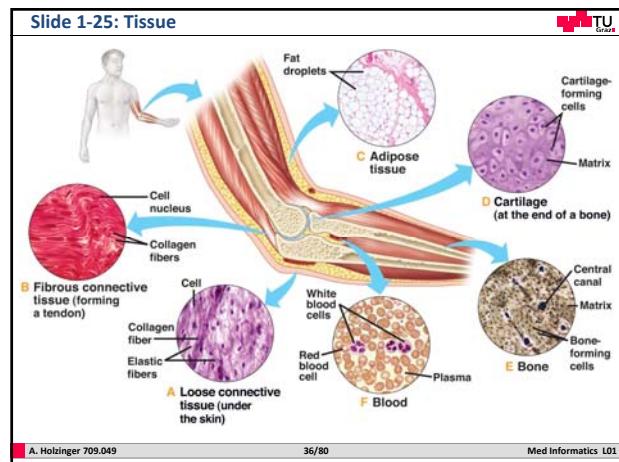
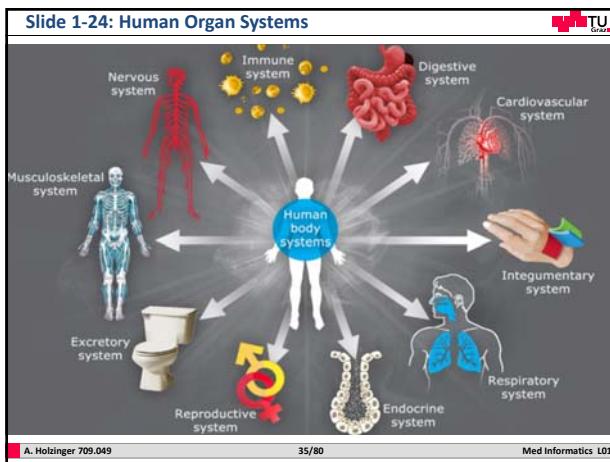
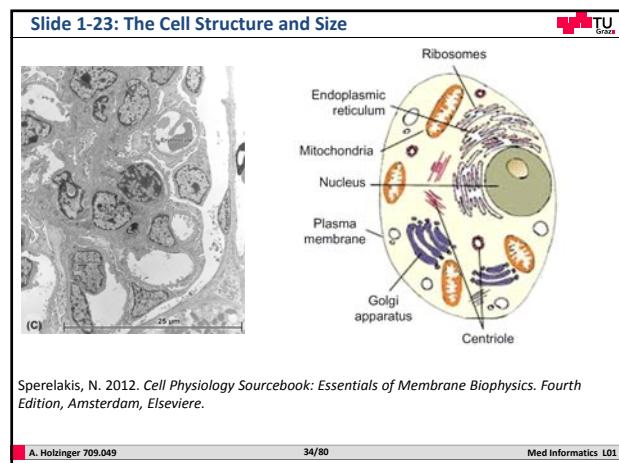
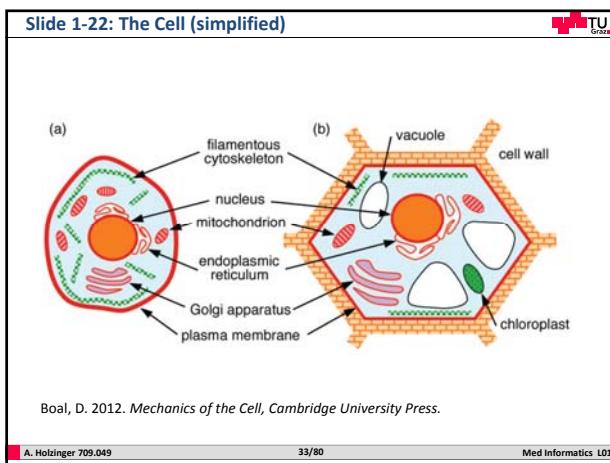
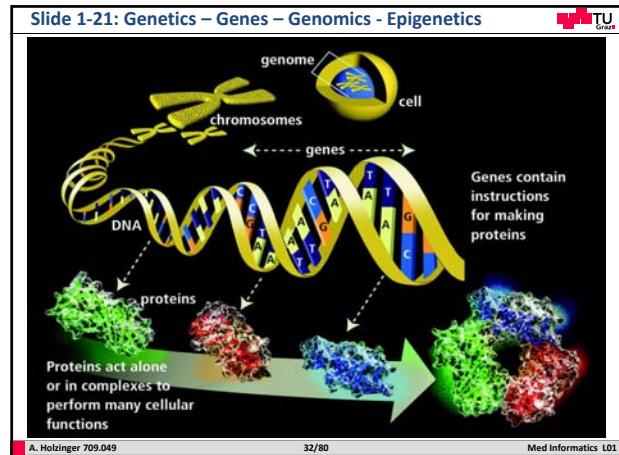
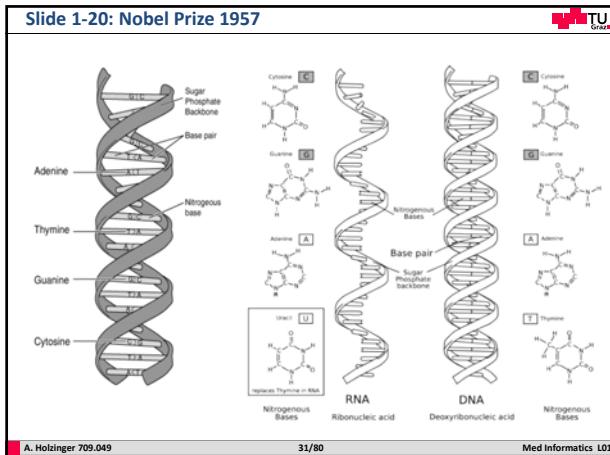
The DNA, the RNA and the proteins are the three major macromolecules essential for all known forms of life.

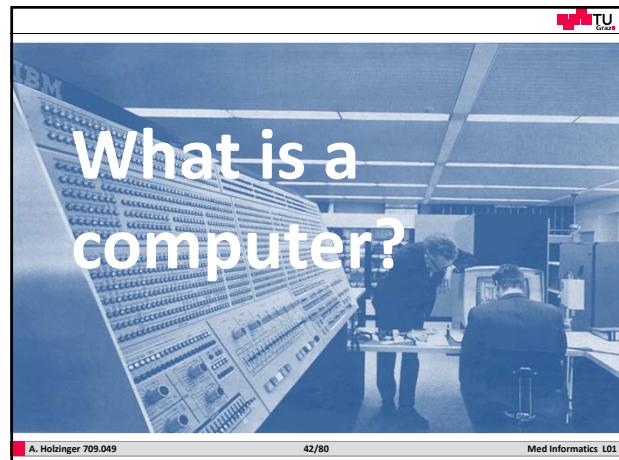
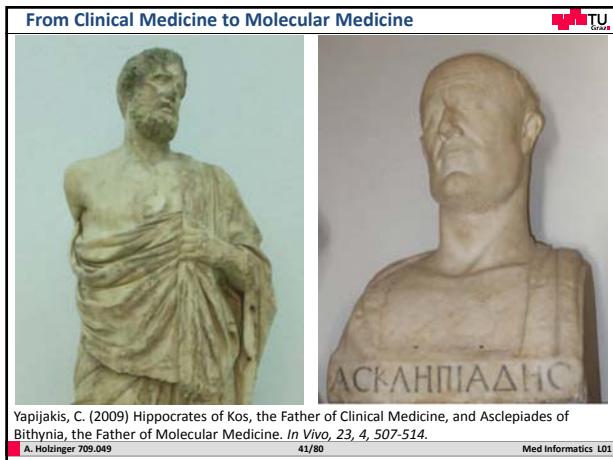
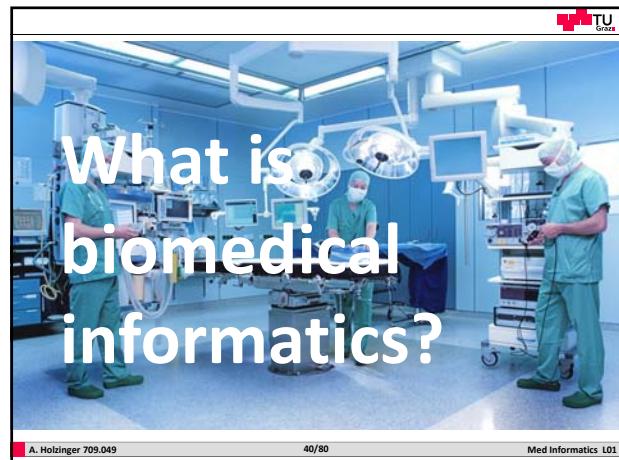
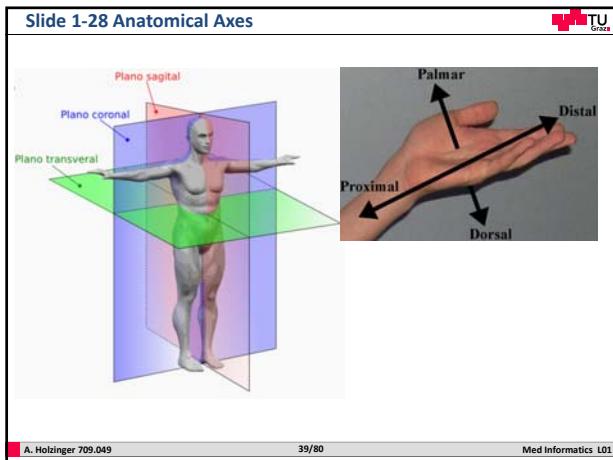
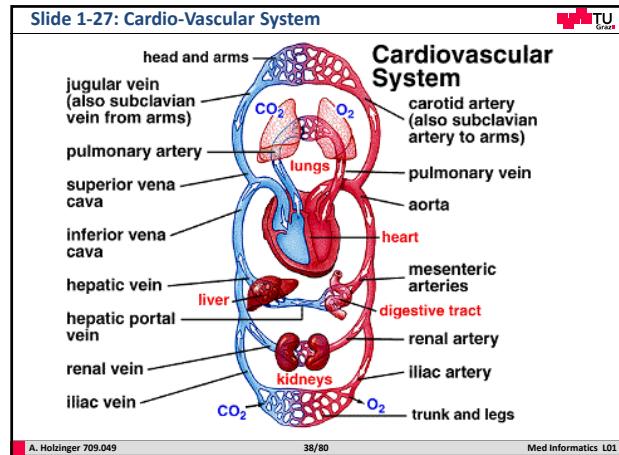
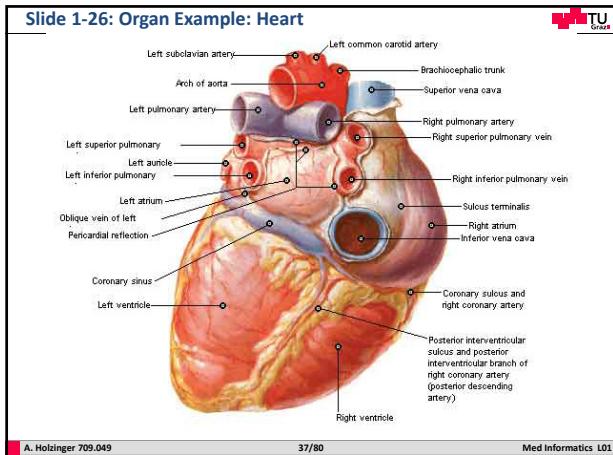
The diagram illustrates the flow of genetic information: DNA contains a promoter and enhancers that regulate transcription. Transcription produces pre-mRNA, which is then spliced to remove introns and joined back together to form mRNA. The mRNA then undergoes translation to produce a protein. Labels include: Promoter, Enhancers, DNA, pre-mRNA, Exon, Intron, mRNA, 5' UTR, 3' UTR, Translation, protein.

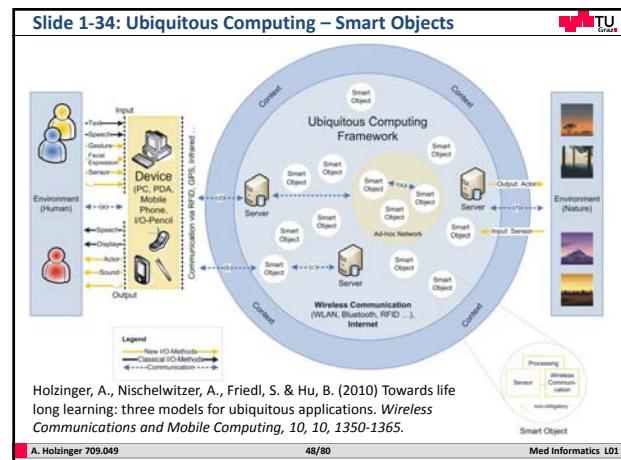
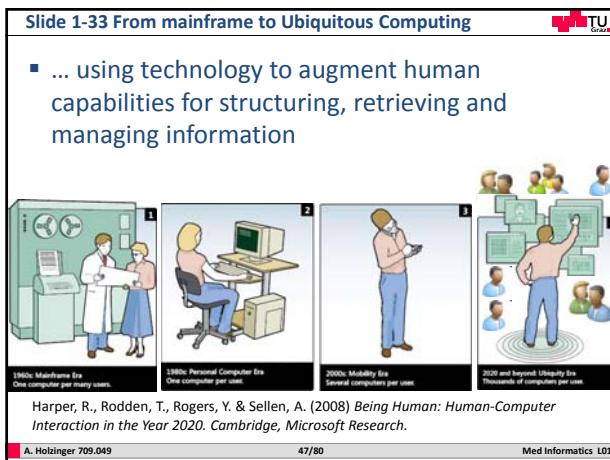
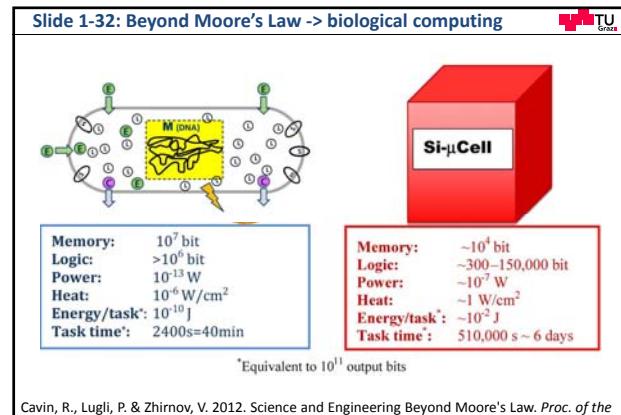
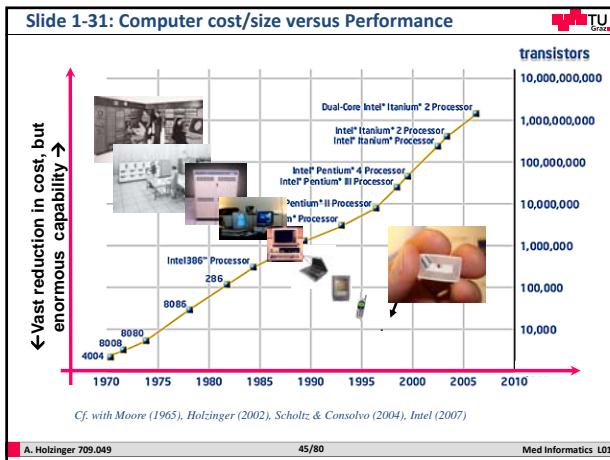
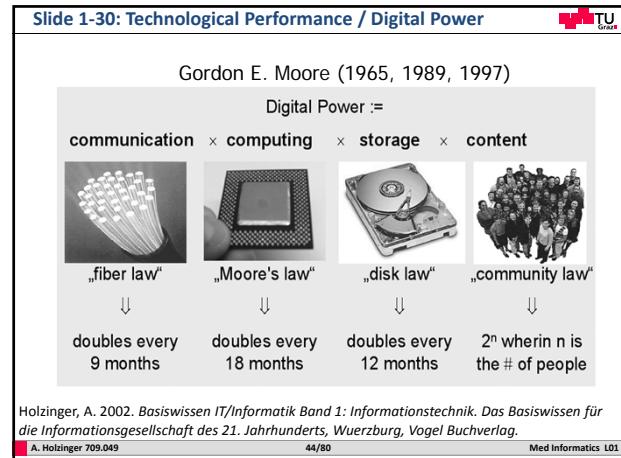
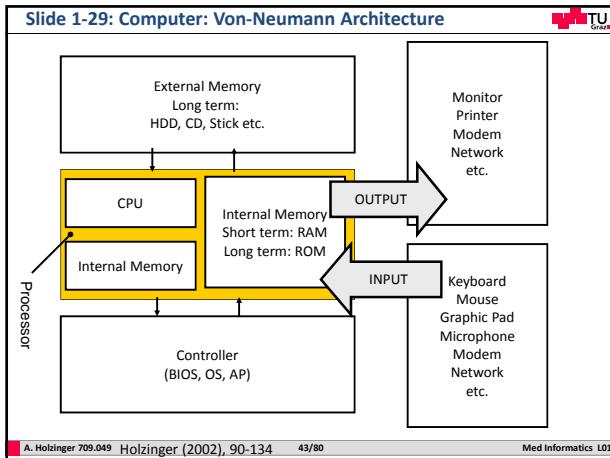
Manca, V. (2013). Infobiotics. Springer.

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**Slide 1-35 Example: Pervasive Health Computing**

Holzinger, A., Schaupp, K. & Eder-Halbedi, W. (2008) An Investigation on Acceptance of Ubiquitous Devices for the Elderly in an Geriatric Hospital Environment: using the Example of Person Tracking In: *Lecture Notes in Computer Science (LNCS 5105)*. Heidelberg, Springer, 22-29.

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**Slide 1-36: Ambient Assisted Living - pHealth**

Alagoz, F., Valdez, A. C., Wilkowska, W., Zieffe, M., Dorner, S. & Holzinger, A. (2010) From cloud computing to mobile Internet, from user focus to culture and hedonism: The crucible of mobile health care and Wellness applications. *5th International Conference on Pervasive Computing and Applications (ICPCA)*. IEEE, 38-45.

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**Slide 1-37: Pervasive Computing in the Hospital**

Holzinger, A., Schwaberger, K. & Weitlaner, M. (2005) Ubiquitous Computing for Hospital Applications: RFID-Applications to enable research in Real-Life environments *29th Annual IEEE International Computer Software & Applications Conference (IEEE COMPSAC)*, 19-20.

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**Slide 1-38: Smart Objects in the pathology**

Holzinger et al. (2005)

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**Slide 1-39 The medical world is mobile (Mocomed)**

Holzinger, A., Kosec, P., Schwantzer, G., Debevc, M., Hofmann-Wellenhof, R. & Fröhlauf, J. 2011. Design and Development of a Mobile Computer Application to Reengineer Workflows in the Hospital and the Methodology to evaluate its Effectiveness. *Journal of Biomedical Informatics*, 44, 968-977.

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**Slide 1-40: 1970 - Turning Knowledge into Data**

Photo by Institute of Medical Informatics, Graz (1970)

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**Slide 1-41: 4 decades from Medical to Biomedical Informatics**



- 1970+ Begin of **Medical Informatics**
  - Focus on data acquisition, storage, accounting (typ. "EDV")
  - The term was first used in 1968 and the first course was set up 1978
- 1985+ Health Telematics
  - Health care networks, Telemedicine, CPOE-Systems etc.
- 1995+ Web Era
  - Web based applications, Services, EPR, etc.
- 2005+ Ambient Era
  - Pervasive & Ubiquitous Computing
- 2010+ Quality Era – **Biomedical Informatics**
  - Information Quality, Patient empowerment, individual molecular medicine, End-User Programmable Mashups

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**Slide 1-42: 2010 - Turning Data into Knowledge**




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**Slide 1-43: Definition of Biomedical Informatics**



- **Biomedical informatics (BMI)** is the interdisciplinary field that studies and pursues the effective use of biomedical data, information, and knowledge for scientific problem solving, and decision making, motivated by efforts to improve human health

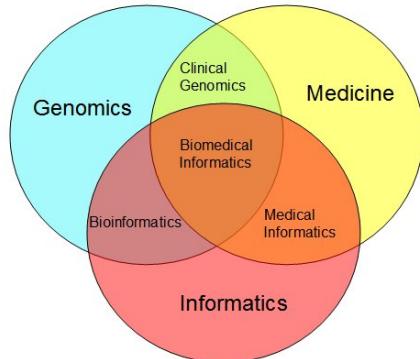
Shortliffe, E. H. (2011). Biomedical Informatics: Defining the Science and its Role in Health Professional Education. In A. Holzinger & K.-M. Simonic (Eds.), *Information Quality in e-Health. Lecture Notes in Computer Science LNCS 7058* (pp. 711-714). Heidelberg, New York: Springer.

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**Slide 1-44: Computational Sciences meet Life Sciences**

<http://www.bioinformaticslaboratory.nl/twiki/bin/view/BioLab/EducationMIK1-2>

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**Slide 1-45 In medicine we have two different worlds ...**



**Our central hypothesis:**  
**Information bridges this gap**

Holzinger, A. & Simonic, K.-M. (eds.) 2011. *Information Quality in e-Health. Lecture Notes in Computer Science LNCS 7058*, Heidelberg, Berlin, New York: Springer.

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**Slide 1-46 Information Quality as the hiatus theoreticus ...**



Holzinger, A. & Simonic, K.-M. (Eds.) (2011) *Information Quality in e-Health. Lecture Notes in Computer Science LNCS 7058*, Heidelberg, New York, Springer.

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Where is the problem in building this bridge

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Slide 1-47 What are the problems?

**Volume of Data**

**High Dimensional**

**Non-Standardized**

**Weakly-structured**

Holzinger, A. (2011) Weakly Structured Data in Health-Informatics. In: INTERACT 2011, Lisbon, IFIP, 5-7.

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Slide 1-48 Big Data – We need machine intelligence ...

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Slide 1-49 Biomed. Big Data Sources (Holzinger, et al. 2014)

Scale	Collective	Individual	Tissue	Cell	Bacteria	Virus	Molecule	Atom
$10^{-12}$								

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Open Problems and Future Challenges

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Slide 1-50 A list of grand challenges by Sittig (1994)

- 1. A unified controlled medical vocabulary (CMV);
- 2. A complete computer-based patient record that could serve as a regional/national/multinational resource and a format to allow exchange of records between systems;
- 3. The automatic coding of free-text reports, patient histories, discharge abstracts, etc.;
- 4. Automated analysis of medical records, yielding
  - a) the expected (most common) clinical presentation and course and the degree of clinical variability for patients with a given diagnosis;
  - b) the resources required in the care of patients compared by diagnosis, treatment protocol, clinical outcome, location, and physician;
- 5. A uniform, intuitive, anticipating user interface;
- 6. The human genome project;
- 7. A complete three-dimensional, digital representation of the body, including the brain, with graphic access to anatomic sections, etc.;
- 8. Techniques to ease the incorporation of new information management technologies into the infrastructure of organizations so that they can be used at the bedside or at the research bench;
- 9. A comprehensive, clinical decision support system.

A. Holzinger 709.049 66/80 Med Informatics L01

**Slide 1-51 An update of the list – 20 years later**

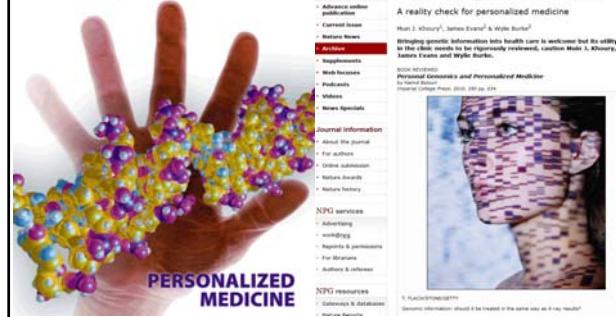
- Grand new challenges from today's perspective include:
- 10. Closing the gap between Science and Practice
- 11. Data fusion and data integration in the clinical workplace
- 12. To provide a trade-off between Standardization and Personalization
- 13. An intuitive, unified and universal, adaptive and adaptable user interface
- 14. Integrated interactive Knowledge Discovery Methods particularly for the masses of still "unstructured data"
- 15. Mobile solutions for the bedside and the clinical bench
- A consequence of 14 and 15 will be the vision of "Watson" on the Smartphone. This goal was announced by IBM for the year 2020. The problem involved are the massive unstructured clinical data sets [1]

1. Holzinger, A., Stocker, C., Ofner, B., Prohaska, G., Brabenetz, A., & Hofmann-Wellenhof, R. (2013). Combining HCI, Natural Language Processing, and Knowledge Discovery – Potential of IBM Content Analytics as an assistive technology in the biomedical domain. Springer Lecture Notes in Computer Science LNCS 7947 (pp. 13-24). Heidelberg, Berlin, New York: Springer.

A. Holzinger 709.049

67/80

Med Informatics L01

**The next big issue ...****Clinical Pharmacology & Therapeutics****nature** international weekly journal of science

Books and Arts

A reality check for personalized medicine

Hans J. Khorana, Jennifer Everett &amp; Wyeth S. Lundquist

Whether the genomic information can be exploited and its utility in the clinic needs to be rigorously reviewed, cautions Hans J. Khorana, Jennifer Everett and Wyeth S. Lundquist

Personal Genomics and Personalized Medicine

D. H. Korn et al. *Nature* 460, 620 pp. 624NPG services Advertising征订  
Marketing  
Reprints & permissions  
For libraries  
Authors & refereesNPG resources Genome & databases  
GeneBank  
Medline

T. FLACKSTEDT ET AL. Genomic information should it be treated in the same way as X-ray results?

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68/80

Med Informatics L01

**Slide 1-52 Between Standardization and Personalization**

EBM CPG

**Standardized Medicine****Person-  
alized  
Medicine****Pervasive Healthcare**

Preventive Health Integration

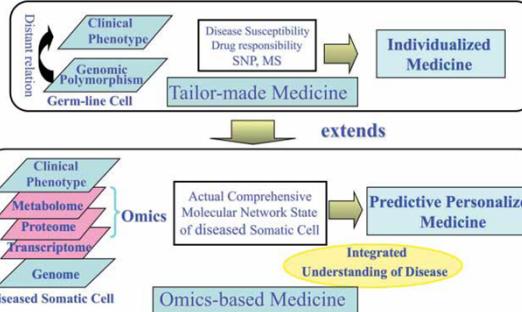
EBM = Evidence Based Medicine  
CPG = Clinical Practice Guideline  
GBM = Genome Based Medicine  
GPM = Genetic Polymorphism

Tanaka, H. (2010)

A. Holzinger 709.049

69/80

Med Informatics L01

**Slide 1-53: Towards Personalized Medicine**

Tanaka, H. (2010) Omics-based Medicine and Systems Pathology A New Perspective for Personalized and Predictive Medicine. *Methods of Information In Medicine*, 49, 2, 173-185.

A. Holzinger 709.049

70/80

Med Informatics L01

**Slide 1-54: Future p-Health Model – A 6 P's paradigm****What Kind of Healthcare Decisions Should Be Made**

**Preventive**  
Strategies that control risk factors of diseases will be implemented based on a mixture of individualised and population approaches.

**Participatory**  
Health care decision making and health information will be shared by individuals and relevant practitioners.

**Pre-emptive**  
Targets of intervention will be broadened beyond treatment response and remission to maintain and restore body health and functions.

**How Healthcare Decisions Should Be Made**

**Personalised**  
Health care decisions will be tailor-made based on individualised modelling from genomic to system levels with reference to statistical analysis of a population.

**Predictive**  
Risk of developing a disease will be constantly assessed based on the health information accumulated up-to-date.

**Pervasive**  
Health services will be available to anyone, anytime and anywhere to facilitate healthcare decisions to be made whenever necessary.

Zhang, Y. T. & Poon, C. C. Y. (2010) Editorial Note on Bio, Medical, and Health Informatics. *Information Technology in Biomedicine, IEEE Transactions on*, 14, 3, 543-545.

A. Holzinger 709.049

71/80

Med Informatics L01

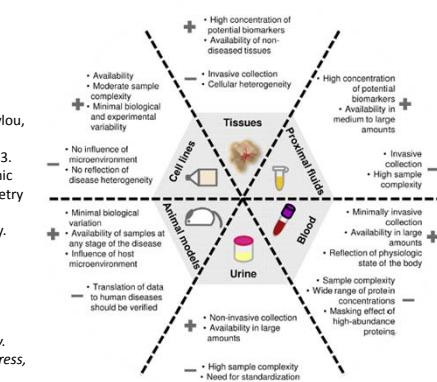
**Slide 1-55: Proteomic Samples for Biomarker Discovery**

Drabovich, A. P., Pavlou, M. P., Batruch, I. & Diamandis, E. P. 2013. Chapter 2 - Proteomic and Mass Spectrometry Technologies for Biomarker Discovery. In: Haleem, J. I. & Timothy, D. V. (eds.) *Proteomic and Metabolomic Approaches to Biomarker Discovery*. Boston: Academic Press, pp. 17-37.

A. Holzinger 709.049

72/80

Med Informatics L01



**nature**  
www.nature.com/nature  
458 | Issue no. 7234 | 5 March 2009  
**What price health?**

A. Holzinger 709.049 73/80 Med Informatics L01

**Thank you!**

A. Holzinger 709.049 74/80 Med Informatics L01

**Sample Questions**

**08** Biomarkers are measured molecules which indicate the presence of an abnormal condition within a patient, and can be a gene (e.g., SNP), protein (e.g., prostate-specific antigen), or metabolite.  Yes  No **2 total**

**06** Part of the definition of Biomedical Informatics is the ...  
 ... effective use of biomedical data.  
 ... motivation to improve computational capacities.  
 ... effort to expand the technological capabilities.  
 ... motivation to improve human health. **4 total**

**02** The Von-Neumann Architecture is the fundamental computer organization structure of nearly all of our todays computing systems (e.g. in your PC, smartphone, microwave oven, car, etc.), please roughly sketch the Von Neumann Architecture and indicate the main parts: **1-28**  
**1 each**  
**6 total**

A. Holzinger 709.049 75/80 Med Informatics L01

**References (2/5)**

- Holzinger, A. 2003. *Basiswissen IT/Informatik Band 1: Informationstechnik*. Wuerzburg, Vogel Buchverlag.
- Holzinger, A. 2003a. *Basiswissen IT/Informatik, Band 2: Informatik*. Wuerzburg, Vogel Buchverlag.
- Holzinger, A. 2003b. Finger Instinct of Mouse Touch Screens as a means of enhancing Universal Access. In: Carbonell, N. & Stephanidis, C. (eds.) *Universal Access: Theoretical Perspectives, Practice and Experience, Lecture Notes in Computer Science (LNCS) 2615*. Berlin, Heidelberg, New York: Springer, pp. 387-397.
- Holzinger, A. 2013. Human-Computer Interaction and Knowledge Discovery (HC4 KDD): What is the benefit of bringing those two fields to work together? In: Cuzzocrea, A., Iamnia, E., Kao, L. (eds.) *Methodologies and Practice for Information Systems*, Springer Lecture Notes in Computer Science (LNCS) 8127. Heidelberg, Berlin, New York: Springer, pp. 319-328.
- Holzinger, A., Basic, L., Pešić, B. & Debevc, M. 2011. Handwriting Recognition on Mobile Devices: State of the art technology, usability and business analysis. *Proceedings of the International Conference on electronic Business and Telecommunications*. Los Alamitos: IEEE, pp. 219-227.
- Holzinger, A., Basic, M. & Juraschek, L. 2012. Knowledge Discover and interactive Data Mining in Bioinformatics - State-of-the-Art, future challenges and research directions. *ICMB Bioinformatics*, 15, (50), 1-1.
- Holzinger, A., Dornig, S., Födinger, M., Valder, A. & Ziefle, M. 2010. Changes of Increasing Youth Health Awareness through Mobile Wellness Applications. In: Leitner, G., Hitz, M. & Holzinger, A. (eds.) *ICD 10 in Work and Leisure, Life and Leisure, Lecture Notes in Computer Science (LNCS) 6305*. Berlin, Heidelberg: Springer, pp. 71-81.
- Holzinger, A., Stocker, W., Wassenberger, S. & Neid, L. 2008. Design, Development and Evaluation of Online Interactive Simulation Software for Learning Human Genetics. *Elektrotechnik & Informatikstechnik (Edi)*, 125, (5), 190-196.
- Holzinger, A., Kosec, P., Schwantner, G., Debevc, M., Hofmann-Wollenhoft, R. & Fröhlich, J. 2011. Design and Development of a Mobile Computer Application to Reengineering Workflows in the Hospital and the Methodology to evaluate its Effectiveness. *Journal of Biomedical Informatics*, 44, (6), 968-977.
- Holzinger, A., Nischwitz, A., Friedl, S. & Hub, B. 2010. Towards life long learning: three models for ubiquitous applications. *Wireless Communications and Mobile Computing*, 10, (10), 1531-1542.
- Holzinger, A., Schäupp, J. & Eder-Holzinger, W. 2008. An Investigation on Acceptance of Ubiquitous Devices for the Elderly in an Geriatric Hospital Environment: using the Example of Person Tracking. In: Miesenberger, K., Klaus, J., Zajer, W. & Karshmer, A. (eds.) *Computers Helping People with Special Needs, Lecture Notes in Computer Science, LNCS 5105*. Heidelberg, Berlin: Springer, pp. 22-29.
- Holzinger, A., Schlegl, M., Pešić, B. & Debevc, M. Preferences of Handwriting Recognition Mobile Information Systems in Medicine: Improving handwriting recognition in mobile devices. *Proceedings of the International Conference on e-Business and Telecommunications, 2010 Athens (Greece)*. INSTICC, 14-21.
- Holzinger, A., Schweiger, K. & Weitlaner, M. 2005. Ubiquitous Computing for Hospital Applications: RFID-Applications to enable research in Real-Life environments. *2nd Annual Conference on Computer Science and Applications (IEEE COMPSAC 2005)*. Edinburgh (UK): IEEE, 19-20. Holzinger, A., Searle, G., Pešić, B. & Debevc, M. 2012. An Analysis of the Acceptance of a "Smart" On-line Learning System on Mobile Devices. *e-Business and Telecommunications, Communications in Computer and Information Sciences, CCS 314*. Heidelberg, Berlin, New York: Springer, pp. 356-367.
- Holzinger, A. & Simonic, K.-M. (eds.) 2011. *Information Quality in e-Health*. Lecture Notes in Computer Science LNCS 7058. Heidelberg, Berlin, New York: Springer.
- Holzinger, A., Stocker, C., Olfert, B., Prostak, C., Brabenetz, A. & Hofmann-Wollenhoft, R. 2013. Combining HCI, Natural Language Processing, and Knowledge Discovery: Potential of IBM Context Analytics as an assistive technology in the biomedical domain. *Springer Lecture Notes in Computer Science LNCS 7947*. Heidelberg, Berlin, New York: Springer, pp. 13-24.
- Holzinger, A., Stocker, C., Pešić, B. & Simonic, K.-M. 2012. On Using Entropy for Enhancing Handwriting Preprocessing. *Entropy*, 14, (11), 2324-2350.

A. Holzinger 709.049 77/80 Med Informatics L01

**References (1/5)**

- Aebischer, F. & Marin, A. 2008. Mass spectrometry-based proteomics. *Nature*, 452, (6984), 198-207.
- Aebischer, F., Marin, A., Valder, A., Wollmack, W., Zeffe, M., Dorner, & Holzinger, A. 2010. From User Focus to Culture and Hedonism - The Crucible of Mobile Health Care and Wellness Applications. *CPCAO International Conference on Pervasive Computer Applications 2010, Maribor (Slovenia)*: IEEE, 1-9.
- Aebischer, F. & Marin, A. 2009. What Proteins Govern the Folding of Protein Chains. *Science*, 31, (4096), 223-230.
- Aral, S. 2011. Identifying Social Influence: A Comment on Opinion Leadership and Social Contagion in New Product Diffusion. *Marketing Science*, 30, (2), 217-223.
- Audia, P. A., Ebner, M., Neblat, D. & Holzinger, A. 2009. Mixing Content and Endless Collaboration - Mashups: Towards Future Personal Learning Environments. In: Stephanidis, C. (ed.) *Universal Access in Human-Computer Interaction HCII, Part III: Applications and Services, Lecture Notes in Computer Science (LNCS) 5525*. Berlin, Heidelberg: Springer, pp. 14-24.
- Banerjee, S., C. James, E. Kao, & X. Li. 2011. Networked sensing: a network-based approach to human disease. *Nature Reviews Genetics*, 12, (1), 56-68.
- Barabási, A. L. & Oltvai, Z. N. 2004. Network biology: understanding the cell's functional organization. *Nature Reviews Genetics*, 5, (2), 101-113.
- Bartram, J. 2013. Activity-Based Support for Mobility and Collaboration in Ubiquitous Computing. In: Baresi, L. (ed.) *Second International Conference on Ubiquitous Computing and Ambient Intelligence (UCAI)*. Berlin, Heidelberg: Springer, pp. 1-10.
- Bianchi, D. W. 2012. From prenatal genomic diagnosis to fetal personalized medicine: progress and challenges. *Not Med.* 18, (7), 1041-1051.
- Blum, A. 2008. *Handwriting of the elderly*. Cambridge University Press.
- Bohne, A. 2008. *Handwriting of the elderly*. Cambridge University Press.
- Brophy, D. G., Burchfield, J. D., Murphy, D. L. & Tomlinson, B. S. 1972. TENEX, apaged time sharing system for the PDP-10. *Communications of the ACM*, 15, (3), 132-140.
- Bogod, S. & McNamee, M. 2003. Biomedical informatics for proteomics. *Nature*, 423, (6920), 233-237.
- Bonacina, G., Ravinder, M., Valente, P. & Wolpert, M. 2011. Science as a public enterprise: the case for open data. *The Lancet*, 377, (9778), 1633-1635.
- Brooks, R. 2001. The relationship between matter and mind. *Nature*, 409, (6818), 409-411.
- Burgin, H. J. & Weinreich, E. 2012. *Science and Engineering Beyond Moore's Law*. Proceedings of the IEEE, 100, (13), 1720-1749.
- Caron, R., Luigi, P. & Zhernov, V. 2012. *Science as a public enterprise: the case for open data*. ACM Ubiquity, 2012, [August], 1-13.
- Chirkov, G. S. 2011. Modeling loop entropy. *Methods in enzymology*, 487, 99.
- Cooper, S. B., Lowrie, B. & Sorbi, A. 2008. New Computational Models for Designing Conceptions of What is Computable. New York, Springer.
- Crisp, J. & Watson, J. 1993. Molecular structure of nucleic acids. *Nature*, 371, (6436), 563-565.
- Crick, F. & Watson, J. 1953. Molecular structure of nucleic acids. *Nature*, 171, (4356), 737-738.
- Dill, K. A., Bromberg, S., Yuz, K., Chan, H. S., Fleibig, K. M., Yeo, D. P. & Thomas, P. D. 1995. Principles of protein folding—a perspective from simple exact models. *Science*, 267, (5207), 1402-1406.
- Drabovich, A., Pavlov, M. P., Butrich, I. & Dimandriis, E. P. 2013. Chapter 2 - Proteomic and Mass Spectrometry Technologies for Biomarker Discovery. In: Holzinger, A. (ed.) *Practical Approaches to Biomarker Discovery*. Boston: Academic Press, pp. 17-37.
- Father, C. J. & Chennapragada, S. 2012. Introduction to Information quality. Bloomington (IN): AuthorHouse.
- Ge, H., Walhout, A. J. M. & Vidal, M. 2003. Integrating 'omic' applications: a bridge between genomics and systems biology. *TRENDS in Genetics*, 19, (10), 551-560.
- Guttmann, M. 2008. *Get Feeling: Smart Cuts to Better Decision Making*. London, Penguin.
- Gronlund, M. 2010. *Protein Bioinformatics*. Amsterdam, Elsevier.
- Hawkins, S. W., Petrone, R. & Atiyah, M. 1996. *The nature of space and time*. Princeton University Press Princeton.
- Hershey, A., Senger, S. & Overington, J. P. 2012. Open data for drug discovery: learning from the biological community. *Future Medicinal Chemistry*, 4, (15), 1865-1887.

A. Holzinger 709.049 76/80 Med Informatics L01

**References (3/5)**

- Hunter, L. 2009. *The Processes of Life: An introduction to molecular biology*. Cambridge (MA): MIT Press.
- Hurst, M. 2007. *Data Mining: Text Mining, Visualization and Social Media* [Online]. Available: [http://datamining.typpedia.com/data\\_mining/2007/01/the\\_blueprint.html](http://datamining.typpedia.com/data_mining/2007/01/the_blueprint.html) [Accessed 2011-05-10].
- Issaq, H. J. & Veenstra, T. D. 2013. Chapter 1 - Biomarker Discovery: Study Design and Execution. In: Haleem, J. I. & Timothy, D. V. (eds.) *Proteomic and Metabolomic Biomarker Discovery and Dissemination*. Elsevier, 1-16.
- Jacobson, J. & Holzinger, A. 2013. A Case Study: In Guzzereata, A., Kittl, C., Simos, D. E., Weißp, G. & Xu, L. (eds.) *Ubiquitous Research and Practice for Information Systems*. Heidelberg, Berlin: Springer, pp. 41-52.
- Jeong, H., Mason, S., Barabási, A. L. & Oltvai, Z. N. 2003. Lethality and centrality in protein networks. *Nature*, 411, (6833), 41-502.
- Kibar, S. & P. 2012. All Eyes on Epigenetics. *Science*, 333, (6069), 637.
- Kilbane, J. 2005. Improving enzymes by using them in organic solvents. *Nature*, 409, (6817), 241-246.
- Konarović, A. L. 1979. The variability and inaccuracy of enzymes. *Proceedings of the Roy. Soc. A*, 67, (9), 1198-1207.
- Kotter, R., Lai, A., Lai, C., Tsui, M. A., Pode, A., Bryn, M., Danes, H., Feustner, H., Gradinger, R. & Hauner, H. 2008. From Molecules to Populations. *Methods of Information in Medicine*, 47, (4), 285-292.
- Mahajan, V. & Scheibenbogen, M. E. F. 1977. The use of computers in hospitals: an analysis of adopters and nonadopters. *Interfaces*, 95-107.
- Marth, J. 2008. A unified vision of the building blocks of life. *Net Cell Biol*, 10, (9), 1015-1015.
- Mitchell, S., Spiteri, M. D., Bates, J. & Coulouris, G. 2000. Context-aware multimedia computing in the intelligent hospital. 2000 Denmark. ACM Press, 13-18.
- Mitrevski, J. 2012. *Mobile Health: Function and diversity of the healthy human microbiome*. *Nature*, 486, 207-214.
- Mojsilović, S., Arribalzaga, G., McKeeegan, K. D., Harrison, T. M., Nutman, A. P. & Friend, C. R. L. 1996. Evidence for life on Earth before 3,800 million years ago. *Nature*, 384, (6604), 55-59.
- Moloy, J. C. 2011. The Open Knowledge Foundation: Open Data Means Better Science. *Plos Biology*, 9, (12).
- Moore, G. E. 1965. Cracking More Components Onto Integrated Circuits. *Electronics*, 38, (B), 114-117.
- Neumann, J. V. 1946. First Draft of a Report on the EDVAC. University of Pennsylvania - Technical Report, 49 pp.
- Ng, P. C., Murray, S. S., Levy, S. & Vertes, J. C. 2009. An agent for personalized medicine. *Nature*, 461, (7265), 724-726.
- Okunade, A. 2008. *Handwriting Recognition and Its Applications*. *Journal of Biomedical Complexity and Ethics*, 4, (1), 387-389.
- Petz, G., Karpuswicz, M., Fürschuß, H., Auinger, A., Srivatski, V. & Holzinger, A. 2013. Opinion Mining on the Web 2.0—Characteristics of User Generated Content and Their Impacts. *Lecture Notes in Computer Science (LNCS) 7947*. Heidelberg, Berlin: Springer, pp. 35-46.
- Petz, G., Karpuswicz, M., Fürschuß, H., Auinger, A., Winkler, S., Schaller, S. & Holzinger, A. 2012. On Text Preprocessing for Opinion Mining Outside of Laboratory Environments. In: Holzinger, A., Ghoshal, S., Yamaguchi, T., Yen, J. & Jin, B. (eds.) *Active Media Technology, Lecture Notes in Computer Science (LNCS) 7661*. Berlin: Springer, pp. 63-72.
- Pevsner, J. 2009. *Biostatistics and functional genomics*. Hoboken (NJ): John Wiley & Sons.
- Rabilou, T., Chevallet, M., Luche, S. & Lelong, C. 2010. Two-dimensional gel electrophoresis in proteomics: past, present and future. *Journal of proteomics*, 73, (11), 2064-2077.
- Rouwakim, J., Rivron, N. C. & Van Blitterswijk, C. A. 2008. Vascularization in tissue engineering. *Trends in biotechnology*, 26, (8), 434-441.

A. Holzinger 709.049 78/80 Med Informatics L01

**References (4/5)**

- Rovelli, L., Wong, G. K. S., Lane, R. P. & Hood, L. 2000. Intellectual property - Publication rights in the era of open data release policies. *Science*, 289, (5486), 1881-1881.
- Sackett, D. L., Rosenberg, W. M., Gray, J., Haynes, R. B. & Richardson, W. S. 1996. Evidence based medicine: what it is and what it isn't. *BMJ: British Medical Journal*, 312, (7023), 71.
- Schidlowski, M. 1988. A 3,800-million-year isotopic record of life from carbon in sedimentary rocks. *Nature*, 333, (6171), 313-318.
- Schmid, F. J., Li, M. & Jokisch, T. A. Sonnen, J., Olson, J. S., Phillips, G. N., Wulff, M. & Amirheidari, P. A. 2003. Watching a protein as it functions with 150 p.s time-resolved X-ray crystallography. *Science*, 300, (5627), 1544-1547.
- Schrödinger, E. 1944. *What is Life? The Physical Aspect of the Living Cell*. Dublin: Dublin Institute for Advanced Studies at Trinity College.
- Shadforth, N., O'hara, K., Berners-Lee, T., Gibbons, N., Glaser, H., Hall, W. & Schraefel, M. 2012. Open Government Data and the Linked Data Web: Lessons from data.gov.uk. *IEEE Intelligent Systems*, 16-16.
- Sheppard, A. & Holzinger, A. 2012. Privacy and motions of loops in protein molecules. *Entropy*, 14, (3), 252-260.
- Shore, D. H. 2011. Biomedical Informatics: Defining the Science and its Role in Health Professional Education. In: Holzinger, A. & Simonic, K.-M. (eds.) *Information Quality in e-Health. Lecture Notes in Computer Science LNCS 7058*. Heidelberg, New York: Springer, pp. 711-714.
- Simonic, K.-M. & Holzinger, A. 2010. Zur Bedeutung von Information in der Medizin. *CCS Journal*, 35, (1), 8.
- Sittig, D. F. 1994. Grand Challenges in Medical Informatics. *Journal of the American Medical Informatics Association*, 1, (5), 412-413.
- Southern, E. M. 1979. Detection of Specific Sequences among DNA Fragments Separated by Gel-Electrophoresis. *Journal of Molecular Biology*, 98, (3), 503-8.
- Sperakis, N. 2012. *Cell Physiology: Sources and Essentials of Membrane Biophysics*. Fourth Edition, Amsterdam, Elsevier.
- Steens, M. 1957. *Handbuch der Anatomie des Menschen* (Deutsche Ausgabe). Stuttgart: Thieme.
- Stork, U., Worm, U., Lalowski, M., Harten, C., Brueckner, A., Goedde, A., Krüger, S., Timm, J., Mintaal, S., Abraham, C., Beck, N., Kettmann, S., Goedde, A., Tokito, E., Droege, A., Knoblich, S., Korn, B., Birchmeier, W., Lehrach, H. & Wanker, E. E. 2005. A Human Protein-Protein Interaction Network: A Resource for Annotating the Proteome. *Cell*, 122, (6), 957-966.
- Tanaka, H. 2010. Omics-based Medicine and Systems Pathology A New Perspective for Personalized and Predictive Medicine. *Methods of Information in Medicine*, 49, (2), 173-185.
- Thompson, M. & Hennegan, C. 2012. BMJ Open Data Campaign: We need to move the debate on open clinical trial data forward. *British Medical Journal*, 345.
- Trent, R. J. 2012. *Molecular Medicine: Genomics to Personalized Healthcare*. 4th Edition, Amsterdam, Elsevier.
- Trygve, T. 2011. *Handbook of Epigenetics*. San Diego, Academic Press.
- Varshney, U. 2009. *Personal Health Computing: EMR/HIS, mHealth, and Health Monitoring*. New York, Springer.
- Walsh, J. I. E. 1980. Designing Medical Database Systems. *Medical Electronics, IEEE Transactions on*, ME-7, (4), 362-366.
- Wittenberg, C. S., Holzinger, A., Emerick, W. & Breitkreuz, F. 2003. Design and Development of Interactive Online-Simulations for e-Learning. In: Hoffmann, R. (ed.) *Frontiers in Simulation - 17th Symposium Simulationstechnik in Magdeburg (Germany)*. Delft: SCS European Publication, pp. 97-105.
- Weiser, M. 1993. The computer for the twenty-first century. *Scientific American*, 265, (3), 94-104.

A. Holzinger 709.049

79/80

Med Informatics LO1

**References (5/5)**

- Westra, R., Turlo, K., Saeyn, Y. & Nowak, A. 2007. Knowledge Discovery and Emergent Complexity in Bioinformatics. In: Tuyls, K., Westra, R., Saeyn, Y. & Nowak, A. (eds.) *Knowledge Discovery and Emergent Complexity in Bioinformatics*. Springer Berlin Heidelberg, pp. 1-9.
- Wilgen, M. & Holzinger, A. 2005. Visualization in Bioinformatics: Protein Structures with Physicochemical and Biological Annotations. In: Zara, J. & Sloup, J. (eds.) *Central European Multimedia and Virtual Reality Conference*. [available in EG Eurographics Library]. Prague: Czech Technical University (CTU), pp. 69-74.
- Wilgen, M., Holzinger, A. & Till, G. P. 2007. Interactive Analysis and Visualization of Macromolecular Interfaces Between Proteins. In: Holzinger, A. (ed.) *HCI and Bioinformatics for Medical Applications and Bioinformatics*. LNCS 4706. Berlin: Heidelberg, New York: Springer, pp. 199-212.
- Xia, W. Z. & Deford, P. J. 2001. Denaturing high-performance liquid chromatography: A review. *Human Mutation*, 17, (6), 439-474.
- Yapijakis, C. 2009. Hippocrates of Kos, the Father of Clinical Medicine, and Asclepius of Bithynia, the Father of Molecular Medicine. *In Vivo*, 23, (4), 507-514.
- Yilmaz, F., Elmekki, I. & Holzinger, A. 2011. On Knowledge Discovery in Open Medical Data on the Example of the FDA Drug Adverse Event Reporting System for Acne-prone (Rosacea). In: Holzinger, A. & Pas, G. (eds.) *Human-Computer Interaction and Knowledge Discovery in Complex, Unstructured, Big Data. Lecture Notes in Computer Science, LNCS 7247*. Berlin Heidelberg: Springer, pp. 195-206.
- Yip, L. Y. & Yong Chan, E. C. 2013. Chapter 3 - Gas Chromatography/Mass Spectrometry-Based Metabolomics. In: Haleem, J. I. & Timothy, D. V. (eds.) *Proteomic and Metabolomic Approaches to Biomarker Discovery*. Boston: Academic Press, pp. 131-144.
- Zhang, Y. T. & Poon, C. Y. 2010. Editorial Note on Bio, Medical, and Health Informatics. *Information Technology in Biomedicine, IEEE Transactions on*, 14, (1), 545-546.
- Ziefle, M., Röcker, C. & Holzinger, A. 2011. Medical Technology in Smart Homes: Exploring the User's Perspective on Privacy, Intimacy and Trust. *35th Annual IEEE Computer Software and Applications Conference Workshops COMPSSAC 2011*. Munich: IEEE, pp. 410-415.

A. Holzinger 709.049

80/80

Med Informatics LO1