

MAKE Decisions: Medical Information Science for Decision Support



Assoc. Prof. Dr. Andreas HOLZINGER (Med. Uni Graz)



<https://hci-kdd.org/mini-course-make-decisions-practice>

Day 1 –Part 2 -19.09.2018

Data, Information and Knowledge

Day 1 - Hot Ideas

01 Information Sciences meets
Life Sciences

02 Data, Information
and Knowledge

03 Decision Making and
Decision Support

04 DSS: from Expert Systems
to explainable AI

Day 2 - Cool Practice

05 Methods of Explainable-AI

Groupwork: Planning of a 500
bed Hospital - Bringing AI into
the workflows

Plenary: Presenting of the
developed concepts

- Data
- Information
- Knowledge
- Dimensionality of data
- Biomedical Ontologies
- Standardized Medical Data
- SNOMED
- UMLS

- ... be aware of the types and categories of different data sets in biomedical informatics;
- ... know some differences between data, information, and knowledge;
- ... be aware of standardized/non-standardized and well-structured/"un-structured" information/data;
- ... have a basic overview on some ontological approaches for standardized medicine;
- ... have some background on classifications

- **Abduction** = cyclical process of generating possible explanations (i.e., identification of a set of hypotheses that are able to account for the clinical case on the basis of the available data) and testing those (i.e., evaluation of each generated hypothesis on the basis of its expected consequences) for the abnormal state of the patient at hand;
- **Abstraction** = data are filtered according to their relevance for the problem solution and chunked in schemas representing an abstract description of the problem (e.g., abstracting that an adult male with haemoglobin concentration less than 14g/dL is an anaemic patient);
- **Artefact/surrogate** = error or anomaly in the perception or representation of information through the involved method, equipment or process;
- **Data** = physical entities at the lowest abstraction level which are, e.g. generated by a patient (patient data) or a (biological) process; data contain no meaning;
- **Data quality** = Includes quality parameter such as : Accuracy, Completeness, Update status, Relevance, Consistency, Reliability, Accessibility;
- **Data structure** = way of storing and organizing data to use it efficiently;
- **Deduction** = deriving a particular valid conclusion from a set of general premises;
- **DIK-Model** = Data-Information-Knowledge three level model
- **Disparity** = containing different types of information in different dimensions
- **Heart rate variability (HRV)** = measured by the variation in the beat-to-beat interval;
- **HRV artifact** = noise through errors in the location of the instantaneous heart beat, resulting in errors in the calculation of the HRV, which is highly sensitive to artifact and errors in as low as 2% of the data will result in unwanted biases in HRV calculations;

- **Induction** = deriving a likely general conclusion from a set of particular statements;
- **Information** = derived from the data by interpretation (with feedback to the clinician);
- **Information Entropy** = a measure for uncertainty: highly structured data contain low entropy, if everything is in order there is no uncertainty, no surprise, ideally $H = 0$
- **Knowledge** = obtained by inductive reasoning with previously interpreted data, collected from many similar patients or processes, which is added to the “body of knowledge” (explicit knowledge). This knowledge is used for the interpretation of other data and to gain implicit knowledge which guides the clinician in taking further action;
- **Large Data** = consist of at least hundreds of thousands of data points
- **Multi-Dimensionality** = containing more than three dimensions and data are multi-variate
- **Multi-Modality** = a combination of data from different sources
- **Multivariate** = encompassing the simultaneous observation and analysis of more than one statistical variable;
- **Reasoning** = process by which clinicians reach a conclusion after thinking on all facts;
- **Spatiality** = contains at least one (non-scalar) spatial component and non-spatial data
- **Structural Complexity** = ranging from low-structured (simple data structure, but many instances, e.g., flow data, volume data) to high-structured data (complex data structure, but only a few instances, e.g., business data)
- **Time-Dependency** = data is given at several points in time (time series data)
- **Voxel** = volumetric pixel = volumetric picture element

- **00 Reflection – follow-up from last lecture**
- **01 What is data?**
- **02 On Standardization**
- **03 Knowledge Representation**
- **04 Biomedical Ontologies**
- **05 Medical Classifications**

00 Reflection

Reflection from last lecture



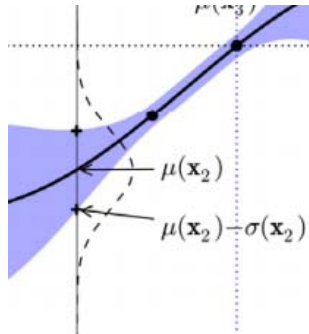
1



2

$$p(\theta|\mathcal{D}) = \frac{p(\mathcal{D}|\theta) * p(\theta)}{p(\mathcal{D})}$$

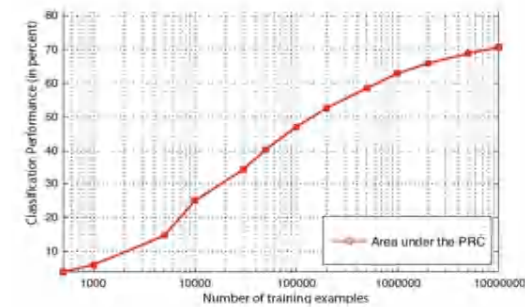
3



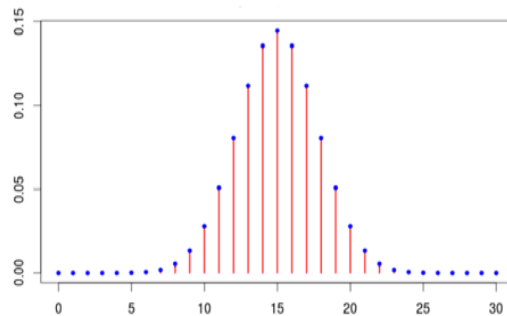
4



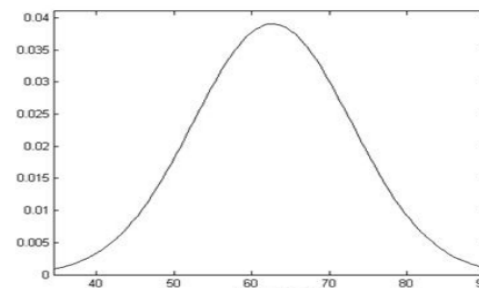
5



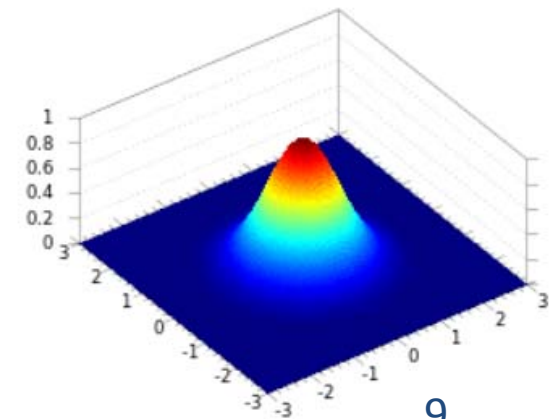
6



7



8



9

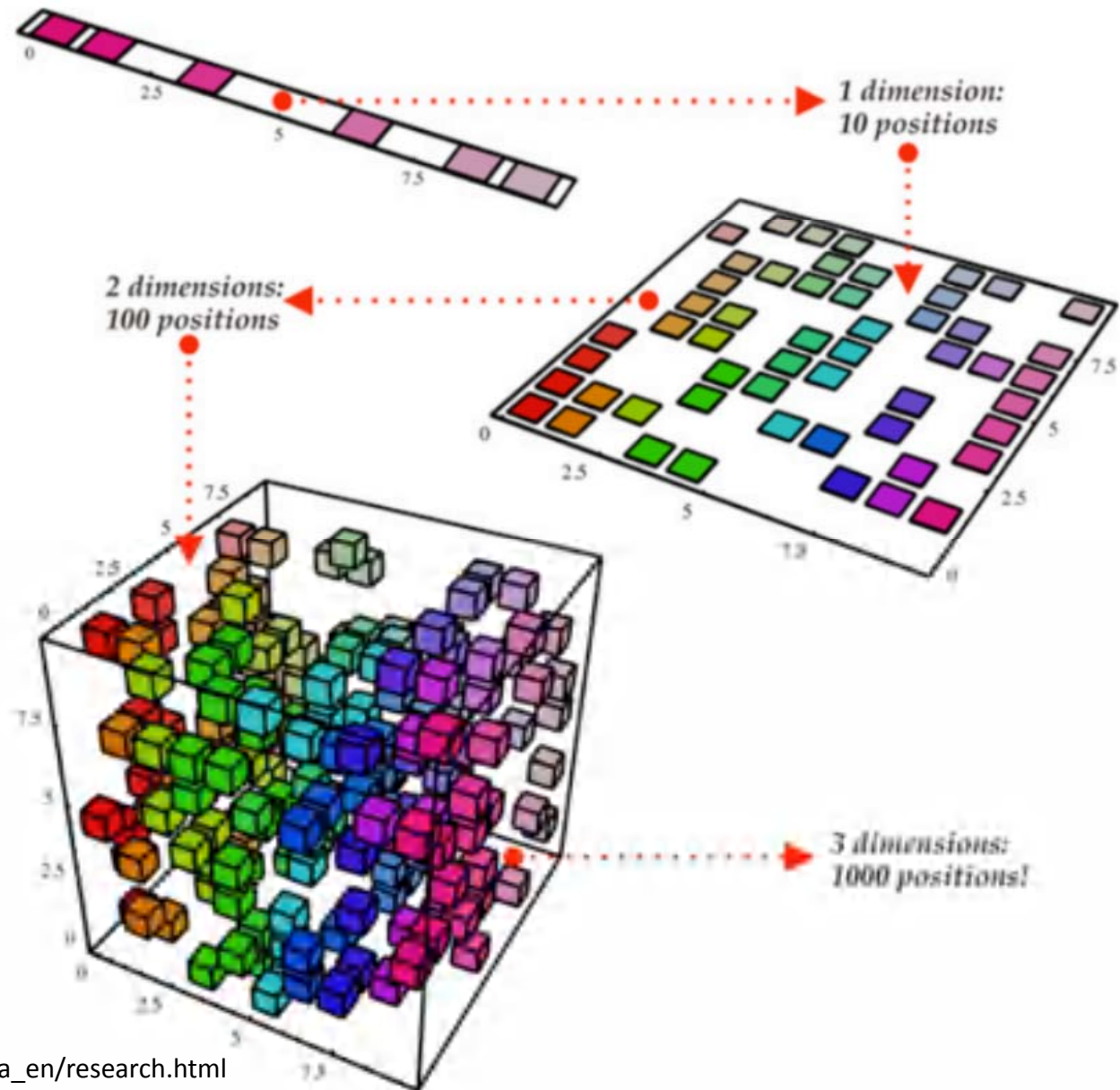
01 Data

<http://www.nytimes.com/2012/05/06/books/review/turings-cathedral-by-george-dyson.html>

- Data in traditional Statistics
- Low-dimensional data ($< \mathbb{R}^{100}$)
- Problem: Much noise in the data
- Not much structure in the data but it can be represented by a simple model
- Data in Machine Learning
- High-dimensional data ($>> \mathbb{R}^{100}$)
- Problem: not noise , but complexity
- Much structure, but the structure can **not** be represented by a simple model

Lecun, Y., Bengio, Y. & Hinton, G. 2015. Deep learning. Nature, 521, (7553), 436-444.

Note: The curse of dimensionality



Bengio, S. & Bengio, Y.
2000. Taking on the curse
of dimensionality in joint
distributions using neural
networks. IEEE Transactions
on Neural Networks, 11,
(3), 550-557.

http://www.iro.umontreal.ca/~bengioy/yoshua_en/research.html

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), I1,

10^{-12}

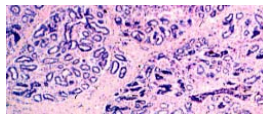
Collective



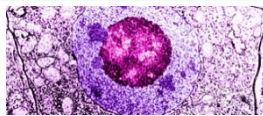
Individual



Tissue



Cell



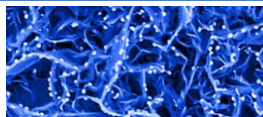
Bacteria



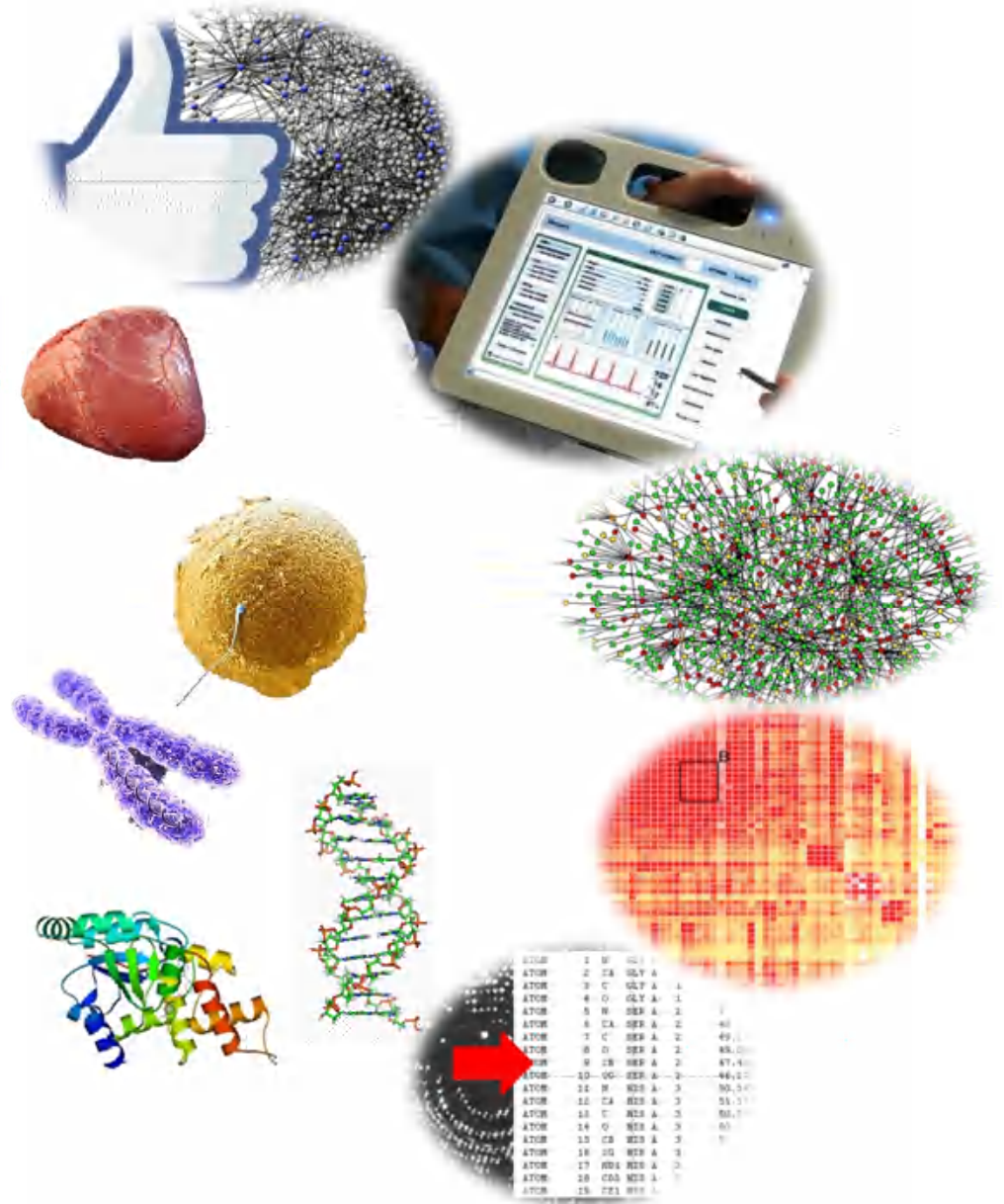
Virus



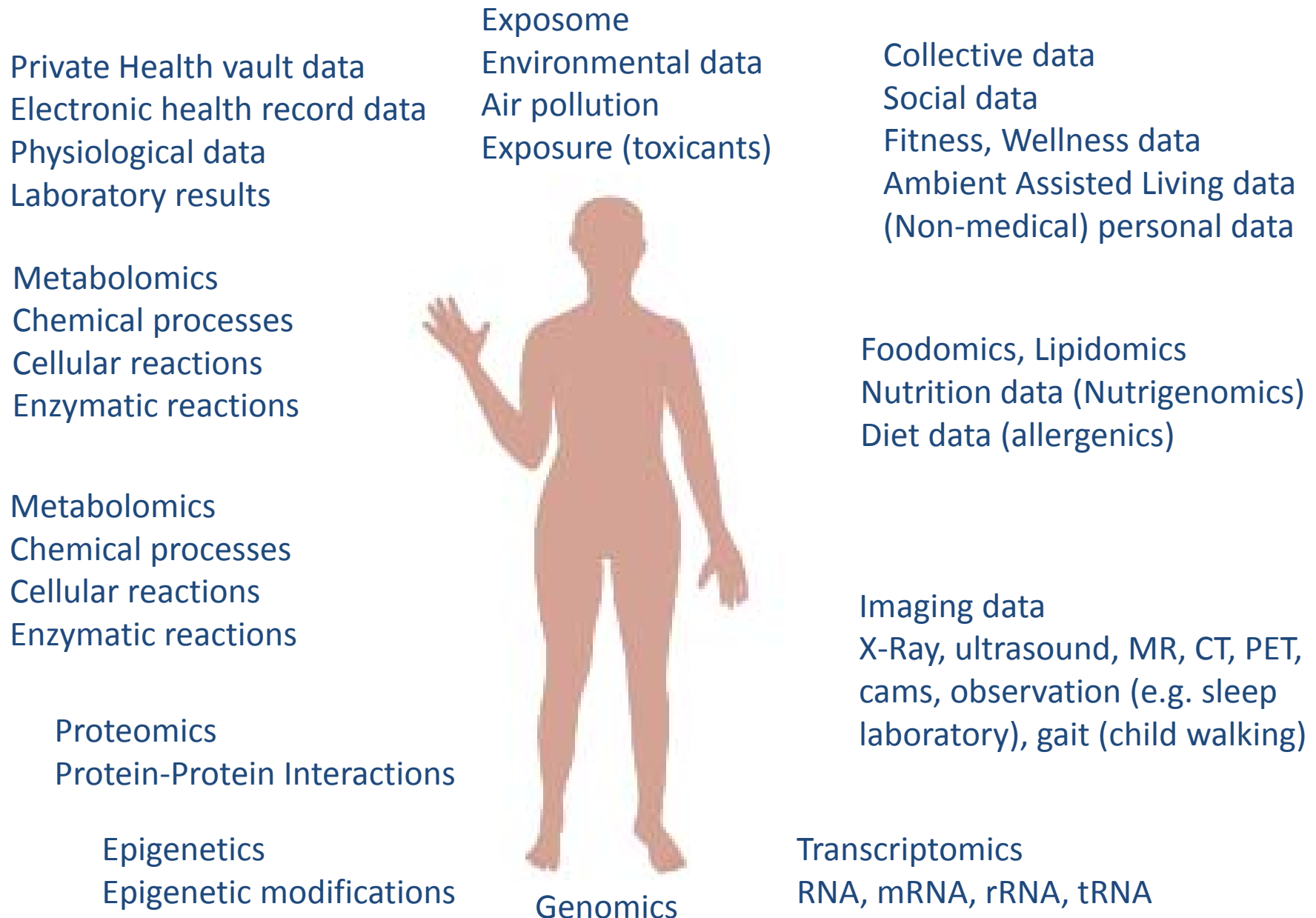
Molecule



Atom



Data for clinical purposes – integration is unsolved!



- **Physical level** -> bit = binary digit = **basic** indissoluble unit (= Shannon, Sh), \neq Bit (!) in Quantum Systems -> qubit
- **Logical Level** -> integers, booleans, characters, floating-point numbers, alphanumeric strings, ...
- **Conceptual (Abstract) Level** -> data-structures, e.g. lists, arrays, trees, graphs, ...
- **Technical Level** -> Application data, e.g. text, graphics, images, audio, video, multimedia, ...
- **“Hospital Level”** -> Narrative (textual) data, genetic data, numerical measurements (physiological data, lab results, vital signs, ...), recorded signals (ECG, EEG, ...), Images (cams, x-ray, MR, CT, PET, ...)

Examples: Imaging Data

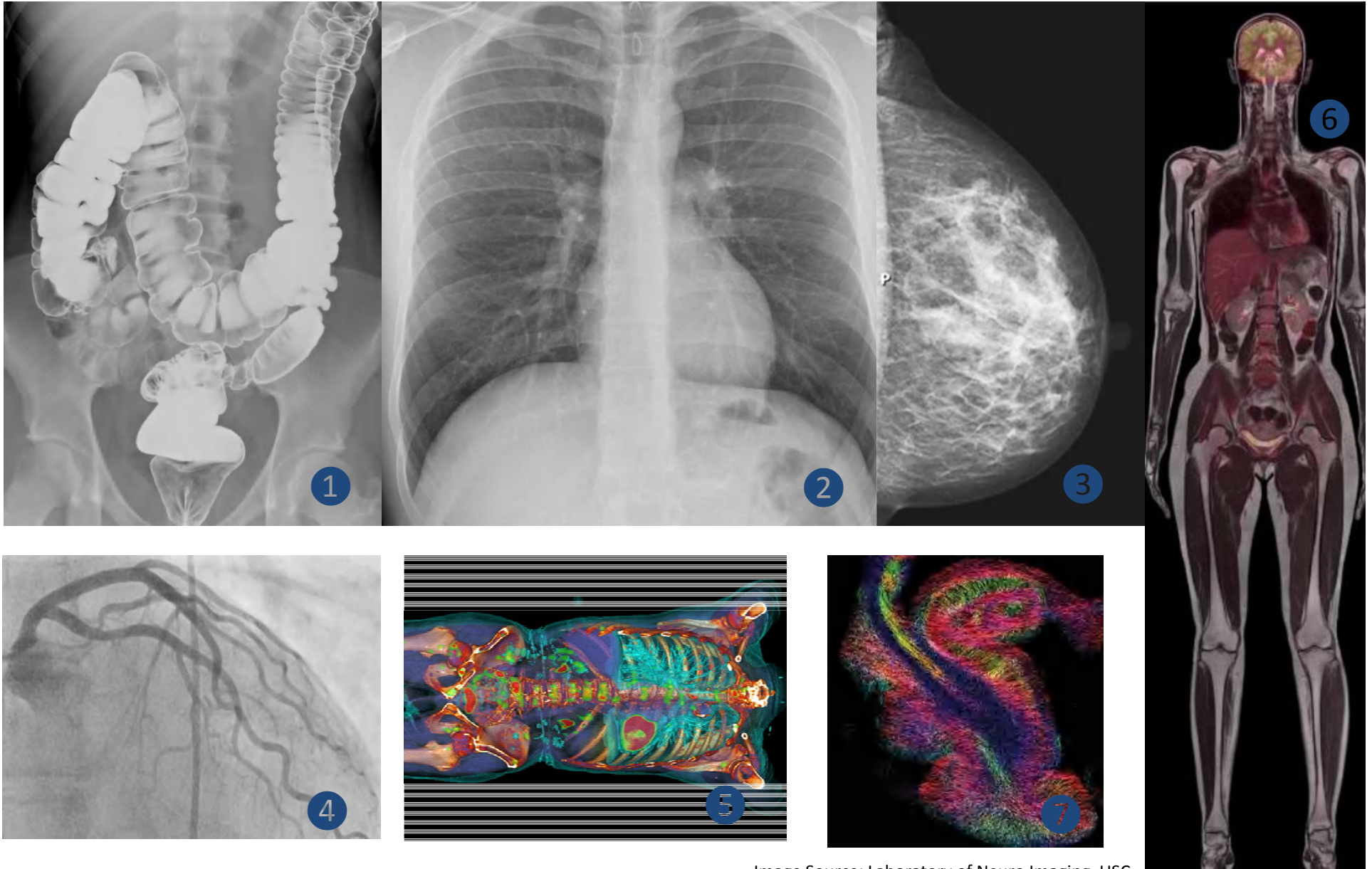
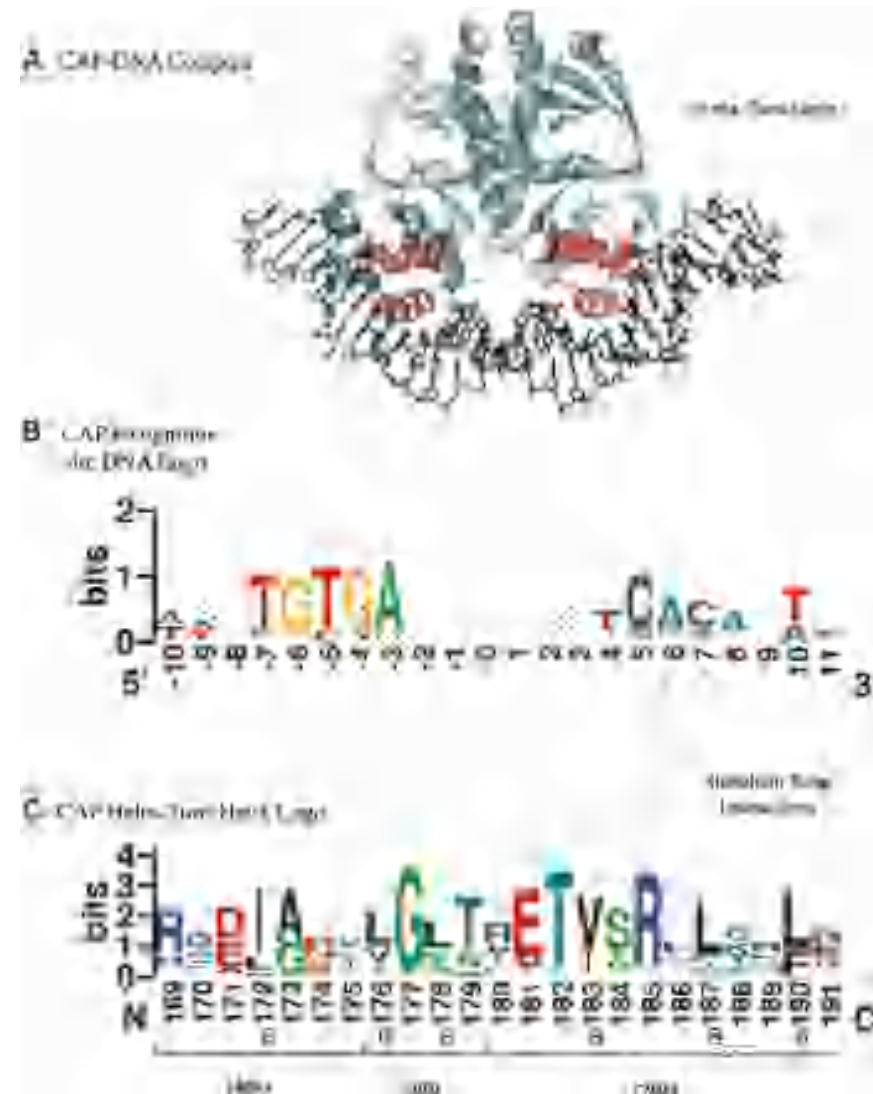
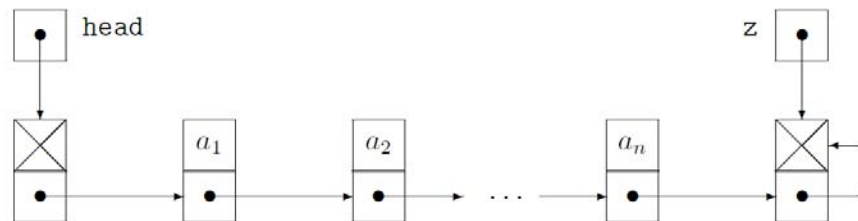


Image Source: Laboratory of Neuro Imaging, USC

Example Data Structures (1/3): List

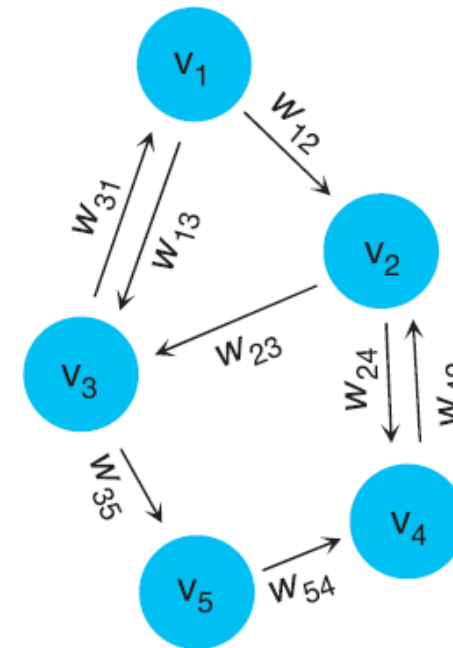
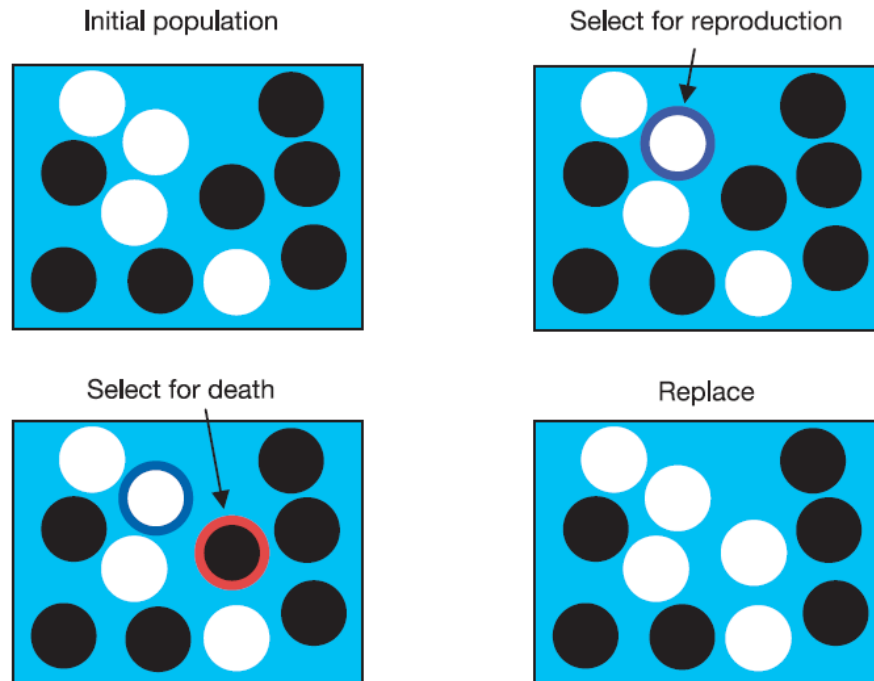
<pre>TYPE link = REF node ; node = RECORD key : ItemType; next : link; END;</pre>	<pre>key next</pre>	<pre>class link { ItemType key; link next; }</pre>
VAR p, q : link ;	p q	link p,q;
p := NEW(link);	p q	p=new link();
p^.key:=x;	p q	p.key=x;
q := NEW(link) ;	p q	q=new link();



Crooks, G. E., Hon, G., Chandonia, J. M. & Brenner, S. E. (2004) WebLogo: A sequence logo generator. *Genome Research*, 14, 6, 1188-1190.

Example Data Structures (2/3): Graph

Evolutionary dynamics act on populations.
Neither genes, nor cells, nor individuals evolve;
only populations evolve.

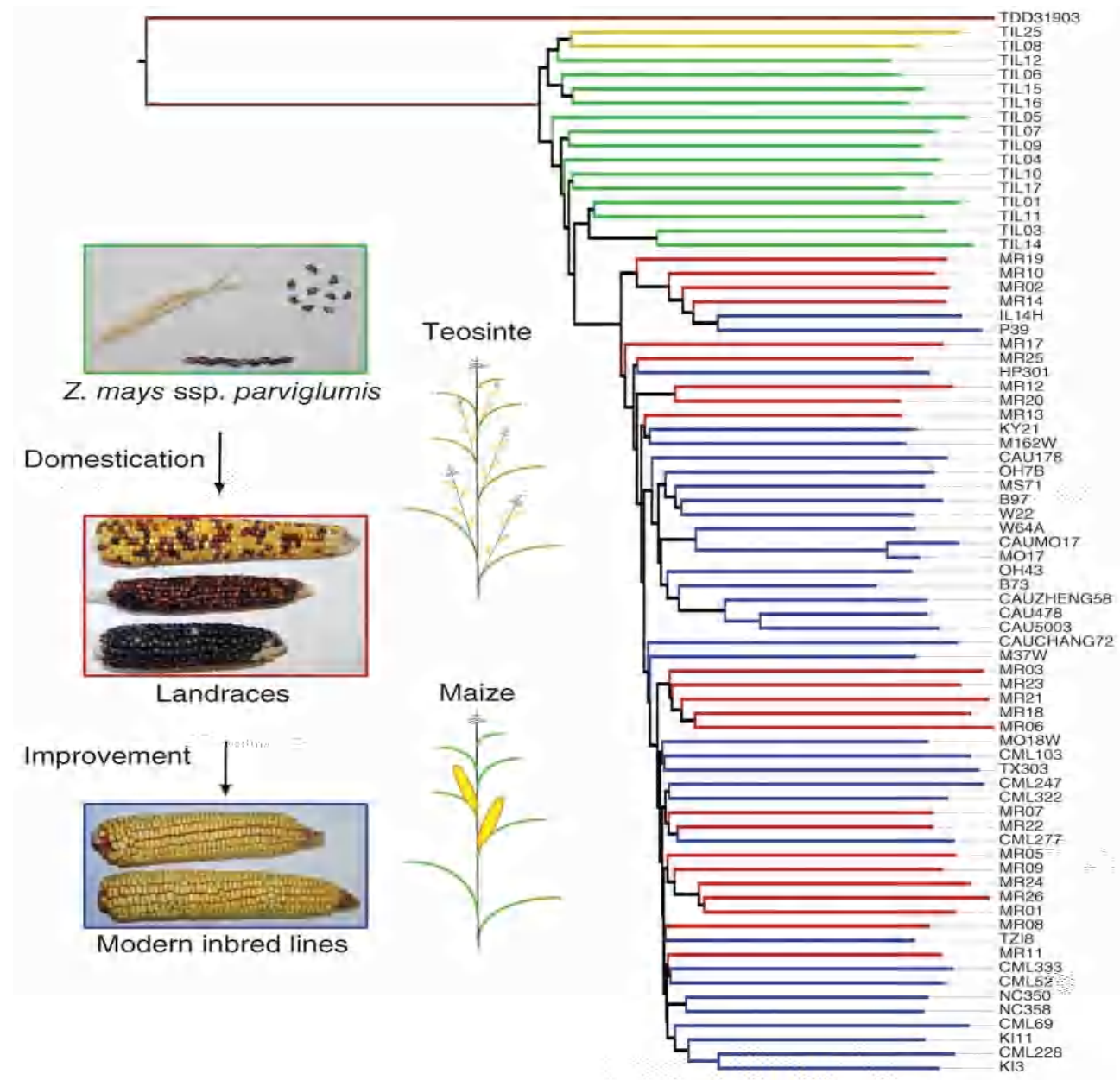


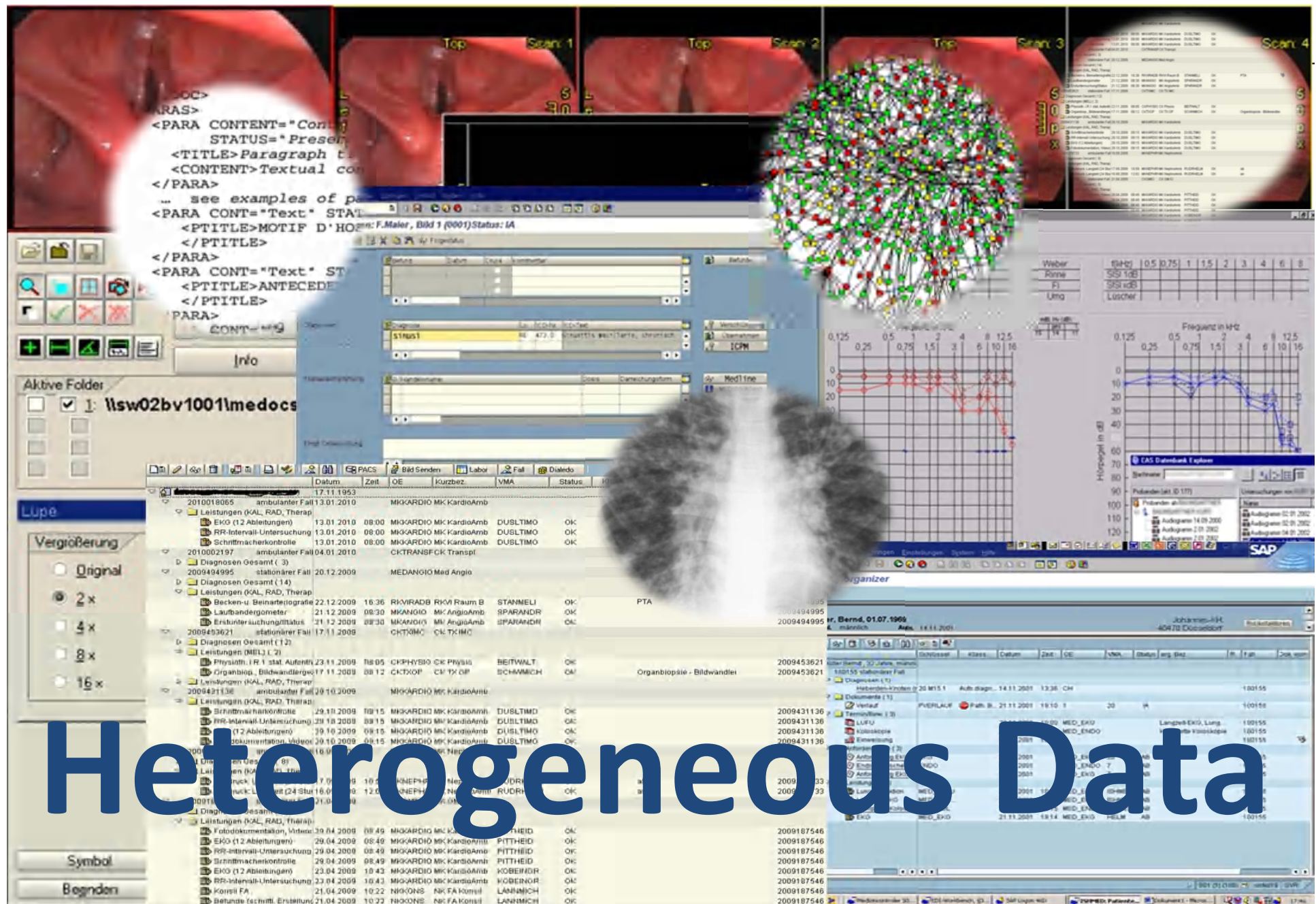
$$W = \begin{bmatrix} 0 & w_{12} & w_{13} & 0 & 0 \\ 0 & 0 & w_{23} & w_{24} & 0 \\ w_{31} & 0 & 0 & 0 & w_{35} \\ 0 & w_{42} & 0 & 0 & 0 \\ 0 & 0 & 0 & w_{54} & 0 \end{bmatrix}$$

Lieberman, E., Hauert, C. & Nowak, M. A.
(2005) Evolutionary dynamics on graphs.
Nature, 433, 7023, 312-316.

Example Data Structures (3/3) Tree

Hufford et. al.
2012. Comparative
population
genomics of maize
domestication and
improvement.
Nature Genetics,
44, (7), 808-811.







Biomedical R&D data
(e.g. clinical trial data)

Clinical patient data
(e.g. EPR, lab, reports etc.)

The combining link is text

Health business data
(e.g. costs, utilization, etc.)

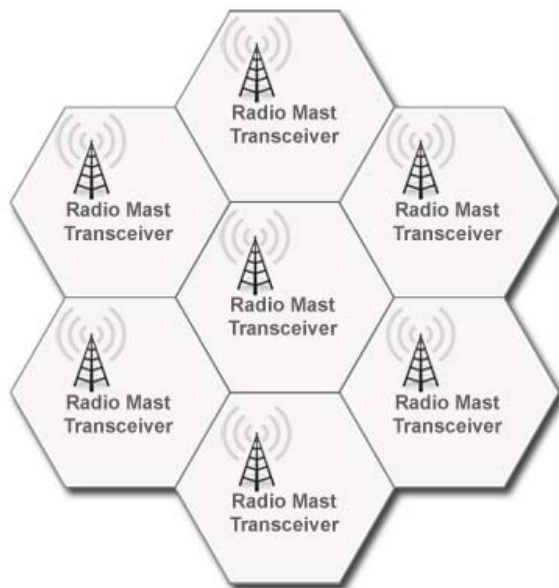
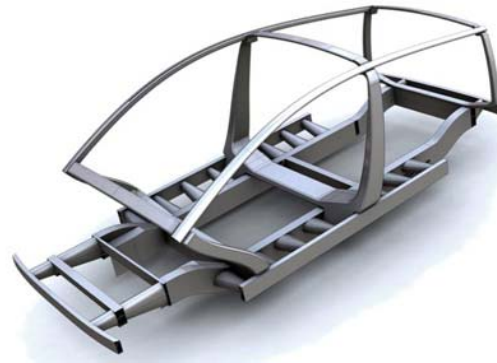
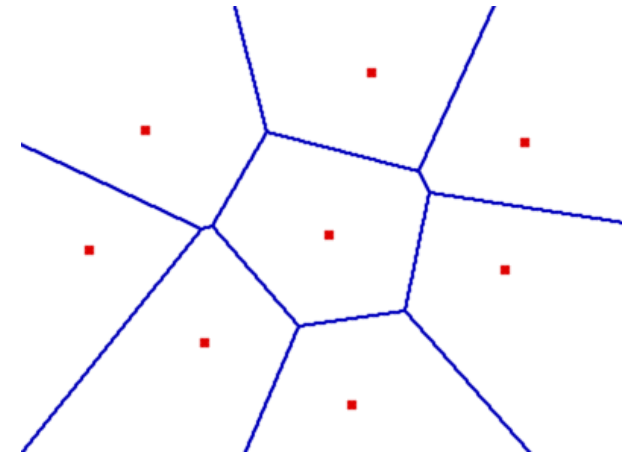
Private patient data
(e.g. AAL, monitoring, etc.)

Manyika, J., Chui, M., Brown, B., Bughin, J., Dobbs, R., Roxburgh, C. & Byers, A. H. (2011) *Big data: The next frontier for innovation, competition, and productivity*. Washington (DC), McKinsey Global Institute.

Problem: Context!



Semantic Ambiguity – Missing Context



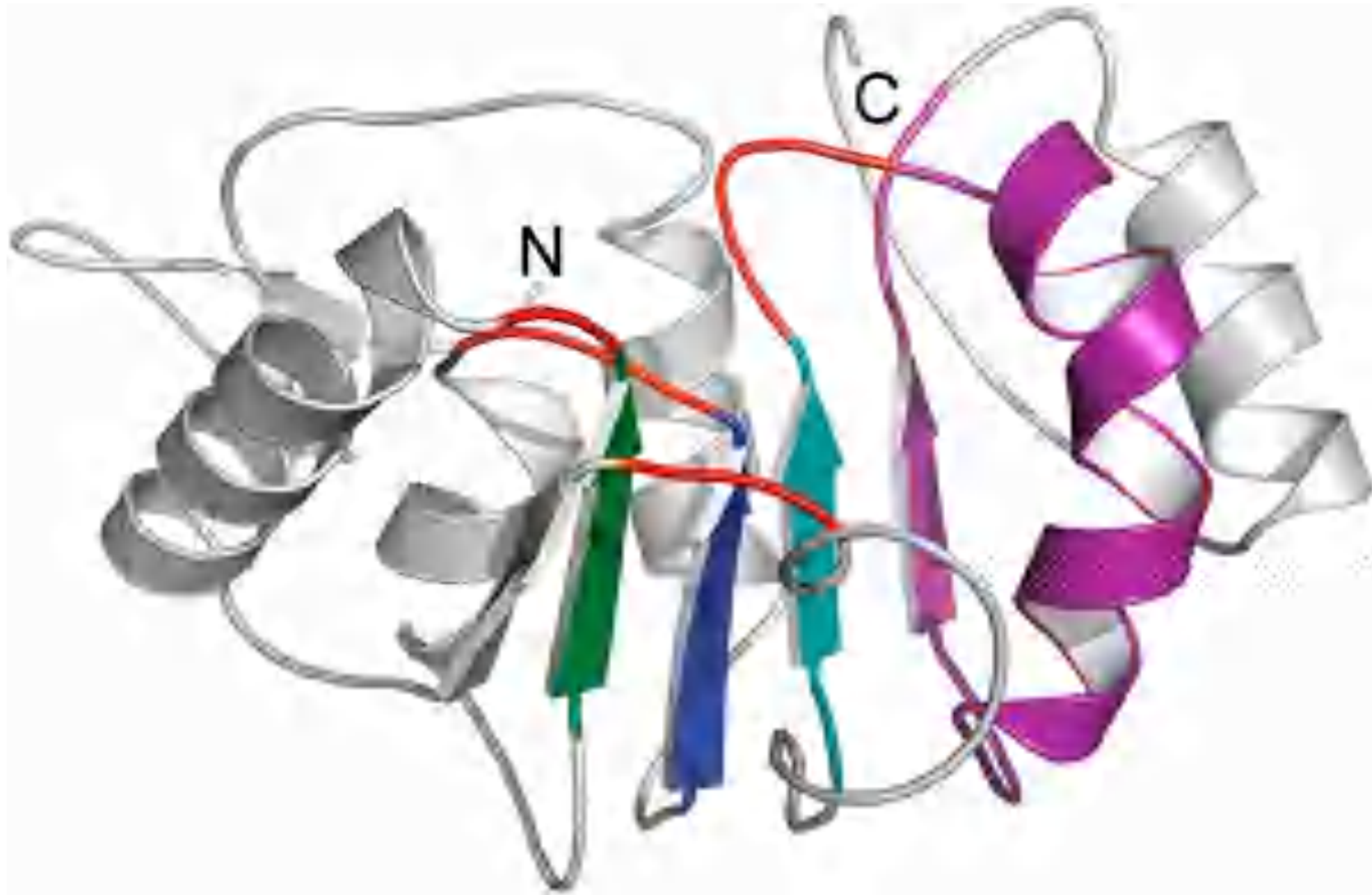
Multiplication table – mixed references

	1	2	3	4	5	6	7	8	9	10
1	1	2	3	4	5	6	7	8	9	10
2	2	4	6	8	10	12	14	16	18	20
3	3	6	9	12	15	18	21	24	27	30
4	4	8	12	16	20	24	28	32	36	40
5	5	10	15	20	25	30	35	40	45	50
6	6	12	18	24	30	36	42	48	54	60
7	7	14	21	28	35	42	49	56	63	70
8	8	16	24	32	40	48	56	64	72	80
9	9	18	27	36	45	54	63	72	81	90
10	10	20	30	40	50	60	70	80	90	100
11	11	22	33	44	55	66	77	88	99	110
12	12	24	36	48	60	72	84	96	108	120



Is a picture really worth a thousand words?

Example: Ribbon Diagram of a Protein Structure



Magnani, R., et al. 2010. Calmodulin methyltransferase is an evolutionarily conserved enzyme that trimethylates Lys-115 in calmodulin. *Nature Communications*, 1, 43.



erstellt am 04.05.2006 09:24
gelesen von
gelesen am 04.05.2006 09:24
Autor: [Name]

Radiologischer Befund

Kurzanamnese: St. SHT

Fragestellung: -

Untersuchung: Thorax eine Ebene liegend

SB

Bewegungsartefakte: Zustand nach Schädelhirntrauma.

Das Cor in der Größenform, keine akuten Stauungszeichen.
Frägliches Interkostal paravert. li. im UF, RV-Enguss li.

Zustand nach Anlage eines ET, die Spitze ca. 5cm cranial der Bifurkation, liegt M/S. orthot.
positioniert. ZVK über m., die Spitze in Proj. auf die VCS. Kein Hinweis auf Pneumothorax.
Der re. Ratenus frei.

Mit kollegialen Grüßen.

Dr. med. [Name]

Holzinger, A., Geierhofer, R. & Errath, M. 2007. Semantische Informationsextraktion in medizinischen Informationssystemen. *Informatik Spektrum*, 30, (2), 69-78.

A picture is worth a thousand words ...







- ... and requires a lot of communication and information exchange ...



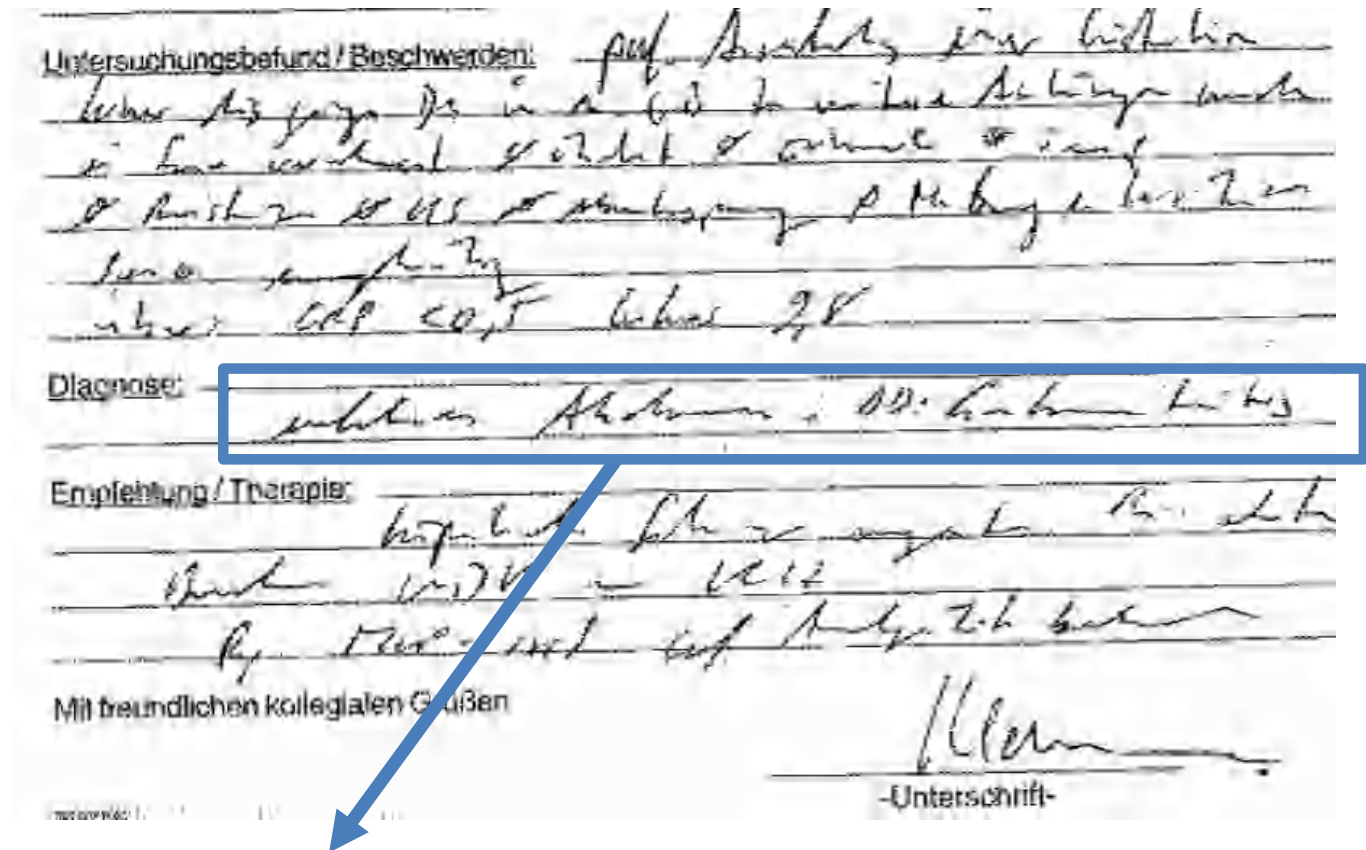
Holzinger, A., Geierhofer, R., Ackerl, S. & Searle, G. (2005). *CARDIAC@VIEW: The User Centered Development of a new Medical Image Viewer*. Central European Multimedia and Virtual Reality Conference, Prague, Czech Technical University (CTU), 63-68.

The medical report is the most important medium

Radiologischer Befund		angelegt am 06.05.2006/20:26 geschr. von gedruckt am 17.11.2006/08:24 Anfo: NCHIN
Kurzanamnese:	St.p, SHT	
Fragestellung:	-	
Untersuchung:	Thorax eine Ebene liegend	
SB		
Bewegungsartefakte. Zustand nach Schädelhirntrauma.		
Das Cor in der Größennorm, keine akuten Stauungszeichen. Fragliches Infiltrat parahilär li. im UF, RW-Erguss li.		
Zustand nach Anlage eines ET, die Spitze ca. 5cm cranial der Bifurkation, lieg. MS, orthotop positioniert. ZVK über re., die Spitze in Proj. auf die VCS. Kein Hinweis auf Pneumothorax. Der re. Rezessus frei.		
Mit kollegialen Grüßen		
*** Elektronische Freigabe durch am 09.05.2006 ***		

**Special Words
Language Mix
Abbreviations
Errors ...**

Holzinger, A., Geierhofer, R. & Errath, M. 2007. Semantische Informationsextraktion in medizinischen Informationssystemen. *Informatik Spektrum*, 30, (2), 69-78.



„die Antrumschleimhaut ist durch Lymphozyten infiltriert“

„lymphozytäre Infiltration der Antrummukosa“

„Lymphoyteninfiltration der Magenschleimhaut im Antrumbereich“

- HWI =

- Harnwegsinfekt
- Hinterwandinfarkt
- Hinterwandischämie
- Hakenwurminfektion
- Halswirbelimmobilisation
- Hip Waist Index
- Height-Width Index
- Heart-Work Index
- Hemodynamically weighted imaging
- High Water Intake
- Hot water irrigation
- Hepatitic weight index
- Häufig wechselnder Intimpartner



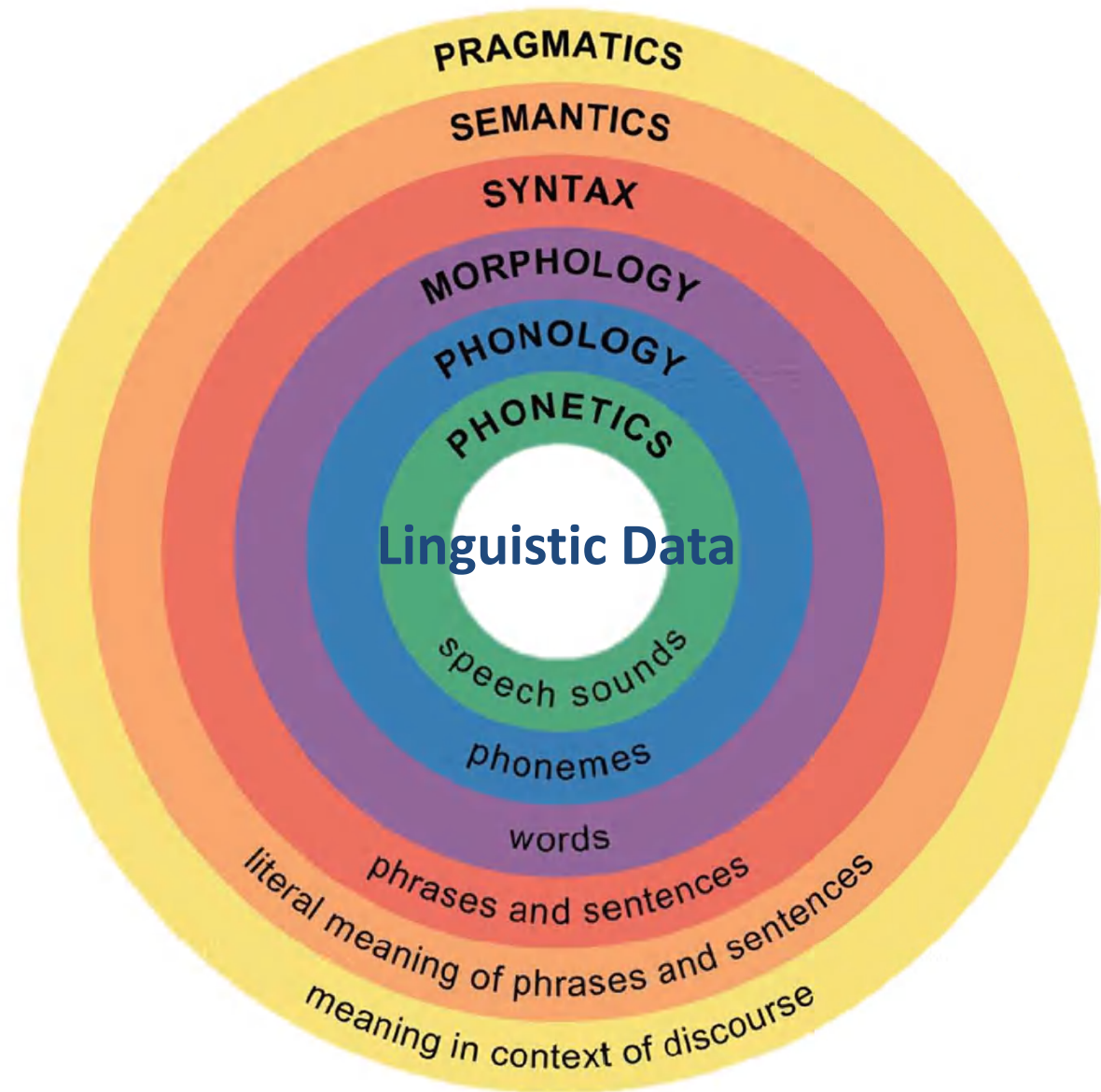
- Leitung = Nervenleitung, Abteilungsleitung, Stromleitung, Wasserleitung, Harnleitung, Ableitung, Vereinsleitung 😊...

- Syntax
- Semantics
- Pragmatics
- Context
- (Emotion)



Andrej Karpathy & Li Fei-Fei. Deep visual-semantic alignments for generating image descriptions. Proceedings of the IEEE conference on computer vision and pattern recognition, 2015. 3128-3137.

Text = Good example for Non-Standardized Data



Thomas, J. J. & Cook, K. A.
2005. *Illuminating the path:
The research and
development agenda for
visual analytics*, New York,
IEEE Computer Society Press.

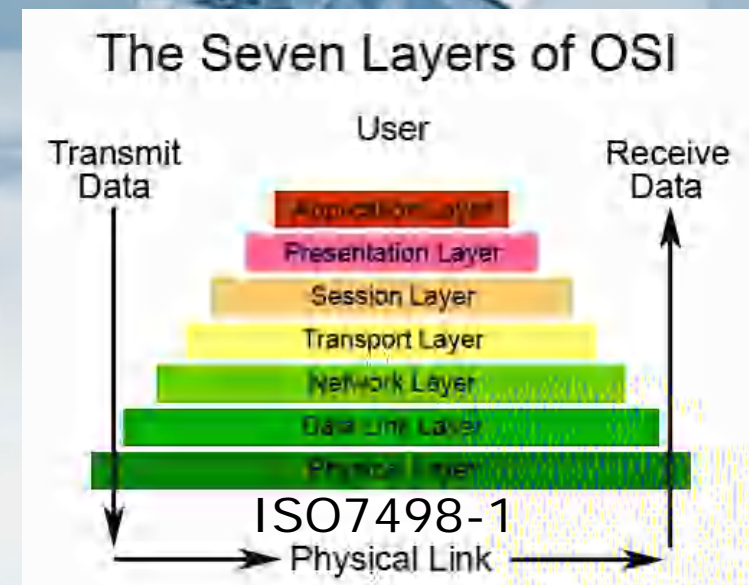
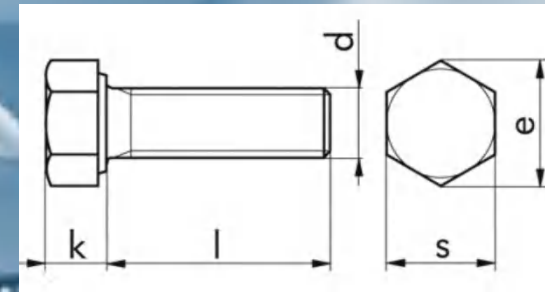
- Increasingly large data sets due to **data-driven medicine** [1]
- Increasing amounts of **non-standardized** data and **un-structured information** (e.g. “free text”)
- Data **quality**, data **integration**, universal **access**
- **Privacy**, security, safety, data protection, data ownership, fair use of data [2]
- **Time** aspects in databases [3]

[1] Shah, N. H. & Tenenbaum, J. D. 2012. The coming age of data-driven medicine: translational bioinformatics' next frontier. Journal of the American Medical Informatics Association, 19, (E1), E2-E4.

[2] Kieseberg, P., Hobel, H., Schrittwieser, S., Weippl, E. & Holzinger, A. 2014. Protecting Anonymity in Data-Driven Biomedical Science. In: LNCS 8401. Berlin Heidelberg: Springer pp. 301-316..

[3] Gschwandtner, T., Gärtner, J., Aigner, W. & Miksch, S. 2012. A taxonomy of dirty time-oriented data. In: LNCS 7465. Heidelberg, Berlin: Springer, pp. 58-72.

Standards



IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, VOL. BME-19, NO. 5, SEPTEMBER 1972

HEWLETT-PACKARD
LIBRARY³³¹

Standardization and Health Care AUG 18 1972

J. H. U. BROWN, SENIOR MEMBER, IEEE, AND DEWITT JAMES LOWELL

NON-CIRCULATING
Do Not Remove
From Library

Abstract—In order to deliver reasonable health care to all people, it is essential that standards be established. Standards vary with the type of control and with the approach desired in determining the quality of care. This paper discusses various kinds of standards and their application in the health care field. Standards may be determined as a process or as a direct regulation. It is probable that regulation of standards by process is the most satisfactory method.

arbiter may be the market place or agencies that rely on expertise from many sources to set acceptable standards of quality or performance. For these reasons, the final moderator may be found in a governmental authority, and its delegation into a system of regulation, law, and judicial action, so that an established code can become the focal point of resolution.

INTRODUCTION

SOCIETY cannot exist without a yardstick by which its accomplishments or failures are measured. Such yardsticks are called *standards*. They are created by the need for regulation and control as an escape from anarchy or to motivate towards greater achievement. In the ultimate, society dictates these limits by the demands it places upon itself. Standards provide opportunities for security and augmentation of process and output by virtue of the goal and process structure that they provide.

THE OBJECTIVES OF STANDARDIZATION

Standards have value within themselves in that they help establish quality. However, they accomplish more for society than the mere establishment of a level of quality and performance. A standard allows coordination of effort between producers so that like products can be produced. It permits the reproduction of similar units in mass quantity and permits the consumer to judge one product or service against another by performance. It establishes *freedom of interchange* of material and ideas, and permits the activity in one part of society

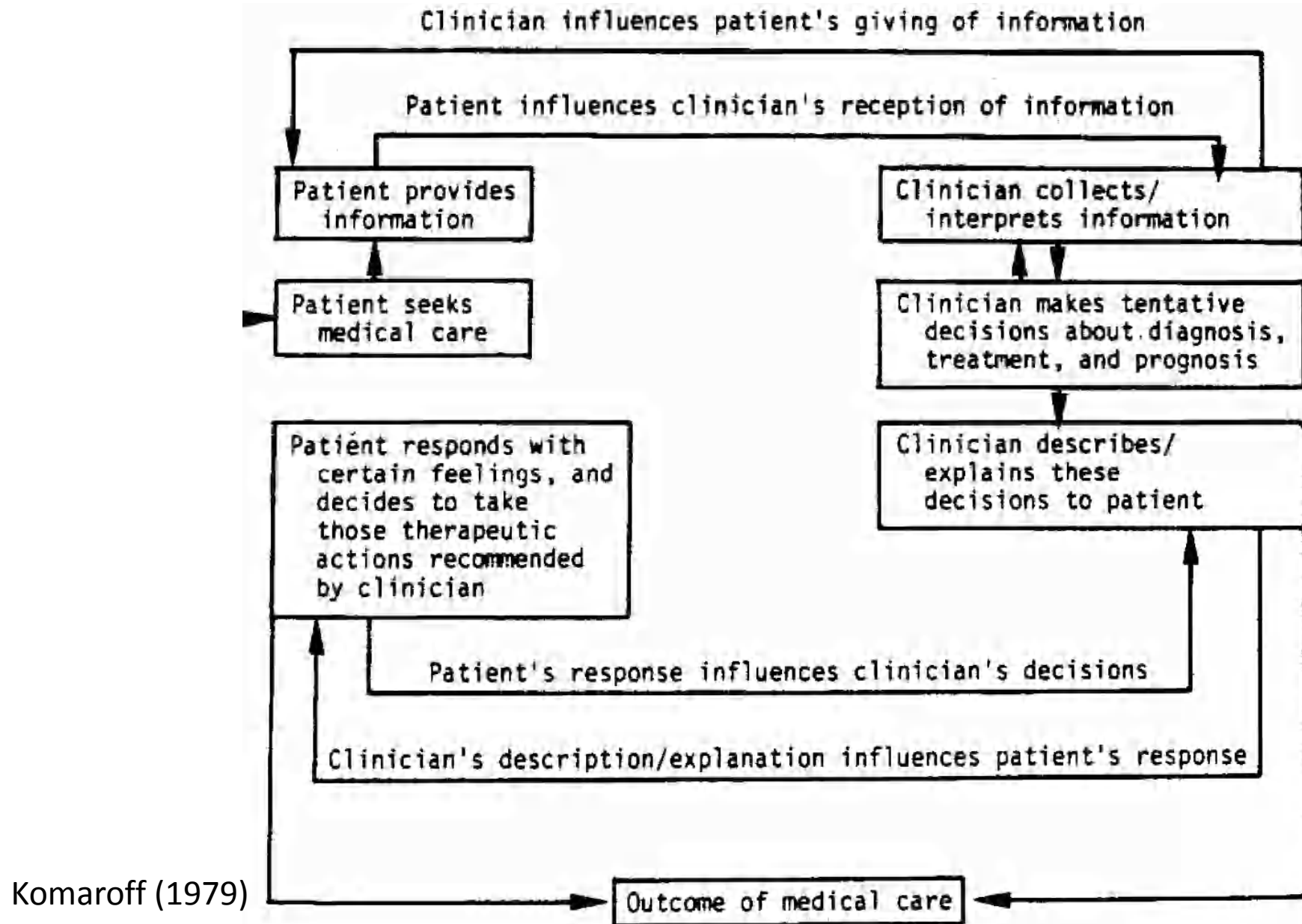
Brown, J. H. U. & Loweli, D. J. (1972) Standardization and Health Care.

IEEE Transactions on Biomedical Engineering, BME-19, 5, 331-334.

- Medical (clinical) data are defined and detected disturbingly “soft” ...
- ... having an obvious degree of **variability** and **inaccuracy**.
- Taking a medical history, the performance of a physical examination, the interpretation of laboratory tests, even the definition of diseases ... are surprisingly **inexact**.
- Data is defined, collected, and interpreted with a degree of variability and inaccuracy which falls far short of the standards **which engineers do expect from most data**.
- Moreover, standards might be **interpreted variably** by different medical doctors, different hospitals, different medical schools, different medical cultures, ...

Komaroff, A. L. (1979) The variability and inaccuracy of medical data.
Proceedings of the IEEE, 67, 9, 1196-1207.

The patient-clinician dialogue (from 1979)



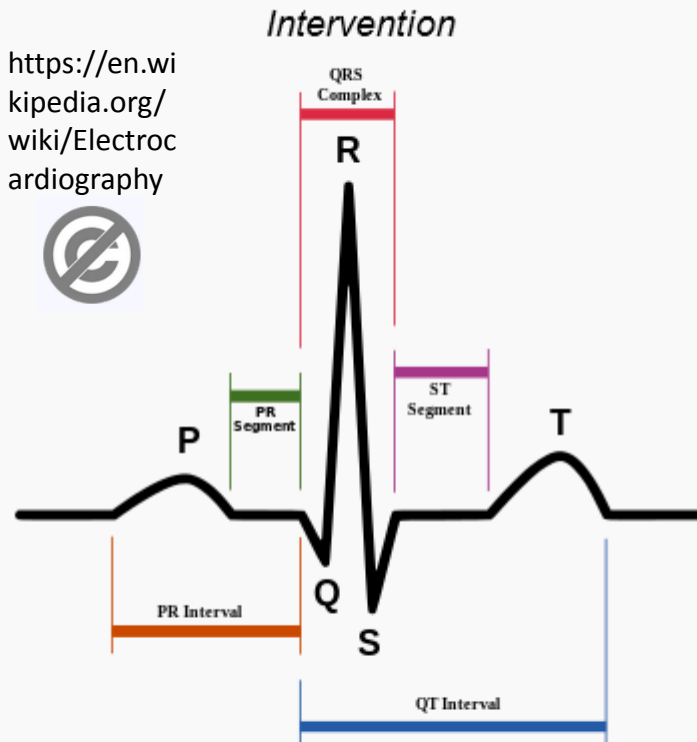
- ... ensures that information is interpreted by all users with the same understanding;
 - supports the reusability of the data,
 - improves the efficiency of healthcare services and
 - avoids errors by reducing duplicated efforts in data entry;
- Data standardization refers to
 - a) the data content;
 - b) the terminologies that are used to represent the data;
 - c) how data is exchanged; and
 - iv) how knowledge, e.g. clinical guidelines, protocols, decision support rules, checklists, standard operating procedures are represented in the health information system (refer to IOM).
- Elements for sharing require standardization of identification, record structure, terminology, messaging, privacy etc.
- The most used standardized data set to date is the **International Classification of Diseases (ICD)**, which was first adopted in 1900 for collecting statistics (Ahmadian et al. 2011)



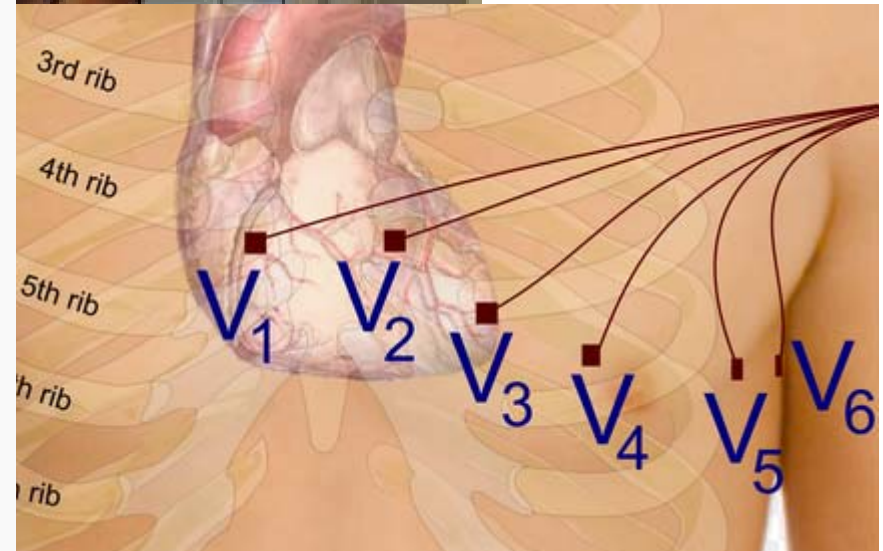
Example: ECG

Electrocardiography

<https://en.wikipedia.org/wiki/Electrocardiography>



ECG of a heart in normal sinus rhythm.



ICD-9-CM

89.52

MeSH

D004562

MedlinePlus

003868



- There has been a large number of ECG storage formats proclaiming to promote interoperability.
- There are three predominant ECG formats:
 - SCP-ECG (1993, European Standard, Binary data)
 - DICOM-ECG (2000, European Standard, Binary data)
 - HL7 aECG (2001, ANSI Standard, XML data)
- A mass of researchers have been proposing their own ECG storage formats to be considered for implementation (= proprietary formats).
- Binary has been the predominant method for storing ECG data

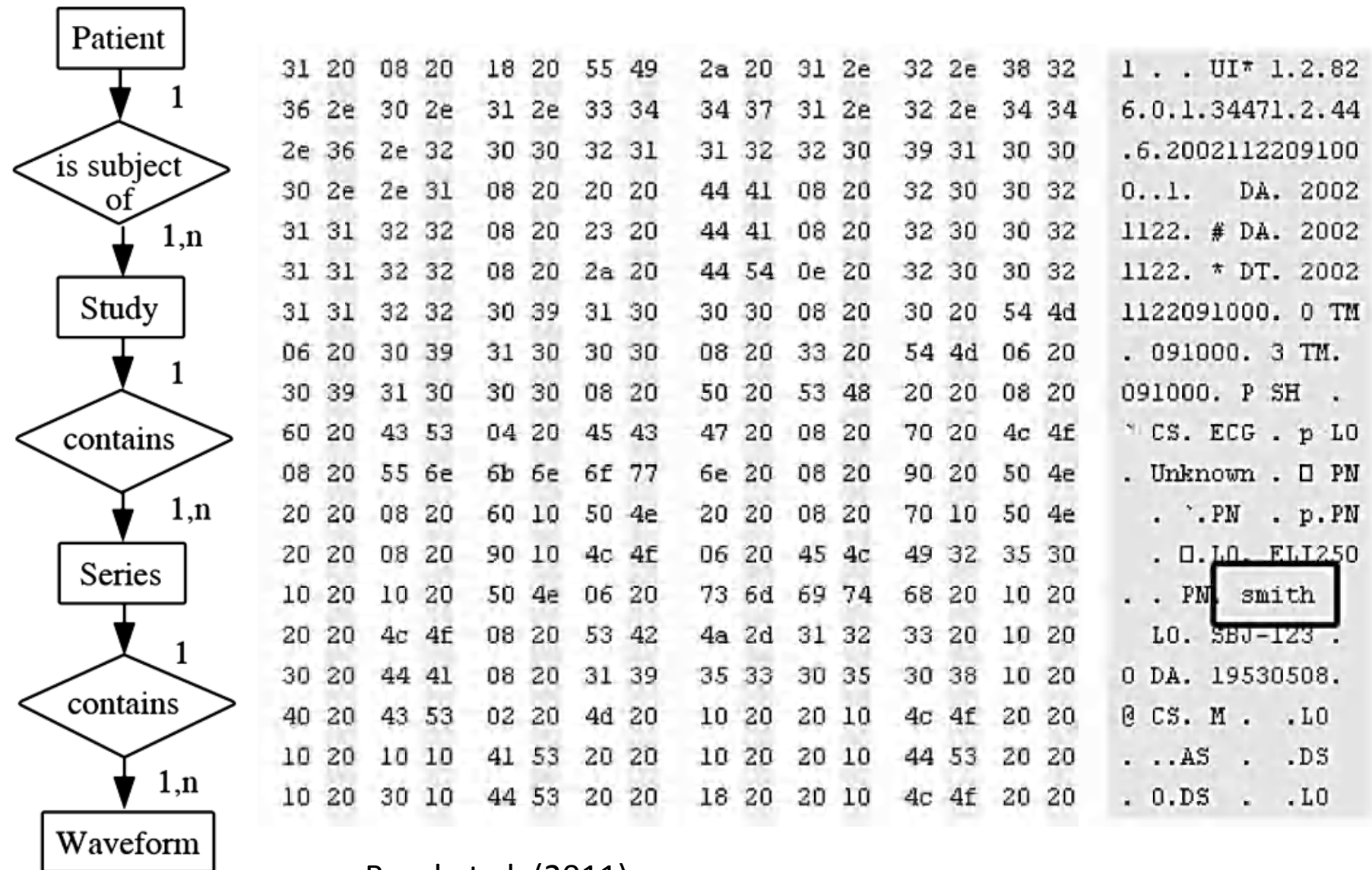
Bond, R. R., Finlay, D. D., Nugent, C. D. & Moore, G. (2011) A review of ECG storage formats. *International Journal of Medical Informatics*, 80, 10, 681-697.

■ Overview on current ECG storage formats

ECG format	Year	Method of implementation	Specification	Viewers
SCP-ECG	1993	BINARY	Can be freely downloaded from the Internet [7].	Freely available SCP-ECG Viewer made by EcgSoft [8].
DICOM-WS 30	2000	BINARY	Can be freely downloaded from the Internet [5].	Freely available DICOM-ECG viewer made by Charruasoft [9].
HL7 aECG	2001	XML	The XML Schema can be used as the specification or the implementation guide by AMPS [6].	Freely available aECG viewer by AMPS [10].
ecgML	2003	XML	Can be freely downloaded from the Internet [11].	None currently exist. Under development.
MFER	2003	BINARY	Can be freely downloaded from the Internet [12].	Freely available MFER viewer [13].
Philips XML	2004	XML	The specification is packaged with the actual product.	Philips viewer. Not freely available.
XML-ECG	2007	XML	Can be freely downloaded from the Internet [14].	XML-ECG viewer [14]. Not freely available.
mECGml	2008	XML	Can be freely downloaded from the Internet [15].	mECGml mobile viewer [15]. Not freely available.
ecgAware	2008	XML	Can be freely downloaded from the Internet [16].	TeleCardio viewer [16]. Not freely available.

Bond, R. R., Finlay, D. D., Nugent, C. D. & Moore, G. (2011) A review of ECG storage formats. *International Journal of Medical Informatics*, 80, 10, 681-697.

Example of a Binary ECG file



Bond et al. (2011)

```
<sequenceSet>

  <component>
    <sequence>
      <code code="TIME_ABSOLUTE" codeSystem="2.16.840.1.113883.5.4"
        codeSystemName="ActCode" displayName="Absolute Time"/>

      <value xsi:type="GLIST_TS">

        <head value="20021122091000.000"/>

        <increment value="0.002" unit="s"/>

      </value>
    </sequence>
  </component>

  <component>
```

Bond et al. (2011)

03 Knowledge Representation

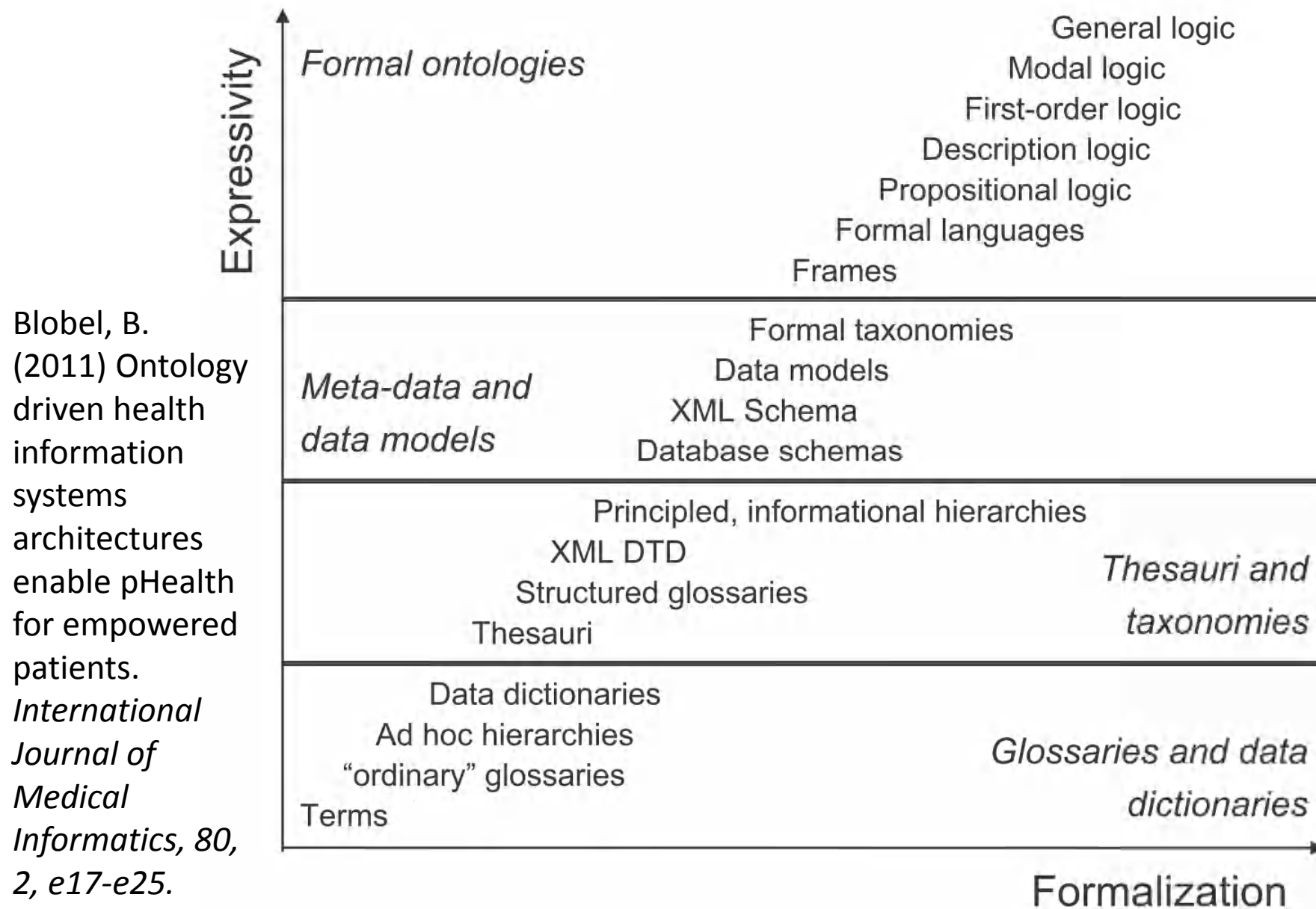
Examples for famous knowledge representations

Mathematical Logic	Psychology	Biology	Statistics	Economics
Aristotle				
Descartes				
Boole	James		Laplace	Bentham Pareto
Frege Peano			Bernoulli	Friedman
Goedel	Hebb	Lashley	Bayes	
Post	Bruner	Rosenblatt		
Church	Miller	Ashby	Tversky, Kahneman	Von Neumann
Turing	Newell, Simon	Lettvin		Simon
Davis		McCulloch, Pitts		Raiffa
Putnam		Heubel, Weisel		
Robinson				
Logic PROLOG	SOAR KBS, Frames	Connectionism	Causal Networks	Rational Agents

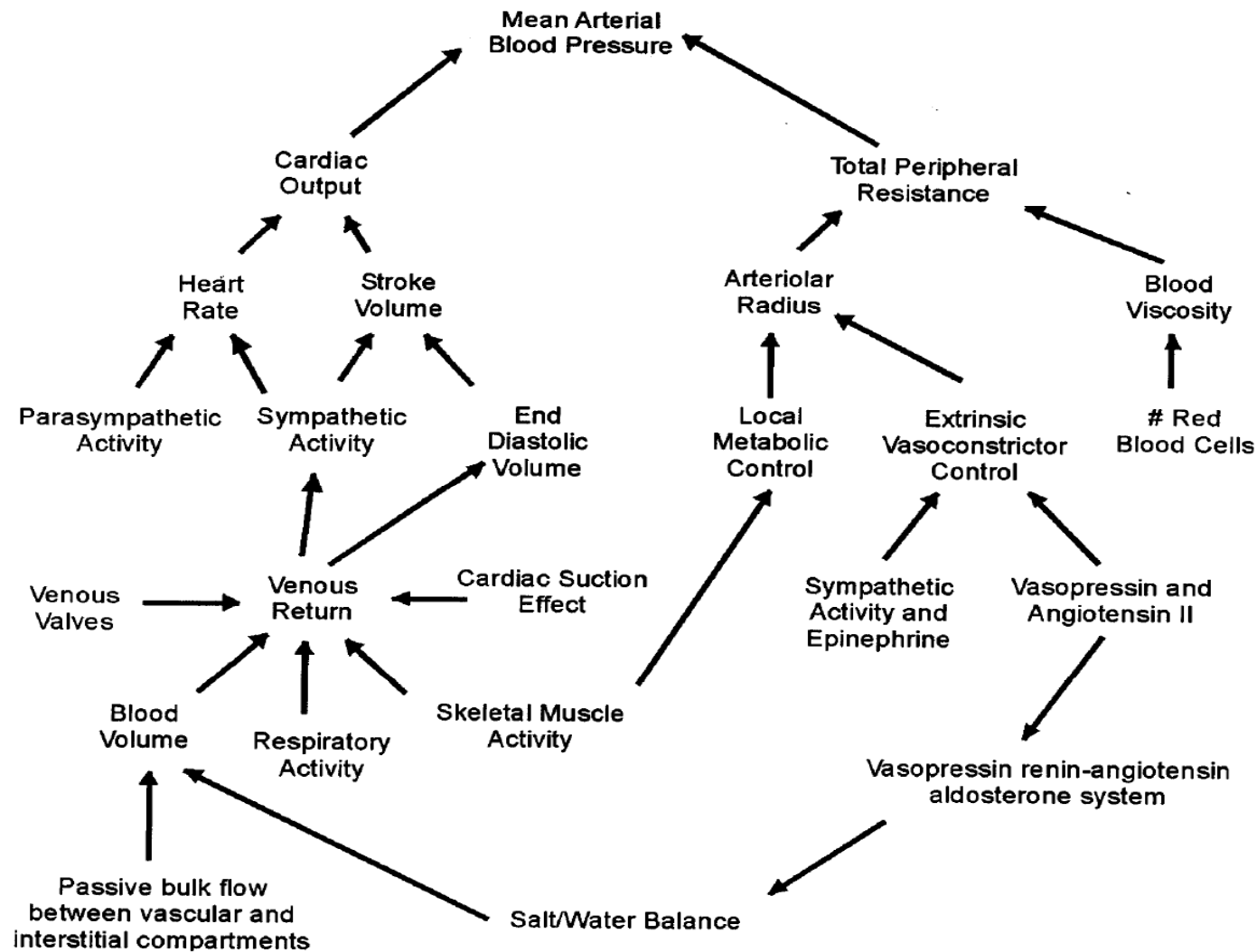
Davis, R., Shrobe, H. , Szolovits, P. 1993 What is a knowledge representation? AI Magazine, 14, 1, 17-33.



Formalization versus Expressivity

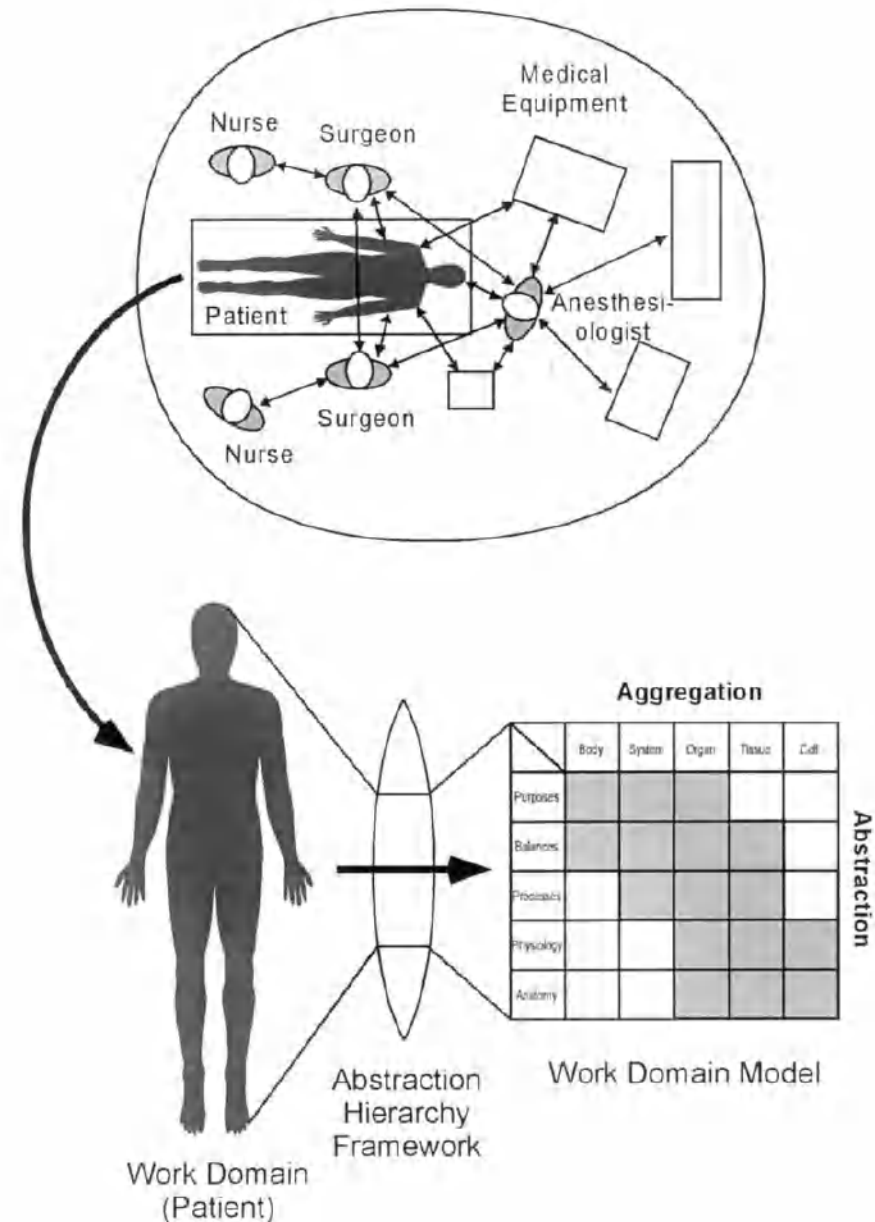


Example for Modeling of biomedical knowledge

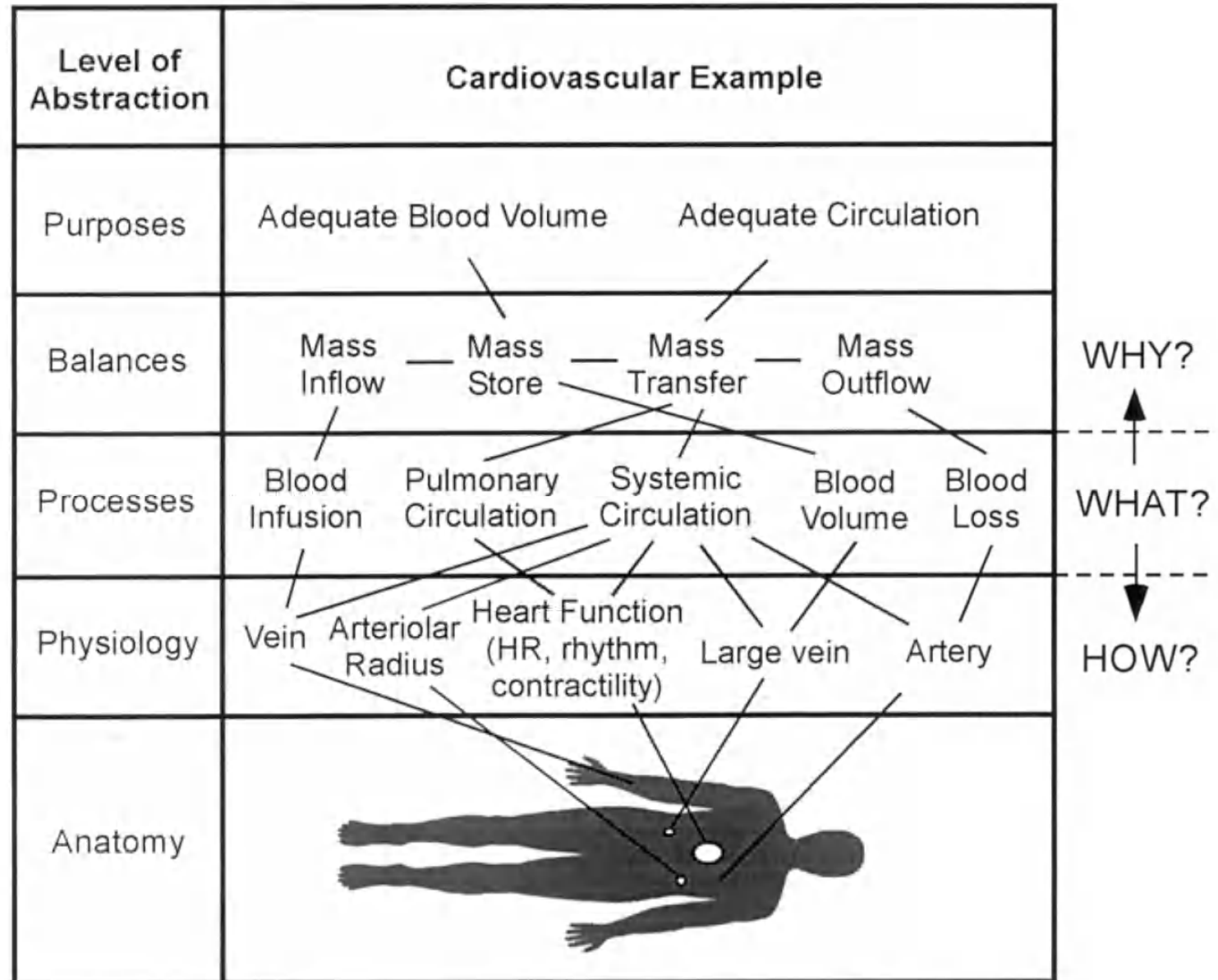


Hajdukiewicz, J. R., Vicente, K. J., Doyle, D. J., Milgram, P. & Burns, C. M. (2001) Modeling a medical environment: an ontology for integrated medical informatics design. *International Journal of Medical Informatics*, 62, 1, 79-99.

Hajdukiewicz, J. R.,
Vicente, K. J., Doyle, D.
J., Milgram, P. & Burns,
C. M. (2001) Modeling a
medical environment: an
ontology for integrated
medical informatics
design. *International
Journal of Medical
Informatics*, 62, 1, 79-99.



Partial abstraction of the cardiovascular system



Hajdukiewicz
et al. (2001)

WDM of: (a) the human body

a)

		Level of Aggregation				
Level of Abstraction		Body	System	Organ	Tissue	Cell
	Purposes	Homeostasis (Maintenance of Internal Environment)	Adequate Circulation, Blood Volume, Oxygenation, Ventilation	Adequate Organ Perfusion, Blood Flow	Adequate Tissue Oxygenation and Perfusion	Adequate Cellular Oxygenation and Perfusion
	Balances	Balances: Mass and Energy Inflow, Storage, and Outflow ★	System Balances: Mass and Energy Inflow, Storage, Outflow, and Transfer ★	Organ Balances: Mass and Energy Inflow, Storage, Outflow, and Transfer ★	Tissue Balances: Mass and Energy Inflow, Storage, Outflow, and Transfer ★	Cellular Balances: Mass and Energy Inflow, Storage, Outflow, and Transfer ★
	Processes	Total Volume of Body Fluid, Temperature, Supply: O ₂ , Fluids, Nutrients, Sink: CO ₂ , Fluids, Wastes	Circulation, Oxygenation, Ventilation, Circulating Volume	Perfusion Pressure, Organ Blood Flow, Vascular Resistance	Tissue Oxygenation, Respiration, Metabolism	Cell Metabolism, Chemical Reaction, Binding, Inflow, Outflow
	Physiology		System Function	Organ Function	Tissue Function	Cellular Function
	Anatomy			Organ Anatomy	Tissue Anatomy	Cellular Anatomy

★ Balances include: Water, Salt, Electrolytes, pH, O₂, CO₂

Hajdukiewicz
et al. (2001)

WDM of: (b) the cardiovascular system

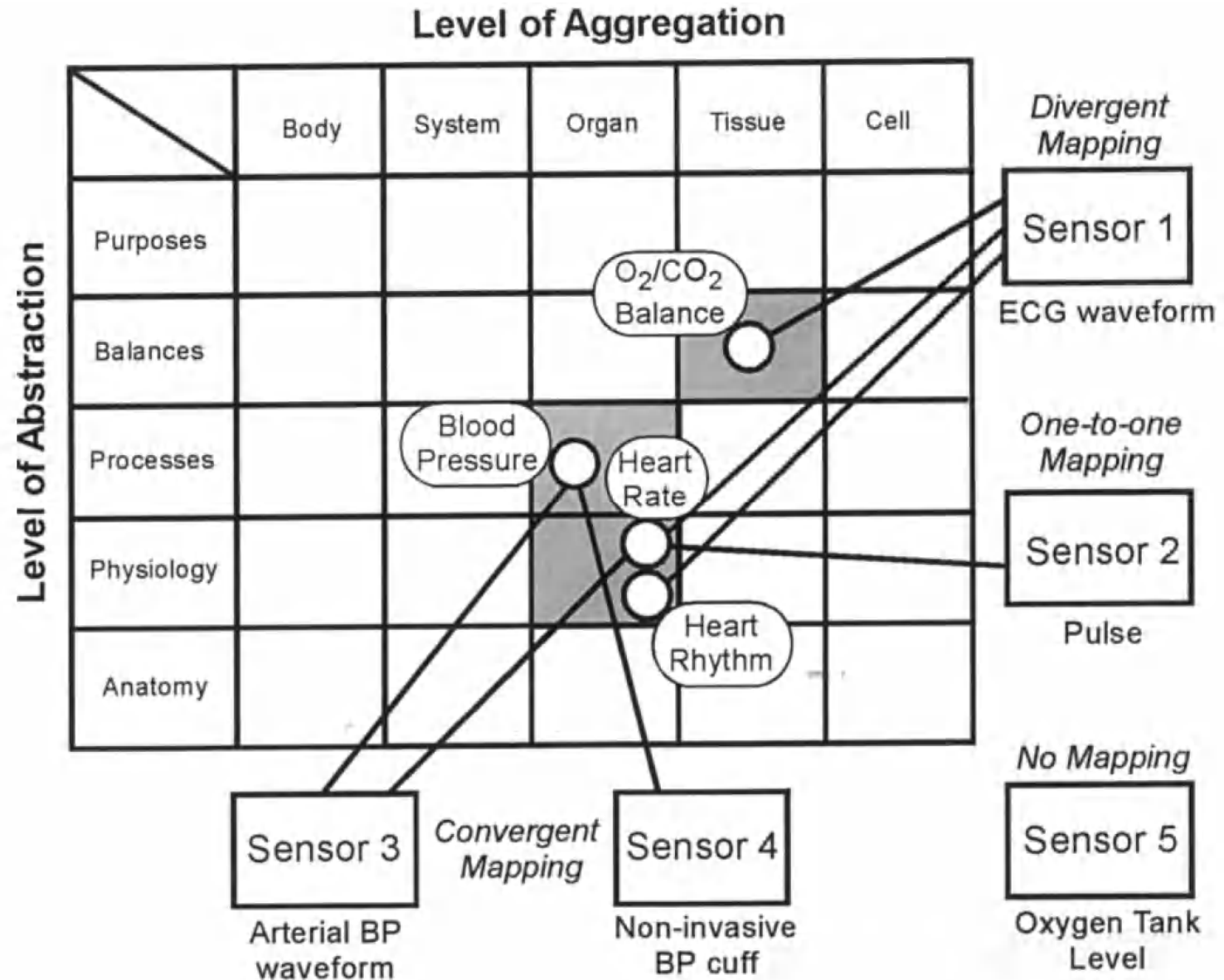
b)

	System	Subsystem	Organ	Component
Purposes	Adequate Circulation and Blood Volume			
Balances	Cardiovascular System: Mass Inflow, Storage, and Outflow	Pulmonary and Systemic Systems: Balance Mass Flows; Mass Inflow, Storage, Outflow, and Transfer	Organ Vascular Network: Balance Mass Flows; Mass Inflow, Storage, Outflow, and Transfer	Vascular Components: Balance Mass Flows, Mass Inflow, Storage, Outflow, and Transfer
Processes	Circulation, Volume, Fluid Supply and Sink	Pulmonary and Systemic Circulation (Pressure, Flow, Resistance) and Volume, Fluid Supply and Sink	Cardiac Output, Organ Circulation (Pressure, Flow, Resistance), Fluid Supply and Sink from each Vascular Network	Circulation through Vascular Components (Pressure, Flow, Resistance), Vascular Blood Volume, Fluid Supply and Sink
Physiology	Cardiovascular System Function	Pulmonary and Systemic System Function	Cardiac Function (Heart Rate, Rhythm)	Atrial and Ventricular Function; Arterial, Arteriolar, Capillary, Venule, Venous Function
Anatomy			Cardiac Anatomy	Atrial, Ventricular, and Vascular Anatomy

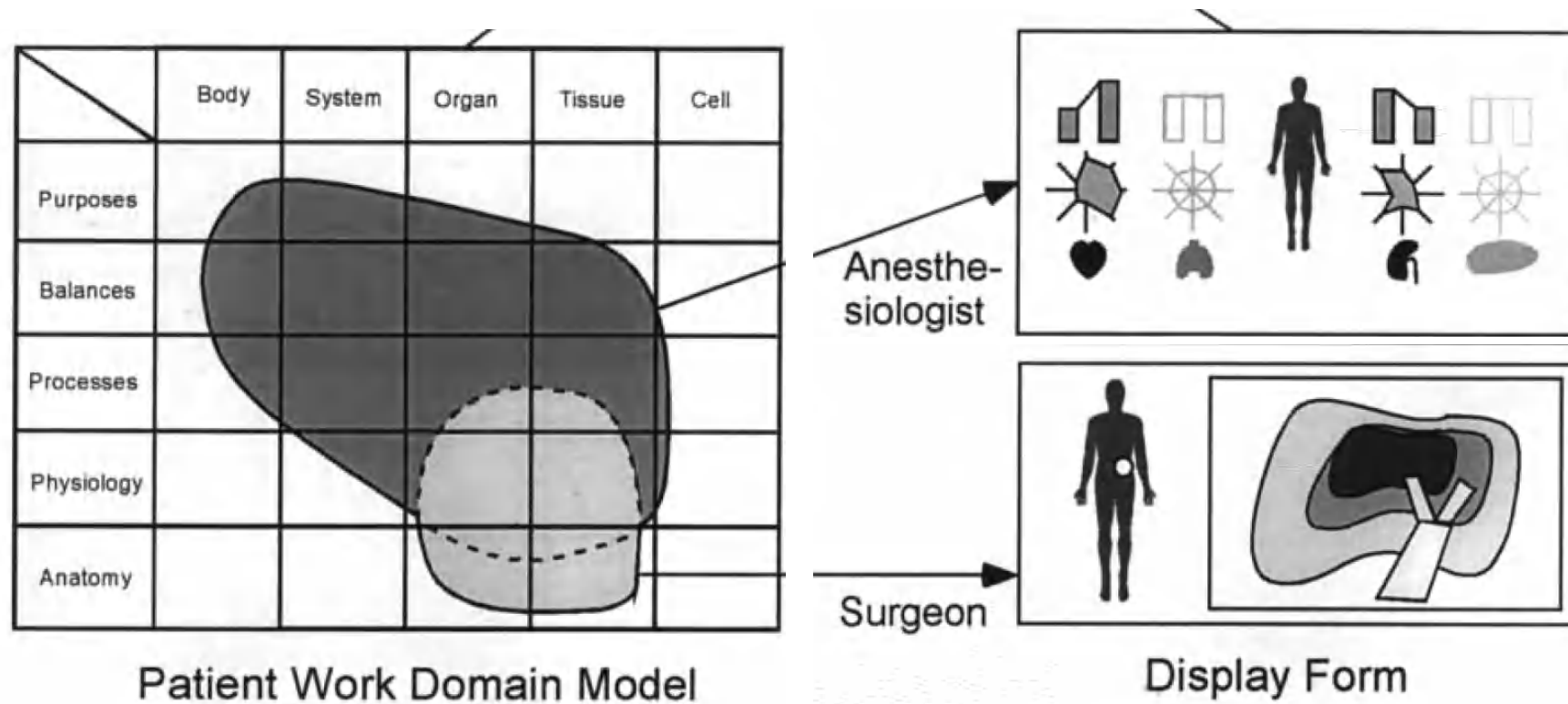
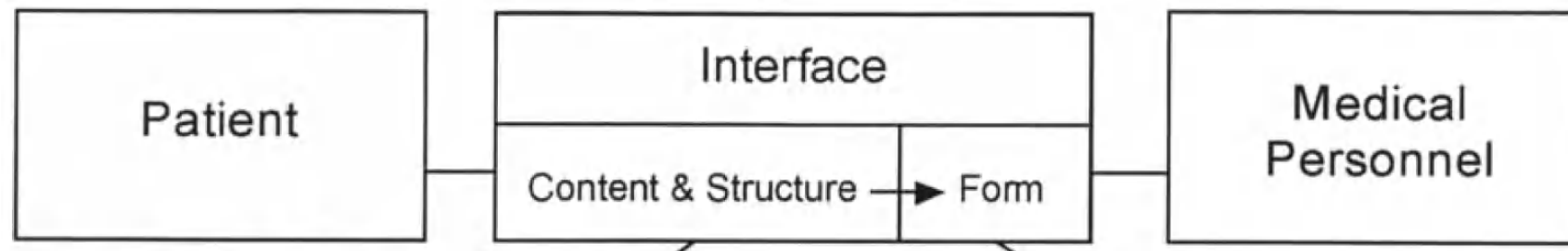
Level of Abstraction

Hajdukiewicz et al. (2001)

Example: Mapping OR sensors onto the WDM



Hajdukiewicz
et al. (2001)



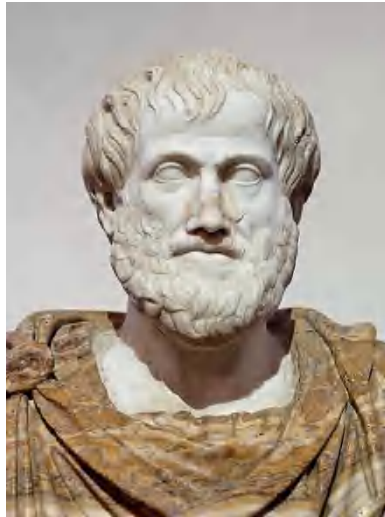
Hajdukiewicz et al. (2001)

04 Ontologies

A simple question: What is a Jaguar?

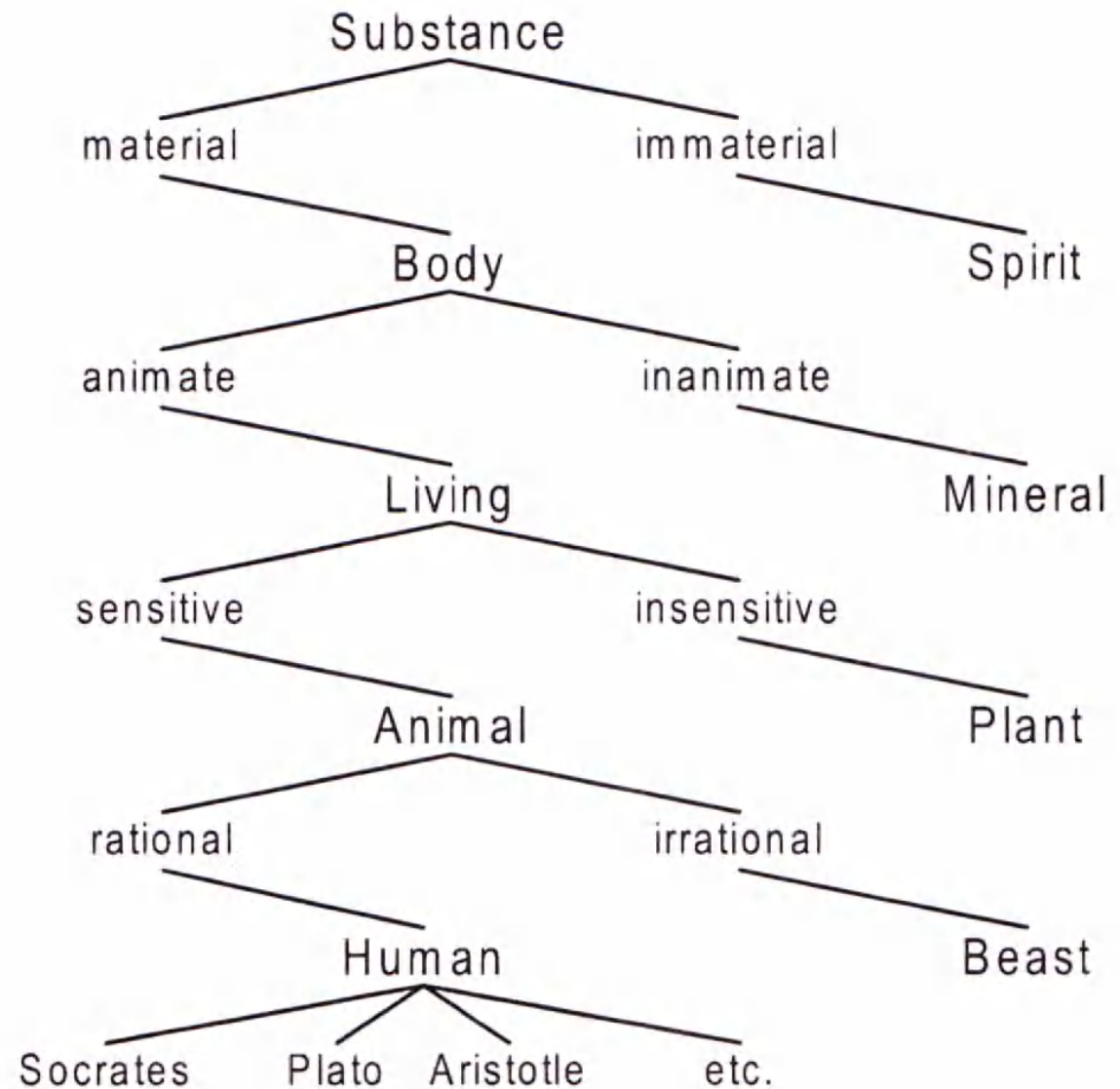


The first “Ontology of what exists”



* 384 BC † 322 BC

Simonet, M., Messai, R., Diallo, G. & Simonet, A. (2009) Ontologies in the Health Field. In: Berka, P., Rauch, J. & Zighed, D. A. (Eds.) *Data Mining and Medical Knowledge Management: Cases and Applications*. New York, Medical Information Science Reference, 37-56.

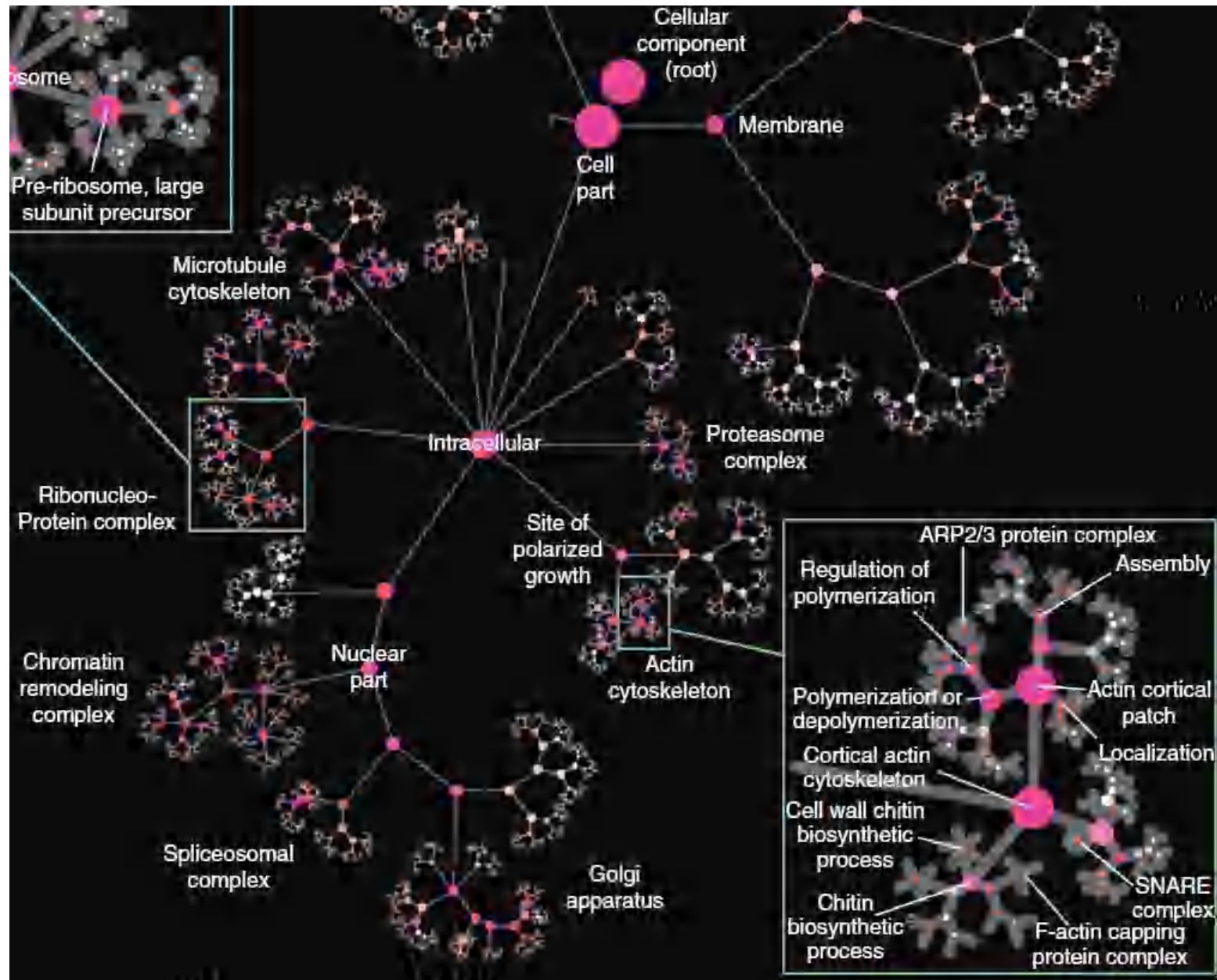


Later: Porphyry (≈ 234-305) ☐ tree

- Aristotle attempted to **classify the things in the world** - where it is employed to describe the existence of beings in the world;
- Artificial Intelligence and Knowledge Engineering deals also with **reasoning about models of the world**.
- Therefore, AI researchers adopted the term 'ontology' to describe **what can be computationally represented** of the world within a program.
- **“An ontology is a formal, explicit specification of a shared conceptualization”.**
 - A 'conceptualization' refers to an **abstract model** of some phenomenon in the world by having identified the relevant concepts of that phenomenon.
 - 'Explicit' means that the type of concepts used, and the constraints on their use are **explicitly defined**.

Studer, R., Benjamins, V. R. & Fensel, D. (1998) Knowledge Engineering: Principles and methods. *Data & Knowledge Engineering*, 25, 1-2, 161-197.

Example: Network-Extracted Ontology of human cell

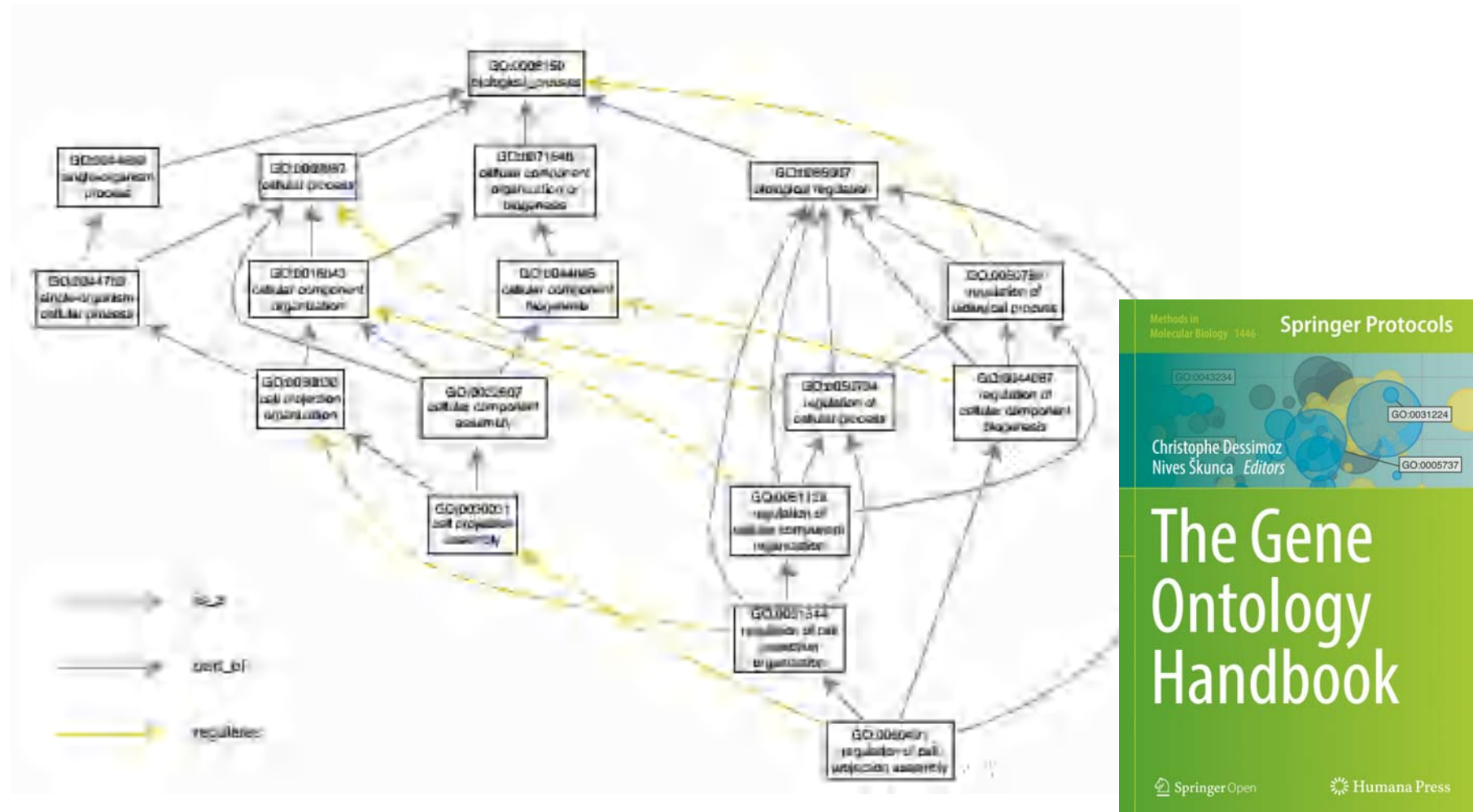


<http://www.kurzweilai.net/images/cell-model.png>

(Credit: UC San Diego School of Medicine)

Example: GO

<http://geneontology.org/>



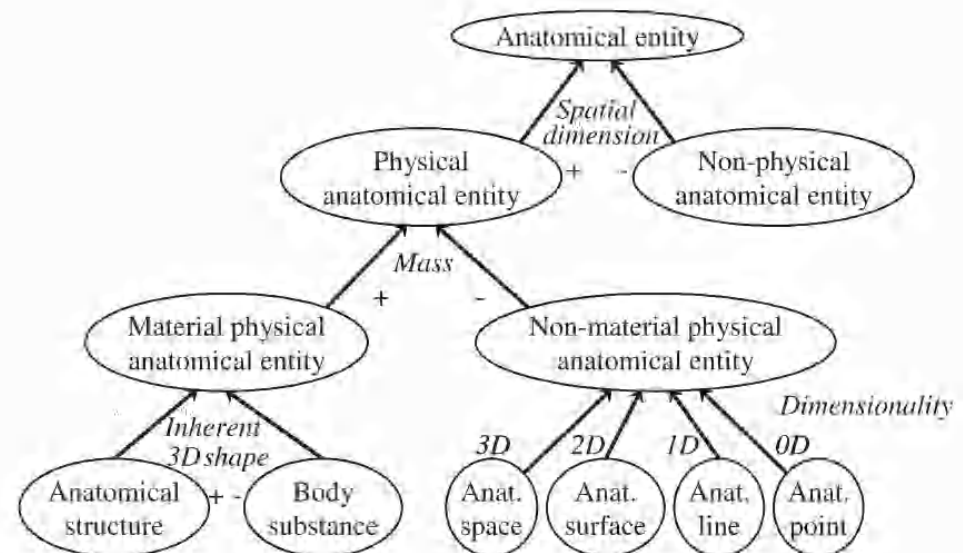
Hastings, J. 2017. Primer on Ontologies. In: Dessimoz, C. & Škunca, N. (eds.) The Gene Ontology Handbook. New York, NY: Springer New York, pp. 3-13, doi:10.1007/978-1-4939-3743-1_1.

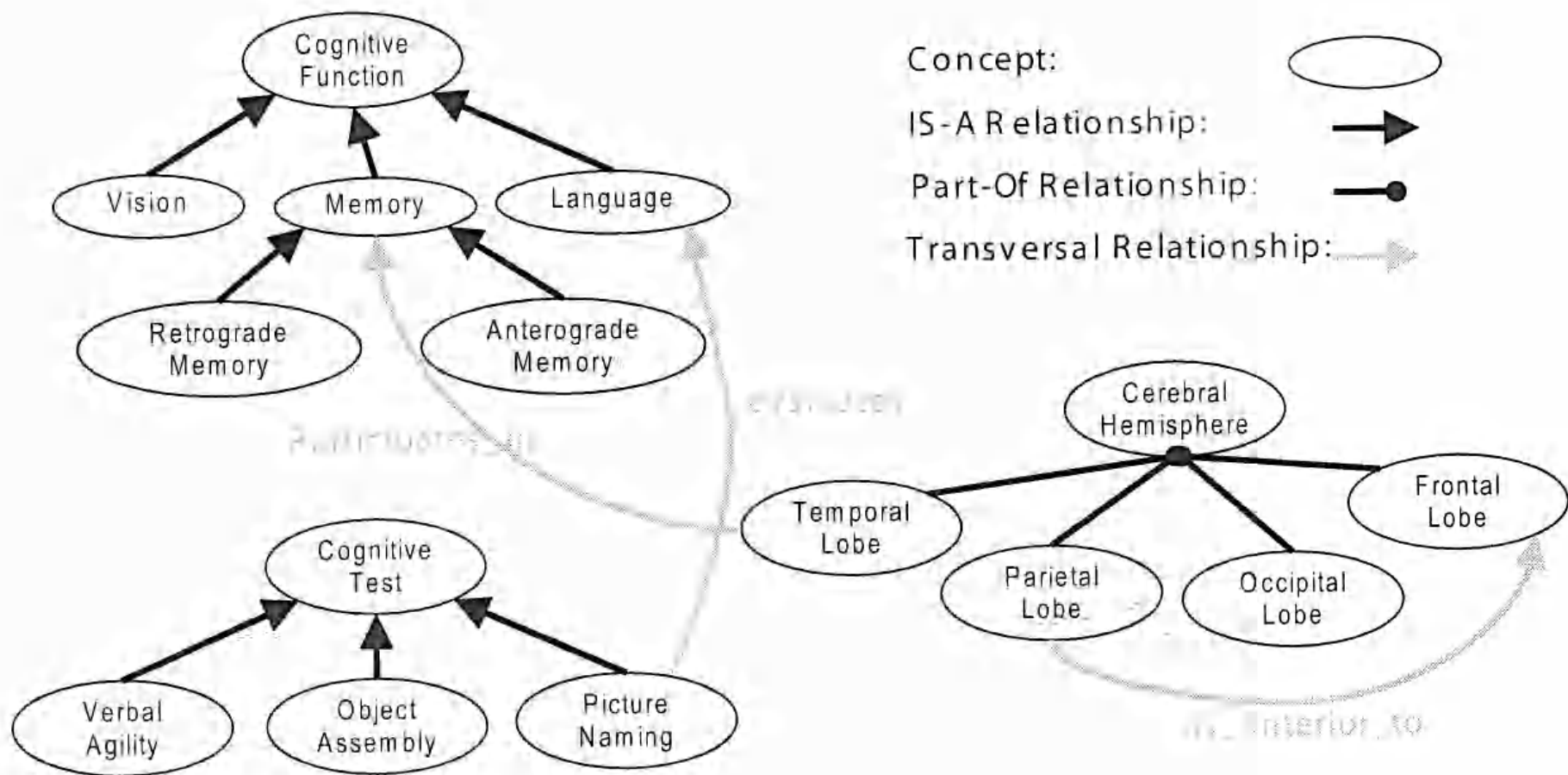
- Ontology = a structured description of a domain in form of **concepts** \leftrightarrow **relations**;
- The **IS-A relation** provides a taxonomic skeleton;
- Other relations reflect the **domain semantics**;
- Formalizes the **terminology** in the domain;
- Terminology = terms definition and usage in the specific **context**;
- Knowledge base = **instance classification** and **concept classification**;
- Classification provides the **domain terminology**
- ...

Additionally an ontology may satisfy:

- (1) In addition to the IS-A relationship, partitive (meronomic) relationships may hold between concepts, denoted by PART-OF. Every PART-OF relationship is irreflexive, asymmetric and transitive. IS-A and PART-OF are also called hierarchical relationships.
- (2) In addition to hierarchical relationships, associative relationships may hold between concepts. Some associative relationships are domain-specific (e.g., the branching relationship between arteries in anatomy and rivers in geography).
- (3) Relationships r and r' are inverses if, for every pair of concepts x and y , the relations (x, r, y) and (y, r', x) hold simultaneously. A symmetric relationship is its own inverse. Inverses of hierarchical relationships are called INVERSE-IS-A and HAS-PART, respectively.
- (4) Every non-taxonomic relation of x to z , (x, r, z) , is either inherited $(\{y, r, z\})$ or refined $(\{y, r, z'\})$ where z' is more specific than z by every child y of x . In other words, every child y of x has the same properties (z) as its parent or more specific properties (z').

Zhang, S. & Bodenreider, O. 2006. Law and order: Assessing and enforcing compliance with ontological modeling principles in the Foundational Model of Anatomy. *Computers in Biology and Medicine*, 36, (7-8), 674-693.





Simonet, M., Messai, R., Diallo, G. & Simonet, A. (2009) Ontologies in the Health Field. In: Berka, P., Rauch, J. & Zighed, D. A. (Eds.) *Data Mining and Medical Knowledge Management: Cases and Applications*. New York, Medical Information Science Reference, 37-56.

Examples of Biomedical Ontologies

Name	Ref.	Scope	# concepts	# concept names				Subs. Hier.	Version / Notes
				Min	Max	Med	Avg		
SNOMED CT	[21]	Clinical medicine (patient records)	310,314	1	37	2	2.57	yes	July 31, 2007
LOINC	[24]	Clinical observations and laboratory tests	46,406	1	3	3	2.85	no	Version 2.21 (no "natural language" names)
FMA	[25]	Human anatomical structures	~72,000	1	?	?	~1.50	yes	(not yet in the UMLS)
Gene Ontology	[28]	Functional annotation of gene products	22,546	1	24	1	2.15	yes	Jan. 2, 2007
RxNorm	[31]	Standard names for prescription drugs	93,426	1	2	1	1.10	no	Aug. 31, 2007
NCI Thesaurus	[34]	Cancer research, clinical care, public information	58,868	1	100	2	2.68	yes	2007_05E
ICD-10	[36]	Diseases and conditions (health statistics)	12,318	1	1	1	1.00	no	1998 (tabular)
MeSH	[38]	Biomedicine (descriptors for indexing the literature)	24,767	1	208	5	7.47	no	Aug. 27, 2007
UMLS Meta.	[41]	Terminology integration in the life sciences	1,4 M	1	339	2	3.77	n/a	2007AC (English only)

Bodenreider, O. (2008) Biomedical ontologies in action: role in knowledge management, data integration and decision support. *Methods of Information In Medicine*, 47, Supplement 1, 67-79.

- **1) Graph notations**
 - Semantic networks
 - Topic Maps (ISO/IEC 13250)
 - Unified Modeling Language (UML)
 - Resource Description Framework (RDF)
- **2) Logic based**
 - Description Logics (e.g., OIL, DAML+OIL, OWL)
 - Rules (e.g. RuleML, LP/Prolog)
 - First Order Logic (KIF – Knowledge Interchange Format)
 - Conceptual graphs
 - (Syntactically) higher order logics (e.g. LBase)
 - Non-classical logics (e.g. Flogic, Non-Mon, modalities)
- **3) Probabilistic/fuzzy**

Example for (1) Graphical Notation: RDF

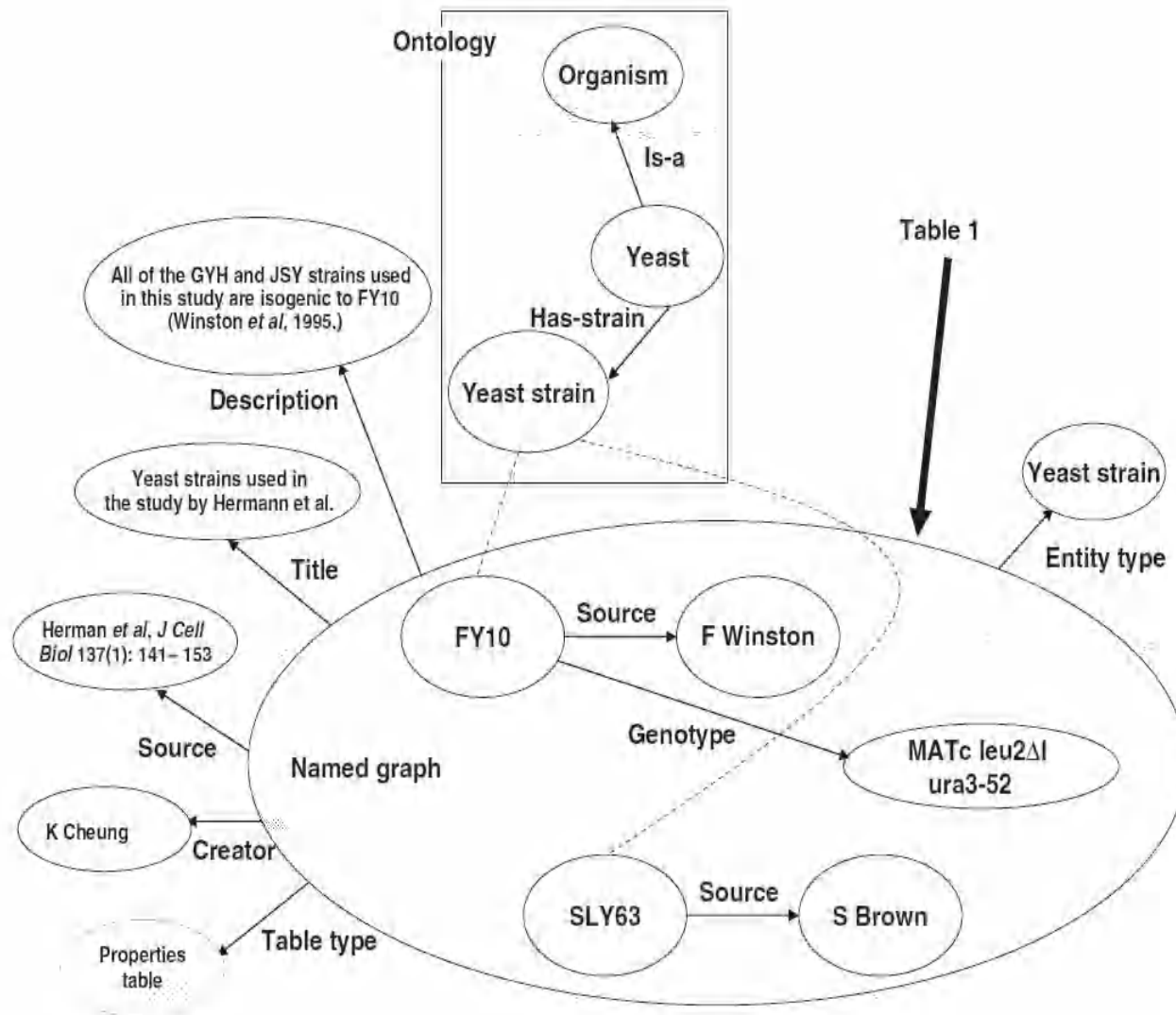


Table 1. Two strains used in the study by Hermann et al. (1997)

Name	Genotype*	Source
FY10	MAT ⁺ leu2ΔI ura3-52	F Winston
FY22	MAT ⁺ his3Δ200 ura3-52	F Winston
GHY1	MAT ⁺ leu2ΔI his3Δ200 ura3-52 his3Δ20-1	This study
JSY707	MAT ⁺ his3Δ200 ura3-52 tpm1D::HIS3	This study
JSY948	MAT ⁺ leu2ΔI leu2ΔI ura3-52 ura3-52	This study
JSY929	MAT ⁺ leu2ΔI his3Δ200 ura3-52	This study
JSY1065	MAT ⁺ leu2ΔI his3Δ200 ura3-52 mdm20D::LEU2	This study
JSY1094	MAT ⁺ leu2ΔI his3Δ200 ura3-52 tpm1D::HIS3	This study
JSY1138	MAT ⁺ leu2ΔI leu2ΔI his3Δ200 ura3-52 ura3-52/ura3-52 tpm1D::HIS3 + mdm20D::LEU2	This study
JSY1185	MAT ⁺ leu2ΔI his3Δ200 ura3-52 tpm2D::HIS3	This study
JSY1340	MAT ⁺ leu2ΔI his3Δ200 ura3-52 mdm20D::LEU2	This study
JSY1374	MAT ⁺ leu2ΔI leu2ΔI his3Δ200 his3Δ200 ura3-52/ura3-52 tpm2D::HIS3 + mdm20D::LEU2	This study
JSY1249	MAT ⁺ leu2-3,11.2 ura3-52 his3Δ01 ade3-101 ade5 hem2 10	A. Reysche
JSY1	MAT ⁺ leu2-3,11.2 his3Δ200 ura3-52 his2-901	A. Adams
SLY63	MAT ⁺ leu2-3,11.2 ura3-52 tpm1D::HIS3 tpm2D::LEU2	S Brown

Cheung, K.-H., Samwald, M., Auerbach, R. K. & Gerstein, M. B. 2010. Structured digital tables on the Semantic Web: toward a structured digital literature. *Molecular Systems Biology*, 6, 403.

Example for (2) Web Ontology Language OWL

DL = Description Logic

Axiom	DL syntax	Example
Sub class	$C_1 \sqsubseteq C_2$	Alga \sqsubseteq Plant \sqsubseteq Organism
Equivalent class	$C_1 \equiv C_2$	Cancer \equiv Neoplastic Process
Disjoint with	$C_1 \sqsubseteq \neg C_2$	Vertebrate $\sqsubseteq \neg$ Invertebrate
Same individual	$x_1 \equiv x_2$	Blue_Shark \equiv Prionace_Glauca
Different from	$x_1 \sqsubseteq \neg x_2$	Sea Horse $\sqsubseteq \neg$ Horse
Sub property	$P_1 \sqsubseteq P_2$	has_mother \sqsubseteq has_parent
Equivalent property	$P_1 \equiv P_2$	treated_by \equiv cured_by
Inverse	$P_1 \equiv P_2^-$	location_of \equiv has_location ⁻
Transitive property	$P^+ \sqsubseteq P$	part_of ⁺ \sqsubseteq part_of
Functional property	$\top \sqsubseteq \leq 1P$	$\top \sqsubseteq \leq 1$ has_tributary
Inverse functional property	$\top \sqsubseteq \leq 1P^-$	$\top \sqsubseteq \leq 1$ has_scientific_name ⁻

Concept equivalence
Speak: C1 is equivalent to C2

Concept inclusion,
Speak: All C1 are C2

Bhatt, M., Rahayu, W., Soni, S. P. & Wouters, C. (2009) Ontology driven semantic profiling and retrieval in medical information systems. *Web Semantics: Science, Services and Agents on the World Wide Web*, 7, 4, 317-331.

Constructor	DL syntax	Example
Intersection	$C_1 \sqcap \dots \sqcap C_n$	Anatomical_Abnormality \sqcap Pathological_Function
Union	$C_1 \sqcup \dots \sqcup C_n$	Body_Substance \sqcup Organic_Chemical
Complement	$\neg C$	\neg Invertebrate
One of	$x_1 \sqcup \dots \sqcup x_n$	Oestrogen \sqcup Progesterone
All values from	$\forall P.C$	\forall co_occurs_with.Plant
Some values	$\exists P.C$	\exists co_occurs_with.Animal
Max cardinality	$\leq nP$	≤ 1 has_ingredient
Min cardinality	$\geq nP$	≥ 2 has_ingredient

Intersection/conjunction of concepts,
Speak: C1 and ... Cn

Universal Restriction
Speak: All P-successors are in C

Existential Restriction
Speak: An P-successor exists in C

Bhatt et al. (2009)

05 Medical Classifications

Ordo secundum queni **METHODI** exhibentur.

U- NI- VER- SA- LES	Fruſu	I CÆSALPINI	pag. 1
		II MORISONI	11
		III RAJI	86
		IV KNAUTHII	106
		V HERMANNI	124
		VI BOENHAAVEN	157
	Corol- le	VII RIVINI	181
		VIII RUPPII	233
		IX LUDWIGII	264
		X KNAUTI	297
	Flora	XI TOURNEFORTII	319
		XII PONTEDERÆ	360
M-E- T-H-O- D-I	Calyce	XIII MAGNOLII	377
		XIV NOSTRA	405
	Gemmae	XV LINNÆI	441
		XVI FRAGMENT	515
	Fructificatione	XVII VAILLANTII	517
		XVIII PONTEDERÆ	525
	Compositorum	XIX ARTEDI	531
		XX MORISONI	533
	Umbelliferorum	XXI RAJI	551
		XXII SCHEUCHZERI	559
P-A- R-T-I- A- L-E-S	Gemmae	CAROLI LINNÆI	
		SIC REXI MITHI SVETIA ARCHIATRI; MEDIC. & BOTAN. PROFESS. UPSAL; EQUITIS AUR. DE STELLA POLARI; SOC. NON ACAD. IMPER. MONSIE. BEROL. TOLOS. UPSAL. STOKH. SOC. & PARIS. COESES.	
	Muscorum	SPECIES	
		PLANTARUM,	
Fungorum	Filicam	EXHIBENTES	
		PLANTAS RITE COGNITAS, AD GENERA RELATAS, CUM	

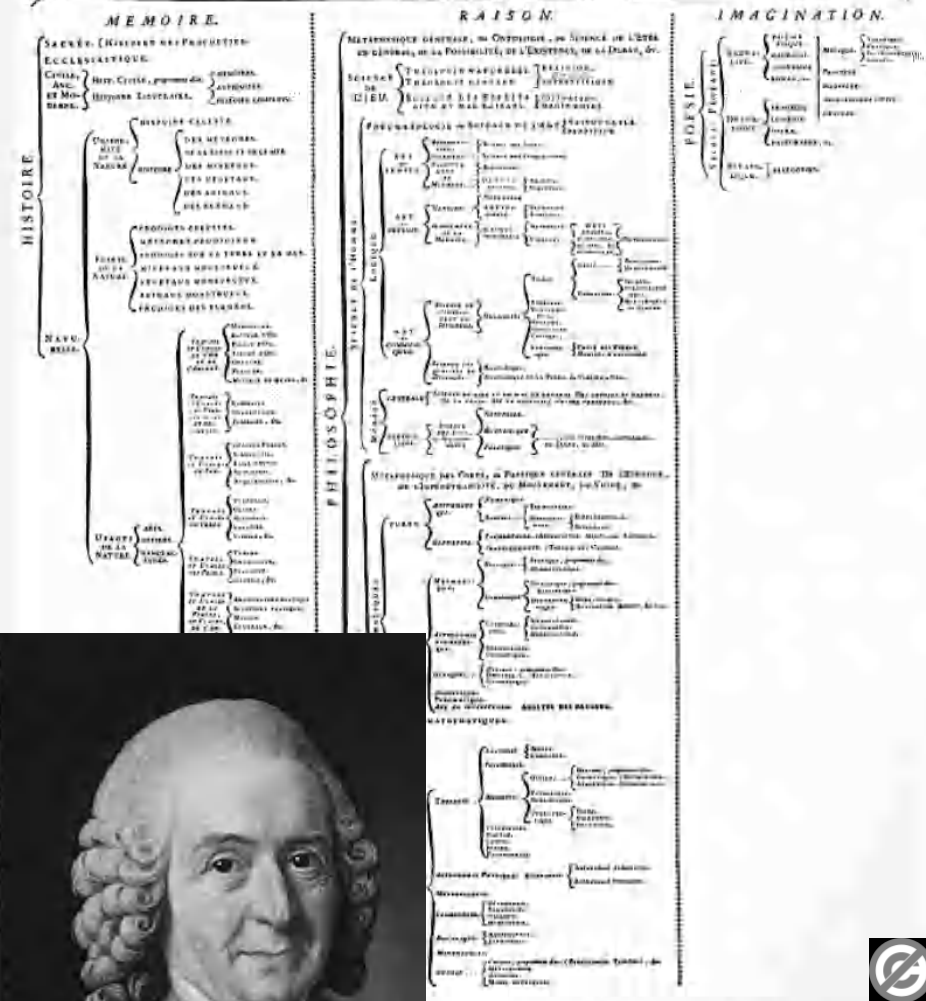
CAROLI LINNÆI
SIC REXI MITHI SVETIA ARCHIATRI; MEDIC. & BOTAN.
PROFESS. UPSAL; EQUITIS AUR. DE STELLA POLARI;
SOC. NON ACAD. IMPER. MONSIE. BEROL. TOLOS.
UPSAL. STOKH. SOC. & PARIS. COESES.

**SPECIES
PLANTARUM,**

EXHIBENTES
PLANTAS RITE COGNITAS,
AD
GENERA RELATAS,
CUM

***SYSTÈME FIGURÉ
DES CONNOISSANCES HUMAINES.**

ENTENDEMENT.



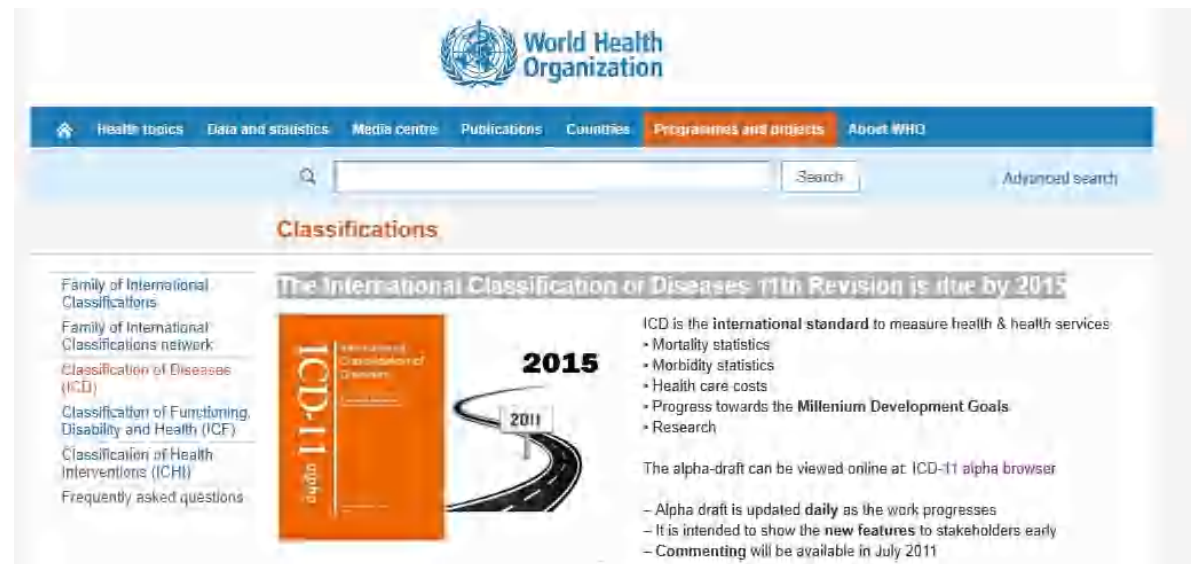
- Since the classification by Carl von Linne (1735) approx. 100+ various classifications in use:
 - International **C**lassification of **D**iseases (ICD)
 - **S**ystematized **N**omenclature of **M**edicine (SNOMED)
 - **M**edical **S**ubject **H**eadings (MeSH)
 - **F**oundational **M**odel of **A**natomy (FMA)
 - **G**ene **O**ntology (GO)
 - **U**nified **M**edical **L**anguage **S**ystem (UMLS)
 - **L**ogical **O**bservation **I**dentifiers **N**ames & **C**odes (LOINC)
 - **N**ational **C**ancer **I**nstitute **T**hesaurus (NCI Thesaurus)



The screenshot shows the WHO Classifications website. At the top is the WHO logo and the text "World Health Organization". Below this is a navigation bar with links: "Health topics", "Data and statistics", "Media centre", "Publications", "Countries", "Programmes and projects", and "About". A search bar is located below the navigation bar. The main heading is "Classifications". On the left is a sidebar with links: "Family of International Classifications", "Family of International Classifications network", "Classification of Diseases (ICD)", "Classification of Functioning, Disability and Health (ICF)", "Classification of Health Interventions (CHI)", and "Frequently asked questions". The main content area features the heading "International Classification of Diseases (ICD)" followed by a paragraph: "ICD-10 was endorsed by the Forty-third World Health Assembly in May 1990 and came into use in WHO Member States as from 1994. The classification is the latest in a series which has its origins in the 1850s. The first edition, known as the International List of Causes of Death, was adopted by the International Statistical Institute in 1893. WHO took over the responsibility for the ICD at its creation in 1948 when the Sixth Revision, which included causes of morbidity for the first time, was published. The World Health Assembly adopted in 1967 the WHO Nomenclature Regulations that stipulate use of ICD in its most current revision for mortality and morbidity statistics by all Member States."

<http://www.who.int/classifications/icd/en>

- 1629 London Bills of Mortality
- 1855 **William Farr** (London, one founder of medical statistics): List of causes of death, list of diseases
- 1893 von Jacques Bertillot: List of causes of death
- 1900 International Statistical Institute (ISI) accepts Bertillot's list
- 1938 5th Edition
- 1948 WHO
- 1965 ICD-8
- 1989 ICD-10
- 2015 ICD-11 due
- 2018 ICD-11 adopt



- 1965 SNOP, 1974 SNOMED, 1979 SNOMED II
- 1997 (Logical Observation Identifiers Names and Codes (LOINC) integrated into SNOMED
- 2000 SNOMED RT, 2002 SNOMED CT



<http://www.isb.nhs.uk/documents/isb-0034/amd-26-2006/techrefguid.pdf>

A

```
24184005|Finding of increased blood pressure (finding) →  
38936003|Abnormal blood pressure (finding) AND  
roleGroup SOME  
  (363714003|Interprets (attribute) SOME  
    75367002|Blood pressure (observable entity))
```

B

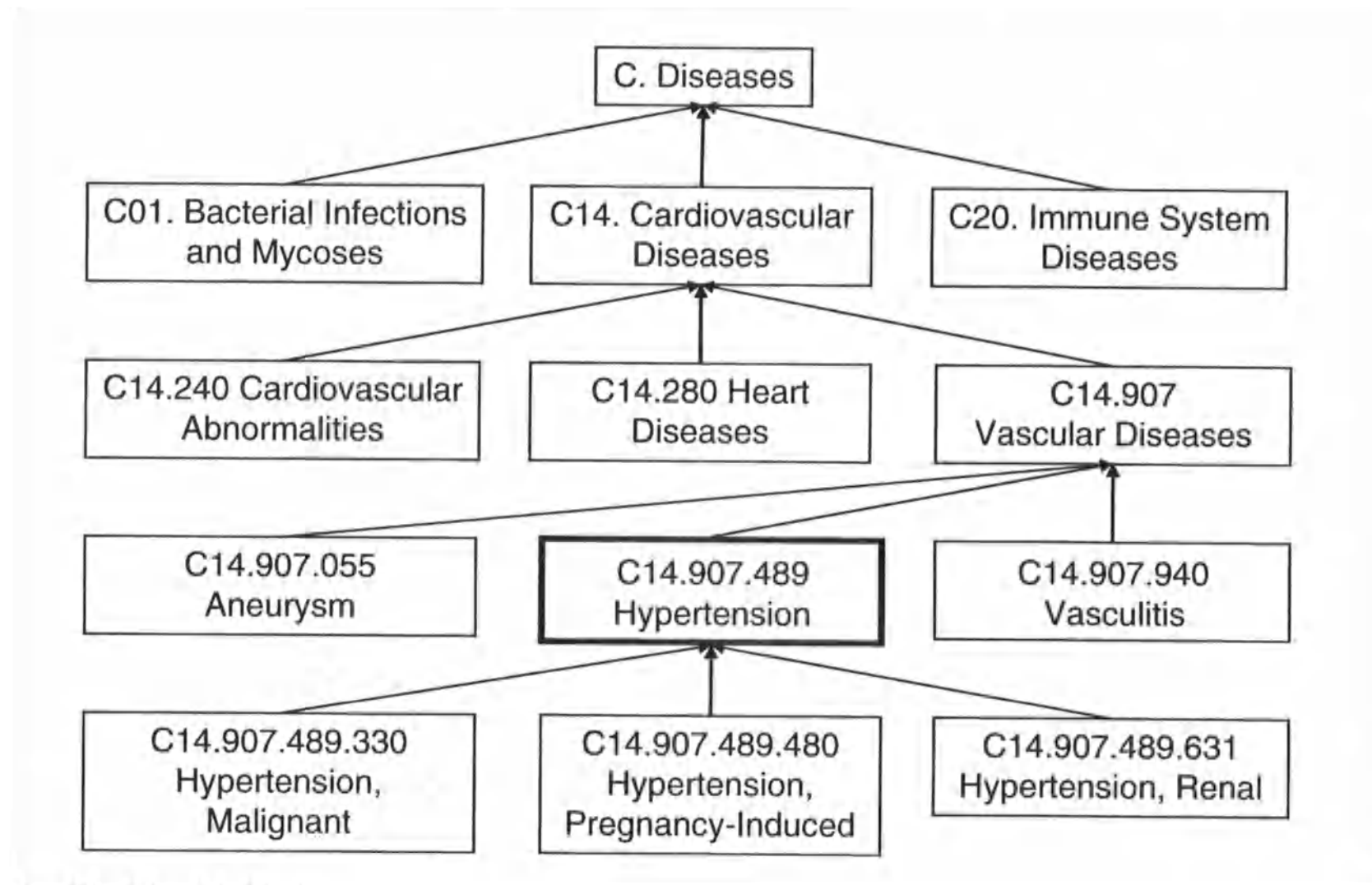
```
12763006|Finding of decreased blood pressure (finding) →  
392570002|Blood pressure finding (finding) AND  
roleGroup SOME  
  (363714003|Interprets (attribute) SOME  
    75367002|Blood pressure (observable entity))
```

Rector, A. L. & Brandt, S. (2008) Why Do It the Hard Way? The Case for an Expressive Description Logic for SNOMED. *Journal of the American Medical Informatics Association*, 15, 6, 744-751.

- MeSH thesaurus is produced by the National Library of Medicine (NLM) since 1960.
- Used for cataloging documents and related media and as an index to search these documents in a database and is part of the metathesaurus of the Unified Medical Language System (UMLS).
- This thesaurus originates from keyword lists of the Index Medicus (today Medline);
- MeSH thesaurus is polyhierarchical, i.e. every concept can occur multiple times. It consists of the three parts:
 - 1. MeSH Tree Structures,
 - 2. MeSH Annotated Alphabetic List and
 - 3. Permuted MeSH.

The 16 trees in MeSH

1. Anatomy [A]
2. Organisms [B]
3. Diseases [C]
4. Chemicals and Drugs [D]
5. Analytical, Diagnostic and Therapeutic Techniques and Equipment [E]
6. Psychiatry and Psychology [F]
7. Biological Sciences [G]
8. Natural Sciences [H]
9. Anthropology, Education, Sociology, Social Phenomena [I]
10. Technology, Industry, Agriculture [J]
11. Humanities [K]
12. Information Science [L]
13. Named Groups [M]
14. Health Care [N]
15. Publication Characteristics [V]
16. Geographicals [Z]



Hersh, W. (2010) *Information Retrieval: A Health and Biomedical Perspective*. New York, Springer.

National Library of Medicine - Medical Subject Headings

2011 MeSH

MeSH Descriptor Data

[Return to Entry Page](#)

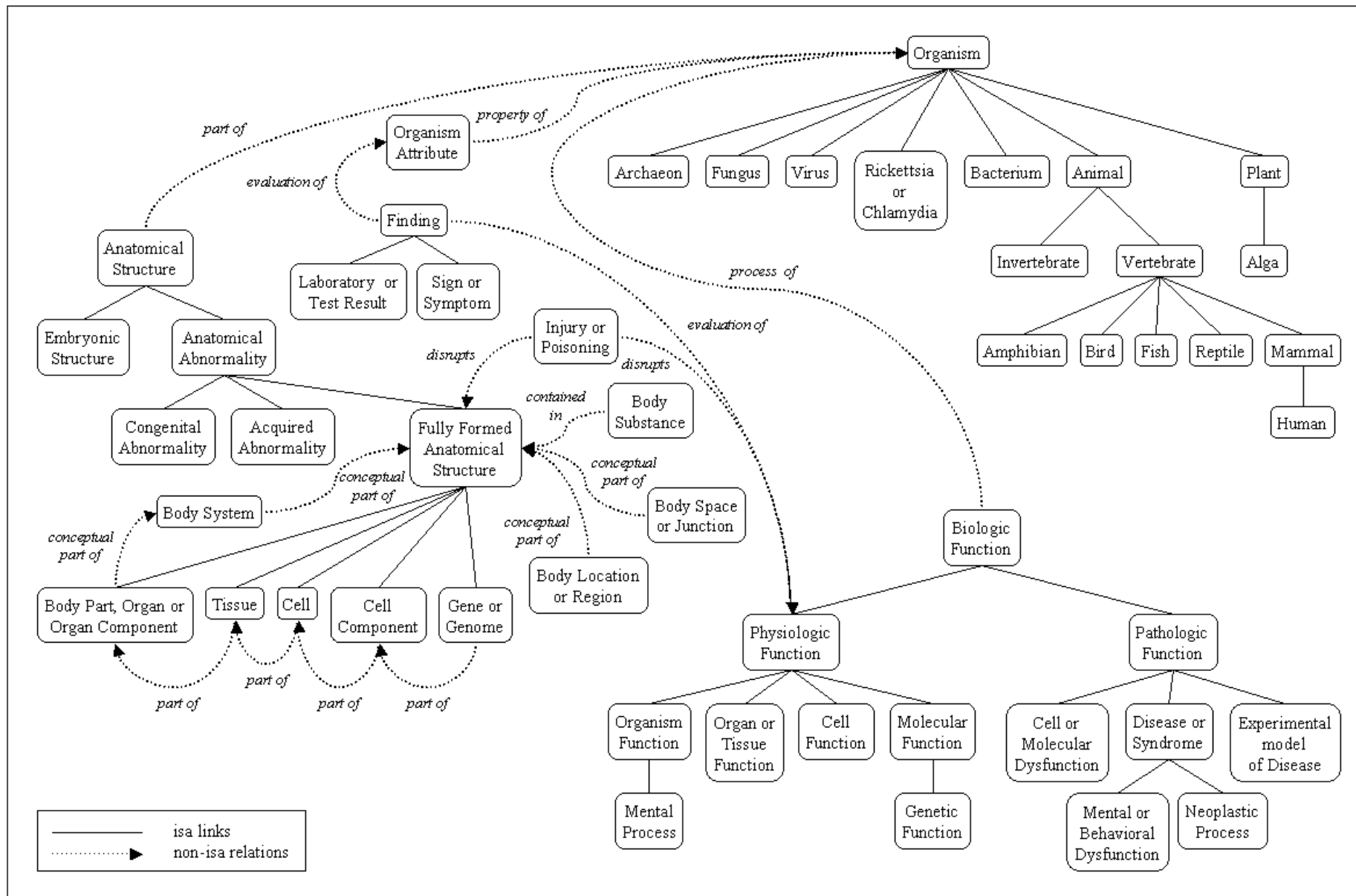
Standard View: [Go to Concept View](#); [Go to Expanded Concept View](#)

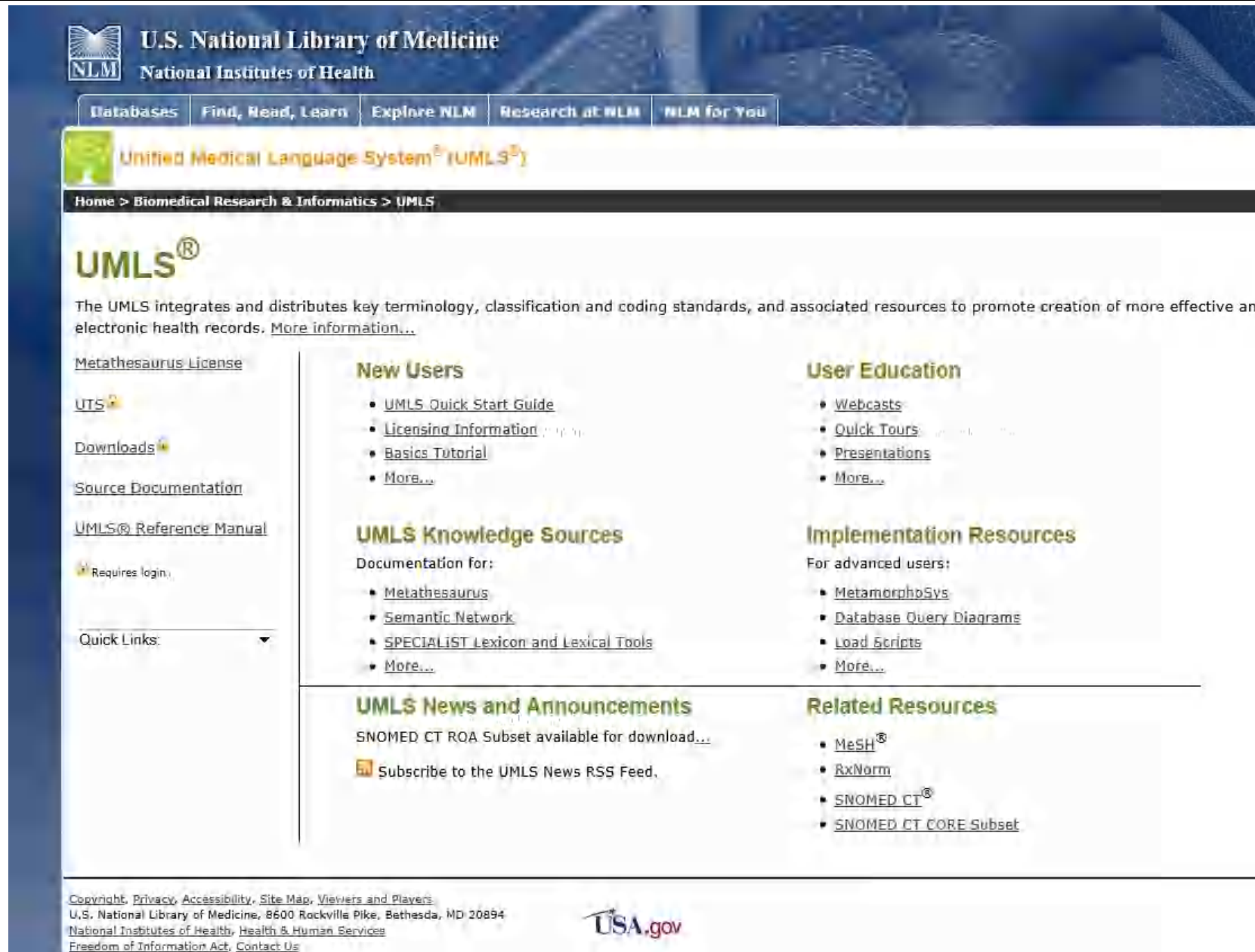
MeSH Heading	Hypertension
Tree Number	C14.907.489
Annotation	not for intracranial or intraocular pressure; relation to BLOOD PRESSURE : Manual 23.27 ; Goldblatt kidney is HYPERTENSION, GOLDBLATT see HYPERTENSION, RENOVASCULAR ; hypertension with kidney disease is probably HYPERTENSION, RENAL , not HYPERTENSION ; venous hypertension; Index under VENOUS PRESSURE (IM) & do not coordinate with HYPERTENSION ; PREHYPERTENSION is also available
Scope Note	Persistently high systemic arterial BLOOD PRESSURE . Based on multiple readings (BLOOD PRESSURE DETERMINATION), hypertension is currently defined as when SYSTOLIC PRESSURE is consistently greater than 140 mm Hg or when DIASTOLIC PRESSURE is consistently 90 mm Hg or more.
Entry Term	Blood Pressure, High
See Also	Antihypertensive Agents
See Also	Vascular Resistance
Allowable Qualifiers	BL CF CI CL CN CO DH DI DT EC EH EM EN EP ET GE HI IM ME MI MO NU PA PC PP PS PX RA RH RI RT SU TH UR US VE VI
Date of Entry	19990101
Unique ID	D006973

<http://www.nlm.nih.gov/mesh/>



Eckert, K. (2008) A methodology for supervised automatic document annotation. *Bulletin of IEEE Technical Committee on Digital Libraries TCDL*, 4, 2.





The screenshot shows the UMLS website interface. At the top, there is a navigation bar with links: Databases, Find, Read, Learn, Explore NLM, Research at NLM, and NLM for You. Below this is a banner for the United Medical Language System (UMLS). The main content area is divided into several sections: a left sidebar with links like Metathesaurus License, UTS, Downloads, Source Documentation, and UMLS® Reference Manual; a central area with sections for New Users (including UMLS Quick Start Guide, Licensing Information, Basics Tutorial, and More...), UMLS Knowledge Sources (documentation for Metathesaurus, Semantic Network, SPECIALIST Lexicon and Lexical Tools, and More...), UMLS News and Announcements (SNOMED CT ROA Subset available for download... and a link to subscribe to the UMLS News RSS Feed), User Education (Webcasts, Quick Tours, Presentations, and More...), Implementation Resources (for advanced users: MetamorphoSys, Database Query Diagrams, Load Scripts, and More...), and Related Resources (MeSH®, RxNorm, SNOMED CT®, and SNOMED CT CORE Subset). The footer contains copyright information, contact details for the U.S. National Library of Medicine, and a USA.gov logo.

U.S. National Library of Medicine
National Institutes of Health

Databases Find, Read, Learn Explore NLM Research at NLM NLM for You

United Medical Language System® (UMLS®)

Home > Biomedical Research & Informatics > UMLS

UMLS®

The UMLS integrates and distributes key terminology, classification and coding standards, and associated resources to promote creation of more effective and electronic health records. [More information...](#)

[Metathesaurus License](#)

[UTS](#)

[Downloads](#)

[Source Documentation](#)

[UMLS® Reference Manual](#)

Requires login.

Quick Links: ▼

New Users

- [UMLS Quick Start Guide](#)
- [Licensing Information](#)
- [Basics Tutorial](#)
- [More...](#)

UMLS Knowledge Sources

Documentation for:

- [Metathesaurus](#)
- [Semantic Network](#)
- [SPECIALIST Lexicon and Lexical Tools](#)
- [More...](#)

User Education

- [Webcasts](#)
- [Quick Tours](#)
- [Presentations](#)
- [More...](#)

Implementation Resources

For advanced users:

- [MetamorphoSys](#)
- [Database Query Diagrams](#)
- [Load Scripts](#)
- [More...](#)

UMLS News and Announcements

SNOMED CT ROA Subset available for download...

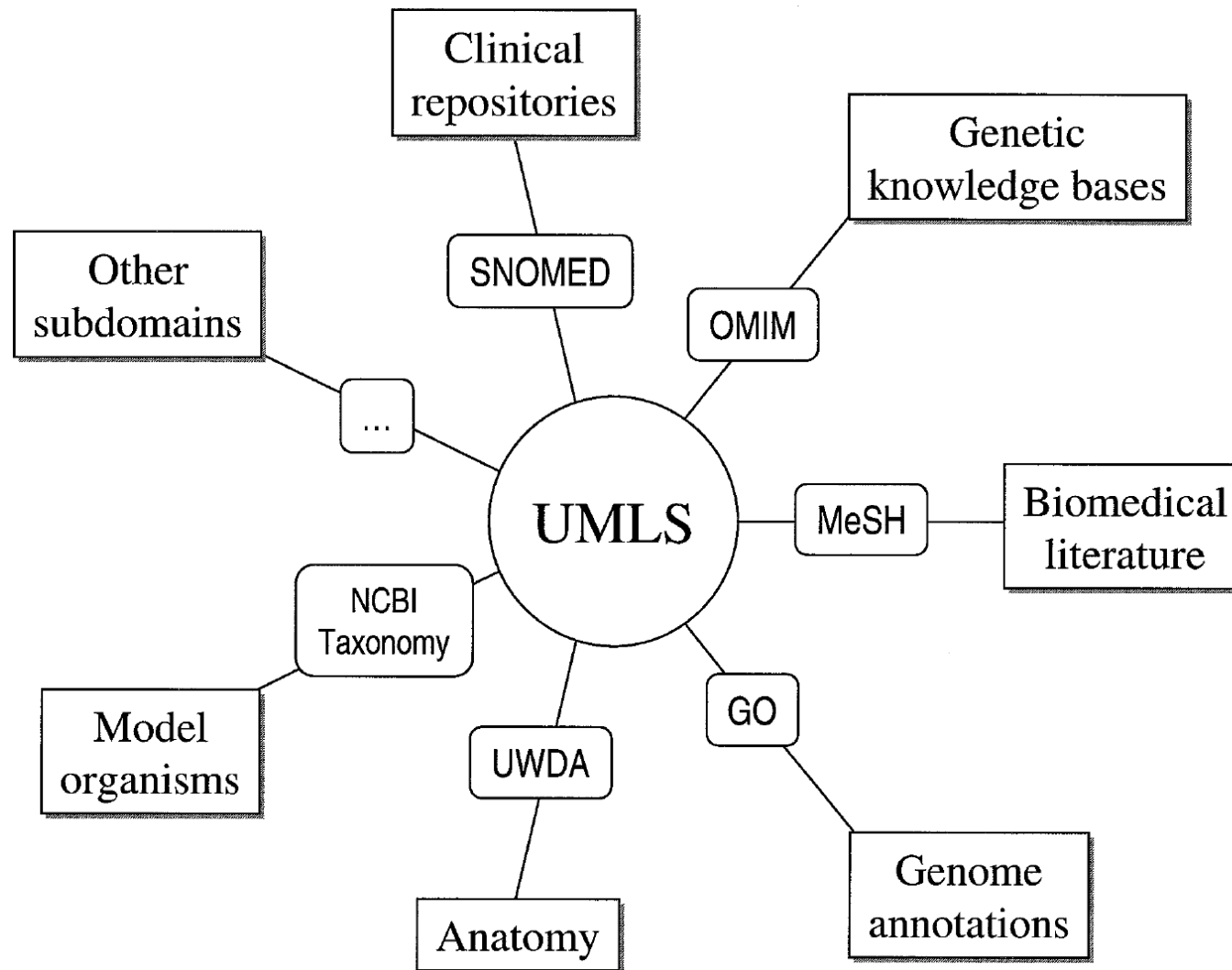
Subscribe to the UMLS News RSS Feed.

Related Resources

- [MeSH®](#)
- [RxNorm](#)
- [SNOMED CT®](#)
- [SNOMED CT CORE Subset](#)

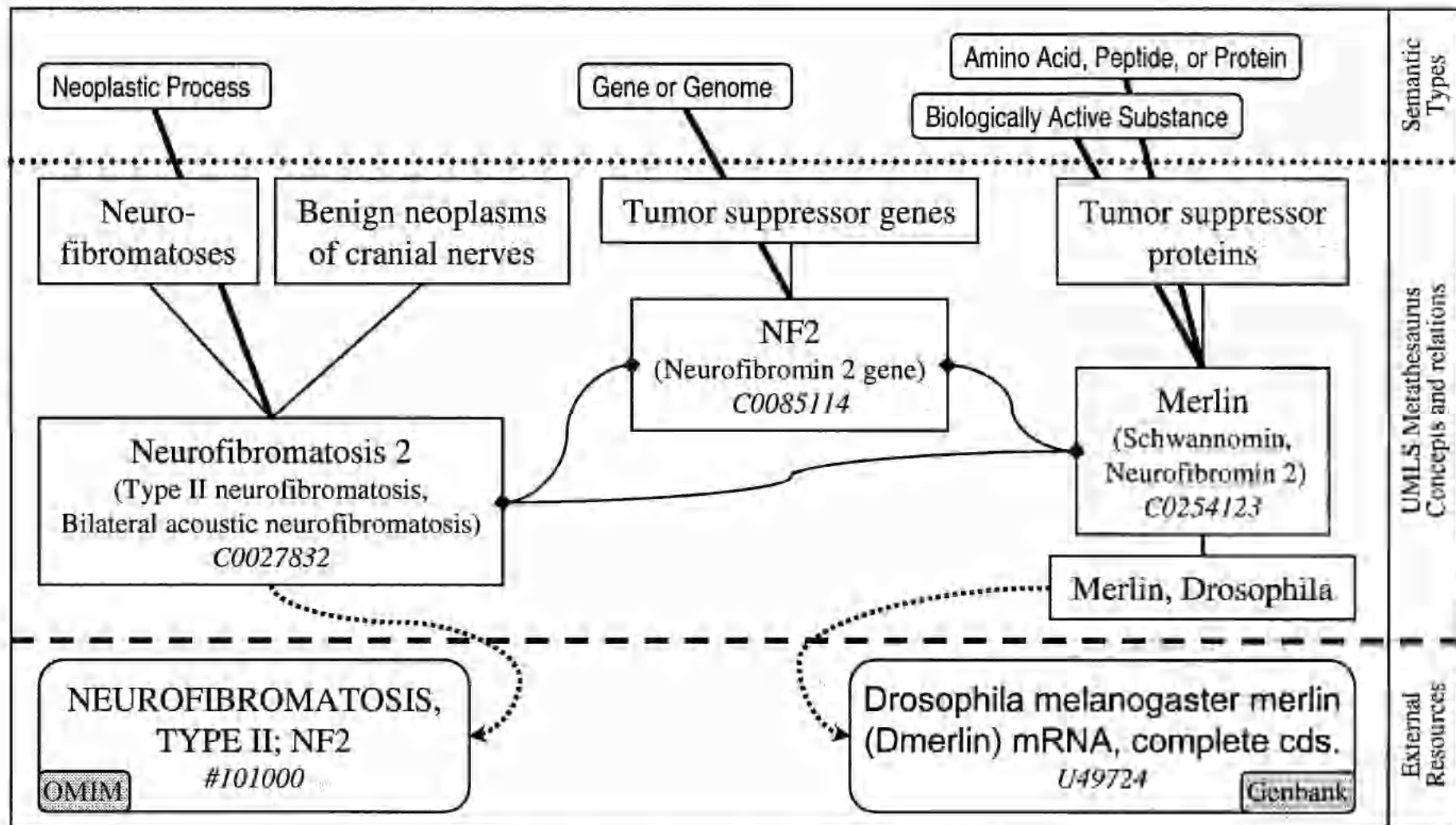
Copyright, Privacy, Accessibility, Site Map, Viewers and Players
U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894
National Institutes of Health, Health & Human Services
Freedom of Information Act, Contact Us

USA.gov



Bodenreider, O. (2004) The Unified Medical Language System (UMLS): integrating biomedical terminology. *Nucleic Acids Research*, 32, D267-D270.

Example of proteins and diseases in the UMLS



Bodenreider, O. (2004) The Unified Medical Language System (UMLS): integrating biomedical terminology. *Nucleic Acids Research*, 32, D267-D270.

Conclusion and Future Challenges

- To find a trade-off between standardization and **personalization** [1];
- The large amounts of **non-standardized data** and **unstructured information** (“free text”) [2];
- **Low integration** of standardized terminologies in the daily clinical practice (Who is using e.g. SNOMED, MeSH, UMLS in daily routine?);
- **Low acceptance** of classification codes amongst practitioners;

1. Holmes, C., McDonald, F., Jones, M., Ozdemir, V., Graham, J. E. 2010. Standardization and Omics Science: Technical and Social Dimensions Are Inseparable and Demand Symmetrical Study. Omics-Journal of Integr. Biology, 14, (3), 327-332.
2. Holzinger, A., Schantl, J., Schroettner, M., Seifert, C. & Verspoor, K. 2014. Biomedical Text Mining: State-of-the-Art, Open Problems and Future Challenges. In: LNCS 8401. Berlin Heidelberg: Springer pp. 271-300.

- Data fusion – Data integration in the life sciences
- Self learning stochastic ontologies [1]
- Interactive, integrative machine learning and interactive ontologies - human-in-the-loop
- Never ending learning machines [2] for automatically building knowledge spaces
- Integrating ontologies in daily work
- Knowledge and **context awareness**

[1] Ongenae, F., Claeys, M., Dupont, T., Kerckhove, W., Verhoeve, P., Dhaene, T. & De Turck, F. 2013. A probabilistic ontology-based platform for self-learning context-aware healthcare applications. *Expert Systems with Applications*, 40, (18), 7629-7646.

[2] Carlson, A., Betteridge, J., Kisiel, B., Settles, B., Hruschka Jr, E. R. & Mitchell, T. M. 2010. Toward an Architecture for Never-Ending Language Learning. *Proceedings of the Twenty-Fourth AAAI Conference on Artificial Intelligence (AAAI-10)*. Atlanta: AAAI. 1306-1313.



Thank you!

Appendix

**Uncertainty
Incompleteness
Probable Information**



**Privacy,
Security, Safety,
Data Protection,
Anonymity,
Fair Use, ...**

EBM CPG

Standardized Medicine



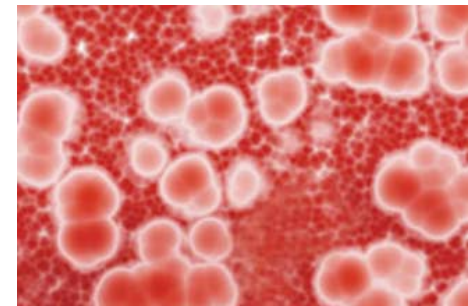
Pervasive Healthcare

Preventive Health Integration

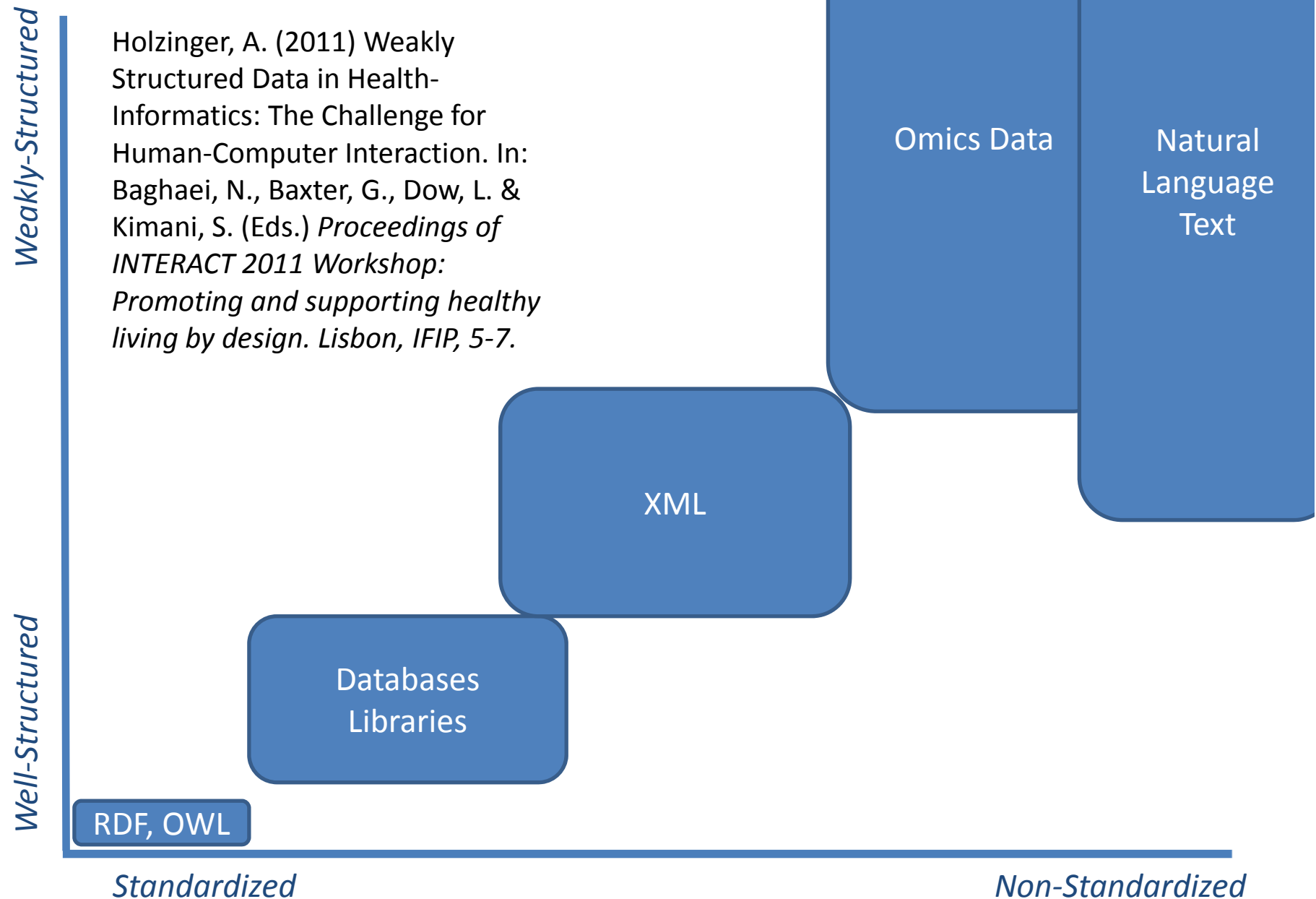
EBM = Evidence Based Medicine
CPG = Clinical Practice Guideline
GBM = Genome Based Medicine
GPM = Genetic Polymorphism

Tanaka, H. (2010)

- **Genomics** (sequence annotation)
- **Transcriptomics** (microarray)
- **Proteomics** (Proteome Databases)
- **Metabolomics** (enzyme annotation)
- **Protein-DNA interactions**
- **Protein-Protein interactions**
- **Fluxomics** (isotopic tracing, metabolic pathways)
- **Phenomics** (biomarkers)
- **Epigenetics**
- **Microbiomics**
- **Lipidomics**



Standardization vs. Structurization



- 0-D data = a data point existing isolated from other data, e.g. integers, letters, Booleans, etc.
- 1-D data = consist of a string of 0-D data, e.g. Sequences representing nucleotide bases and amino acids, SMILES etc.
- 2-D data = having spatial component, such as images, NMR-spectra etc.
- 2.5-D data = can be stored as a 2-D matrix, but can represent biological entities in three or more dimensions, e.g. PDB records
- 3-D data = having 3-D spatial component, e.g. image voxels, e-density maps, etc.
- H-D Data = data having arbitrarily high dimensions

SMILES (Simplified Molecular Input Line Entry Specification)

... is a compact machine and human-readable chemical nomenclature:

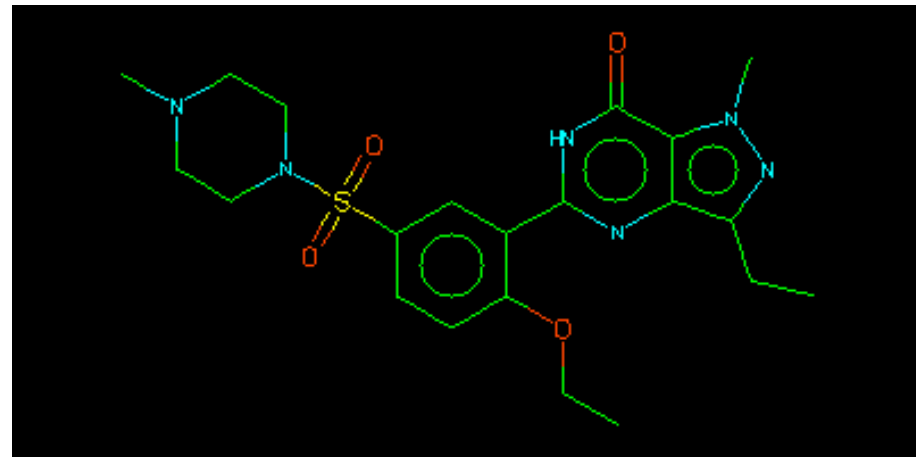
e.g. Viagra:

```
CCc1nn(C)c2c(=O)[nH]c(nc12)c3cc(ccc3OCC)S(=O)(=O)N4CCN(C)CC4
```

...is Canonicalizable

...is Comprehensive

...is Well Documented



http://www.daylight.com/dayhtml_tutorials/languages/smiles/index.html

- The Quiz-Slide will be shown during the course

