



Andreas Holzinger
185.A83 Machine Learning for Health Informatics
2017S, VU, 2.0 h, 3.0 ECTS
Lecture 10 - Module 08 – Week 22 – 30.05.2017



Multi Agent Interaction with the human-in-the-loop

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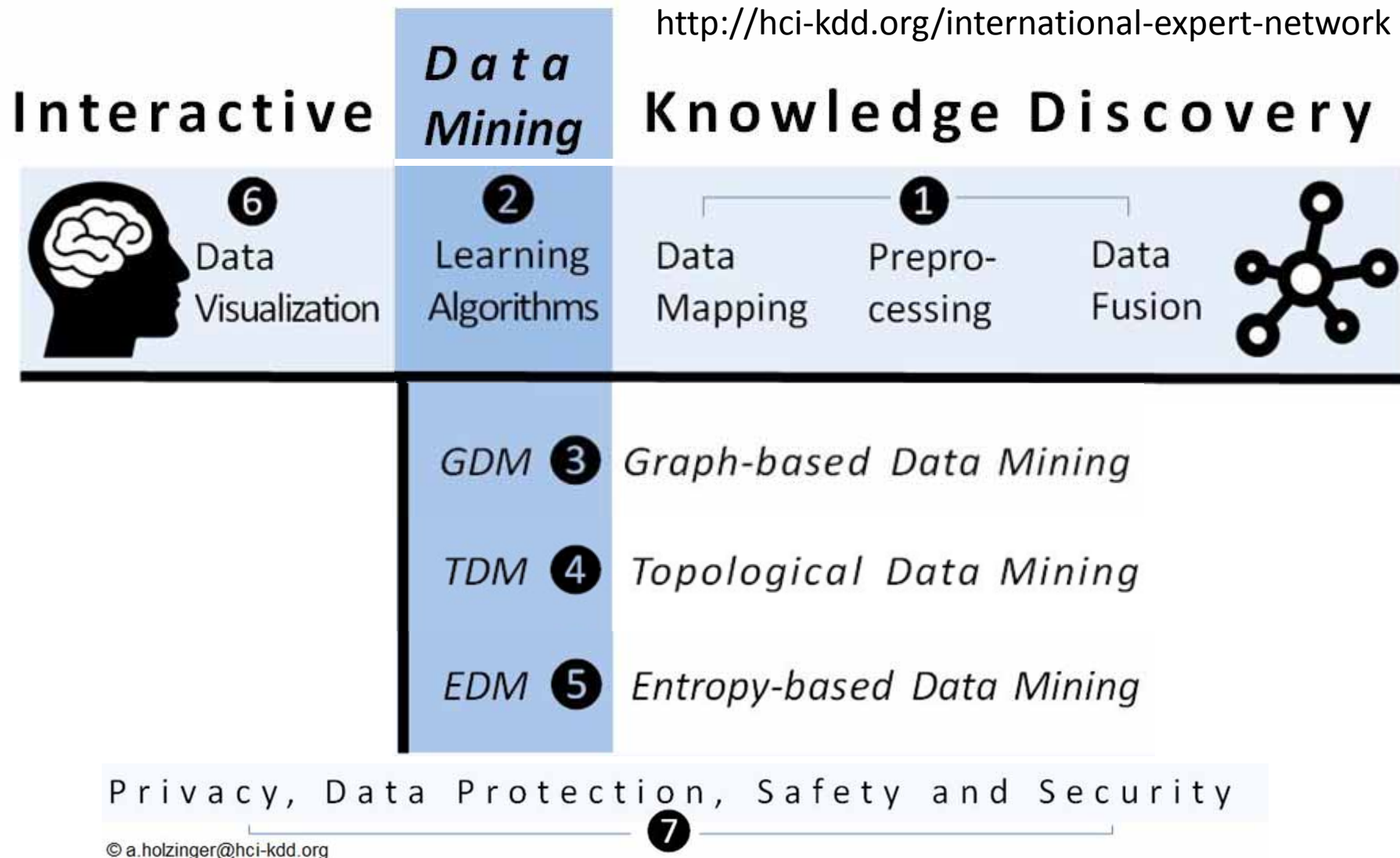
<http://hci-kdd.org/machine-learning-for-health-informatics-course>



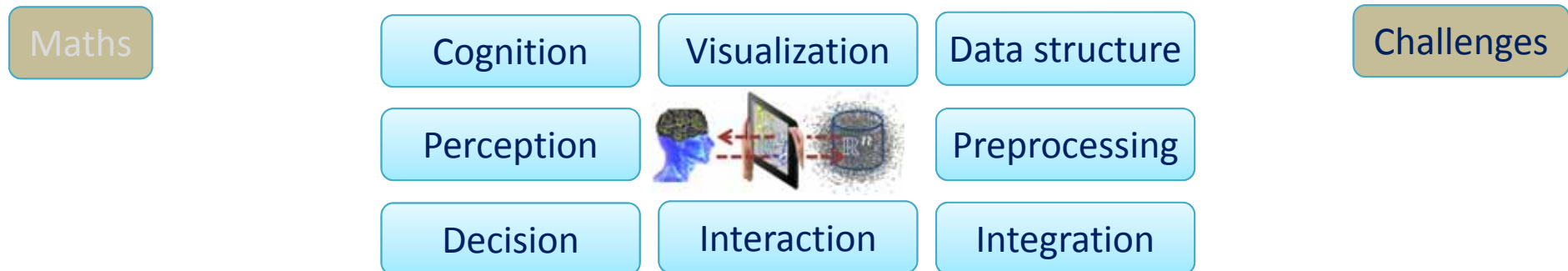


Science is to test crazy ideas –
Engineering is to put these ideas into Business
Lucky Students 😊

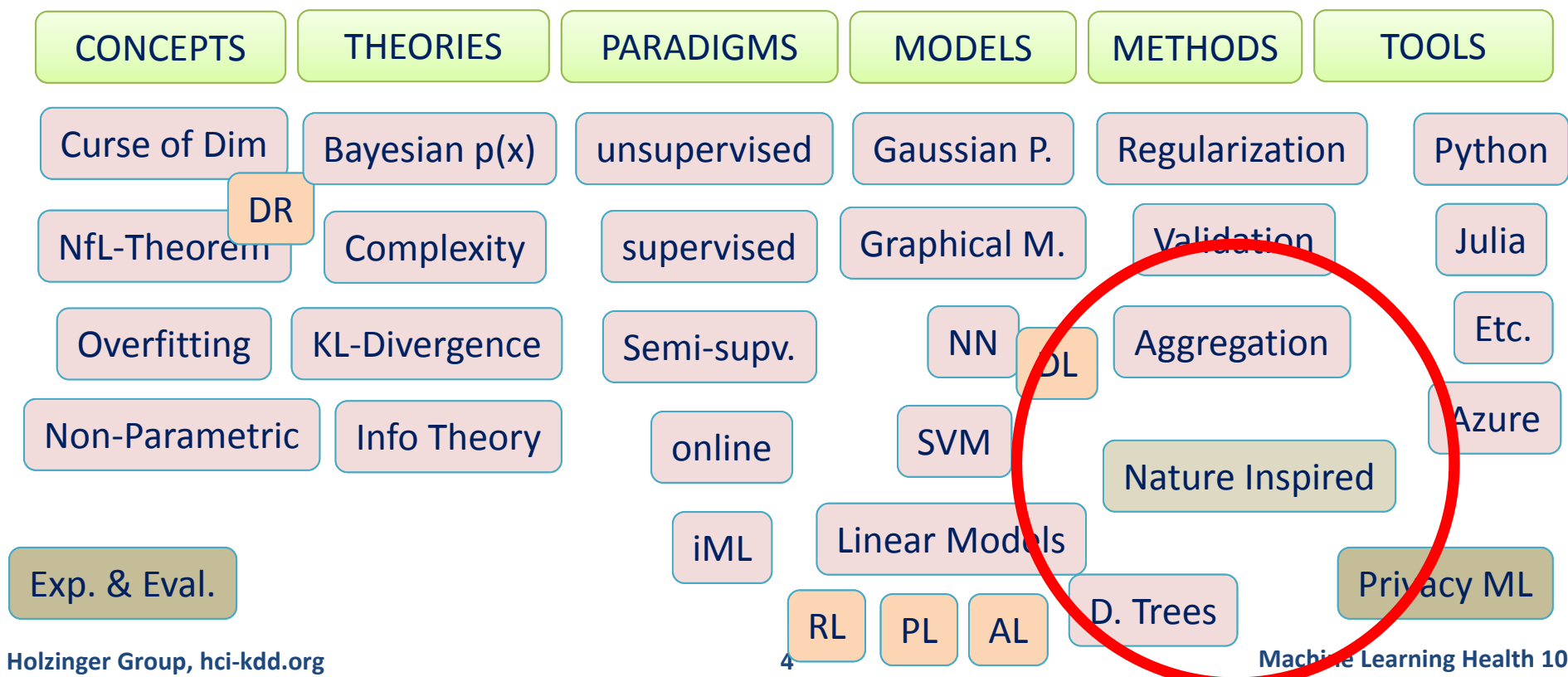
<http://hci-kdd.org/international-expert-network>



Holzinger, A. 2014. Trends in Interactive Knowledge Discovery for Personalized Medicine: **Cognitive Science meets Machine Learning**. IEEE Intelligent Informatics Bulletin, 15, (1), 6-14.

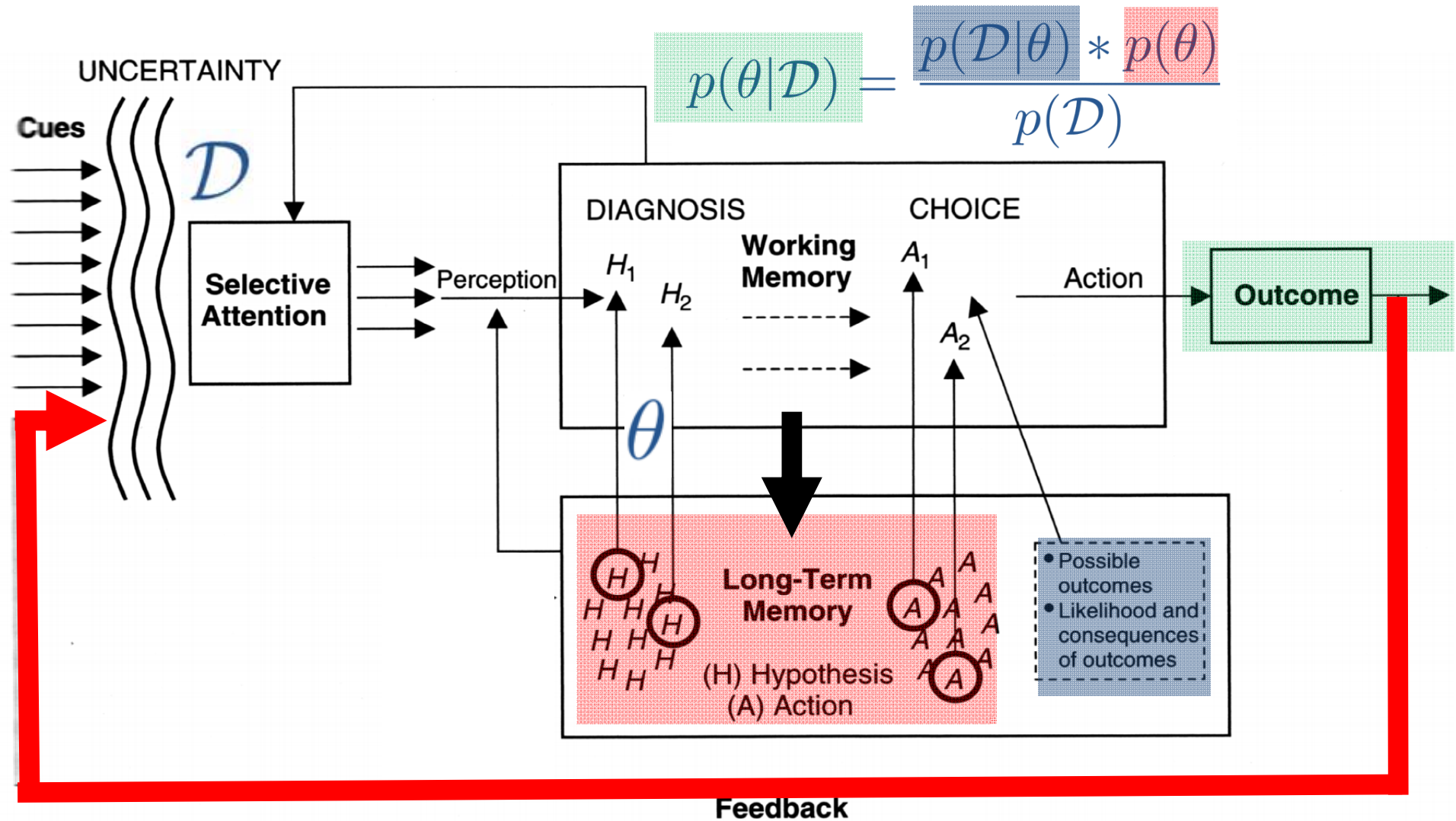


Always with a focus/application in health informatics



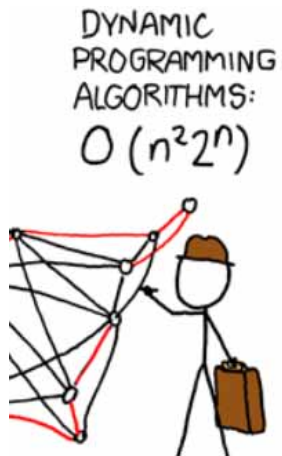
- **00 Reflection**
- **01 Intelligent Agents**
- **02 Multi-Agent (Hybrid) Systems**
- **03 Applications in Health**
- **04 Medical Decision**
- **05 iML Gamification**

00 Reflection

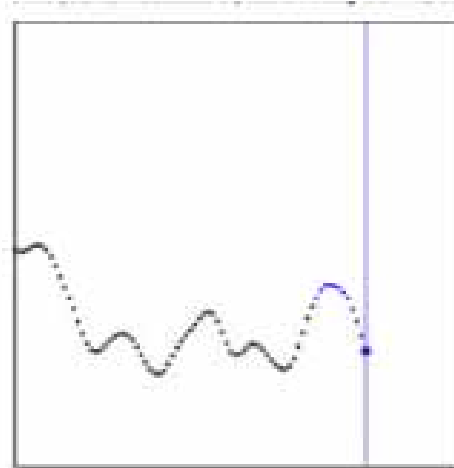


Wickens, C. D. (1984) *Engineering psychology and human performance*.
Columbus (OH), Charles Merrill, Altered by Holzinger, A. (2017)

1



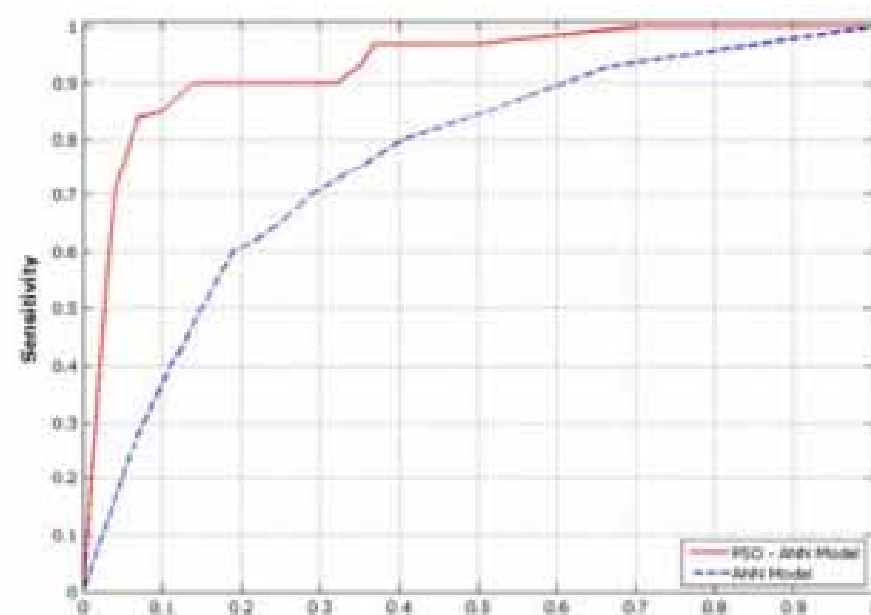
2



3



4



5

External context

Verbal suggestions:
“This is going to make you feel better”

Place cues:
Doctor’s office

Social cues:

- Eye gaze
- Body language
- Voice cues
- White coat



Treatment cues:

- Syringe
- Needle puncture

Internal context

- **Outcome expectancies:**
“My pain will go away”
- **Emotions:**
“I am less anxious”
- **Meaning schema:**
“I am being cared for”
- **Explicit memories**
- **Pre-cognitive associations**

Nature Reviews | Neuroscience

Wager, T. D. & Atlas, L. Y. 2015. The neuroscience of placebo effects: connecting context, learning and health. Nat Rev Neurosci, 16, (7), 403-418, doi:10.1038/nrn3976

01 Intelligent Agents



- Symbolic ML
 - First order logic, inverse deduction
 - Tom Mitchell, Steve Muggleton, Ross Quinlan, ...
- Bayesian ML
 - Statistical learning
 - Judea Pearl, Michael Jordan, David Heckermann, ...
- Cognitive ML
 - Analogisms from Psychology, Kernel machines
 - Vladimir Vapnik, Peter Hart, Douglas Hofstadter, ...
- Connectionist ML
 - Neuroscience, Backpropagation
 - Geoffrey Hinton, Yoshua Bengio, Yann LeCun, ...
- **Evolutionary ML**
 - Nature-inspired concepts, genetic programming
 - John Holland (1929-2015), John Koza, Hod Lipson, ...

- I) Machine Learning: Evolutionary computation is a key concept in ML [1]
- II) Health Informatics: Evolutionary computation is widely applied in medical problem solving [2]
- Whenever a **decision** is required, it is possible to apply evolutionary techniques, e.g.
 - 1) Learning, Knowledge Discovery, Mining, ... applied to both diagnosis and prognosis (=prediction)
 - 2) Medical imaging, signal processing, ... and
 - 3) Planning and scheduling

[1] Zhang, J., Zhan, Z.-H., Lin, Y., Chen, N., Gong, Y.-J., Zhong, J.-H., Chung, H. S., Li, Y. & Shi, Y.-H. 2011. Evolutionary computation meets machine learning: A survey. Computational Intelligence Magazine, IEEE, 6, (4), 68-75

[2] Pena-Reyes, C. A. & Sipper, M. 2000. Evolutionary computation in medicine: an overview. Artificial Intelligence in Medicine, 19, (1), 1-23, doi:10.1016/S0933-3657(99)00047-0.

- Study of the design of **intelligent agents**
- Set of *nature-inspired* methodologies to solve complex real-world problems, when traditional methods might be useless, because:
 - 1) the processes might be too **complex** for mathematical reasoning within the given time,
 - 2) the problem contains a lot of **uncertainties**
 - 3) the problem/process is **stochastic** in nature

Kruse, R., Borgelt, C., Klawonn, F., Moewes, C., Steinbrecher, M. & Held, P. 2013. Computational Intelligence: A Methodological Introduction, Heidelberg, New York, Springer.
Online in both German and English: <http://www.computational-intelligence.eu/>

IFIP WG 12.9 <http://www.ifip.org/bulletin/bulltcs/memtc12.htm>

- Subfield of CI which studies evolutionary algorithms [1] based on **evolutionary principles** (e.g. Darwin, Baldwin, Lamarck, Mendel [2]),
- **Trial-and-error problem solvers**, considered as
- **Global optimization** methods with metaheuristic or stochastic optimization character – mostly applied for black-box problems (with exception of interactive machine learning approaches, where the black box is opened to a glass box [3])

[1] Eiben, A. E. & Smith, J. E. 2015. *Introduction to evolutionary computing. Second Edition*, Berlin, Springer. Online: <http://www.evolutionarycomputation.org/>

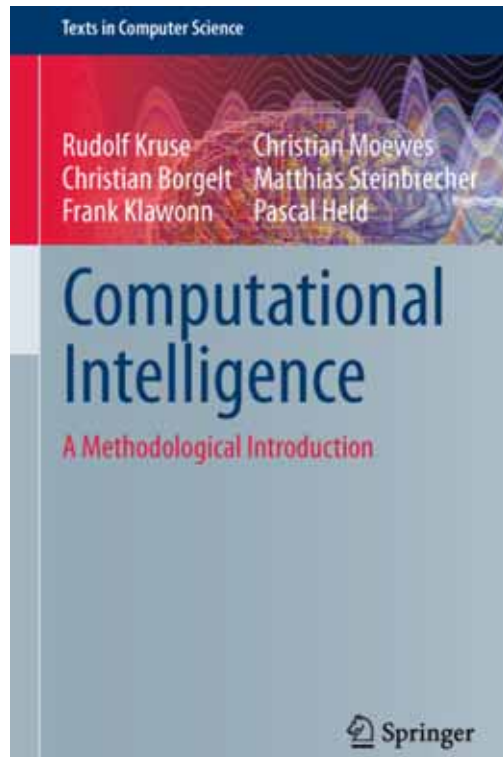
[2] Holzinger, K., Palade, V., Rabadan, R. & Holzinger, A. 2014. Darwin or Lamarck? Future Challenges in Evolutionary Algorithms for Knowledge Discovery and Data Mining. In: *Lecture Notes in Computer Science LNCS 8401*. Berlin: Springer, pp. 35-56, doi:10.1007/978-3-662-43968-5_3.

[3] Holzinger, A. 2016. Interactive Machine Learning for Health Informatics: When do we need the human-in-the-loop? *Brain Informatics*, 3, (2), 119-131, doi:10.1007/s40708-016-0042-6.

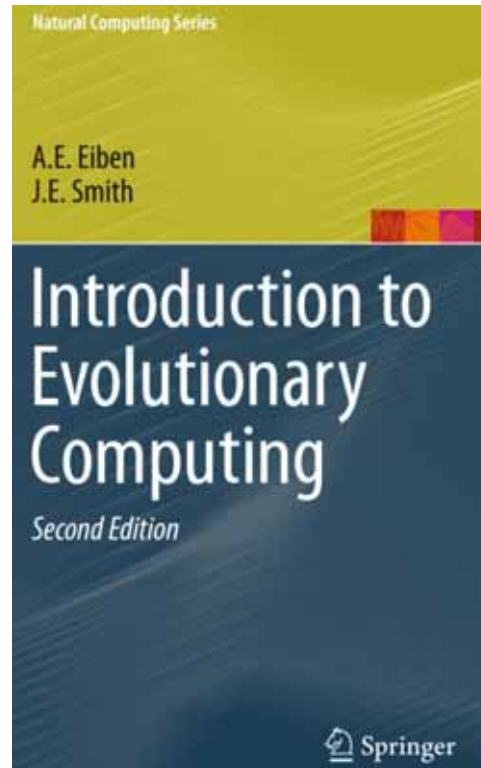
- search heuristic mimicking the process of **natural selection** used to generate useful solutions to optimization and search problems [1];
- particularly making use of techniques inspired by natural evolution (competing for resources), such as inheritance, reproduction, recombination, mutation, selection, inversion and crossover, according to a
- **fitness function (evaluation function)** [2].

[1] Mitchell, Melanie (1996). An Introduction to Genetic Algorithms. Cambridge, MA: MIT Press

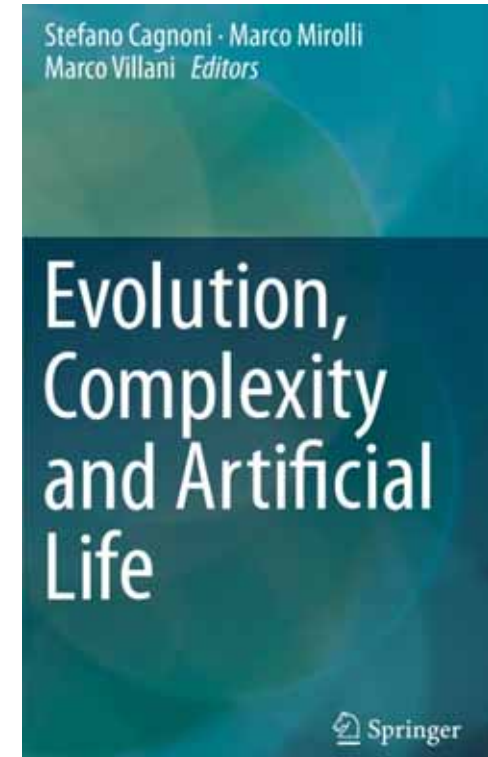
[2] Kallel, L., Naudts, B. & Reeves, C. 2001. Properties of fitness functions and search landscapes. In: Kallel, L. (ed.) Theoretical Aspects of Evolutionary Computing. Heidelberg: Springer, pp. 175-206.



Kruse, R., Borgelt, C., Klawonn, F., Moewes, C., Steinbrecher, M. & Held, P. 2013. Computational Intelligence: A methodological Introduction, Heidelberg, New York, Springer.



Eiben, A. E. & Smith, J. E. 2010. Introduction to evolutionary computing, Springer Berlin.



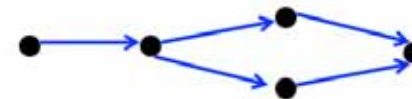
Cagnoni, S., Mirolli, M. & Villani, M. 2014. *Evolution, Complexity and Artificial Life*, Springer.

02 Multi-Agent (Hybrid*) Systems

*) not in the sense as we use it in “interactive ML”, i.e.

The classical meaning of “hybrid” is the attempt to combine classical symbolic AI approaches (from the 1950ies) with newer approaches as e.g. the subsumption architecture (from the 1990ies)

Discrete System (FSM)



Continuous System



Hybrid System

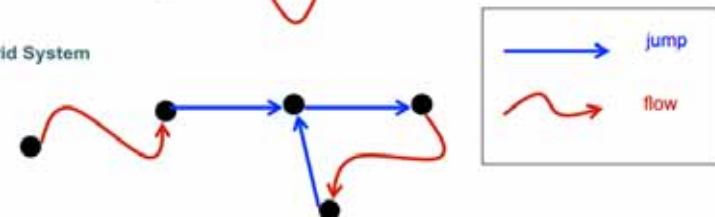


Image credit to Andreas Podelski, University of Freiburg



Michael Wooldridge

University of Oxford

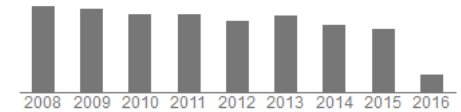
multi-agent systems, multiagent systems, knowledge representation, artificial intelligence, computer science

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Title 1–20

Cited by

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M Wooldridge, NR Jennings
Knowledge engineering review 10 (2), 115-152

9433

1995

An introduction to multiagent systems

M Wooldridge
John Wiley & Sons

8083

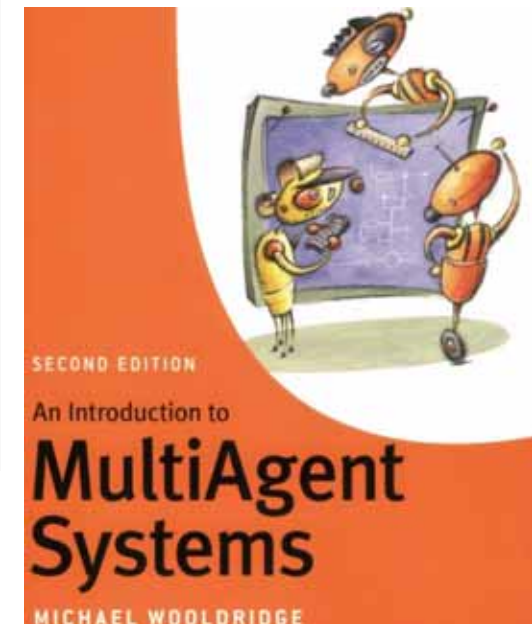
2009

A roadmap of agent research and development

NR Jennings, K Sycara, M Wooldridge
Autonomous agents and multi-agent systems 1 (1), 7-38

2909

1998



Wooldridge, M. 2009. An introduction to multiagent systems, John Wiley & Sons

<http://www.cs.ox.ac.uk/people/michael.wooldridge/pubs/imas/IMAS2e.html>

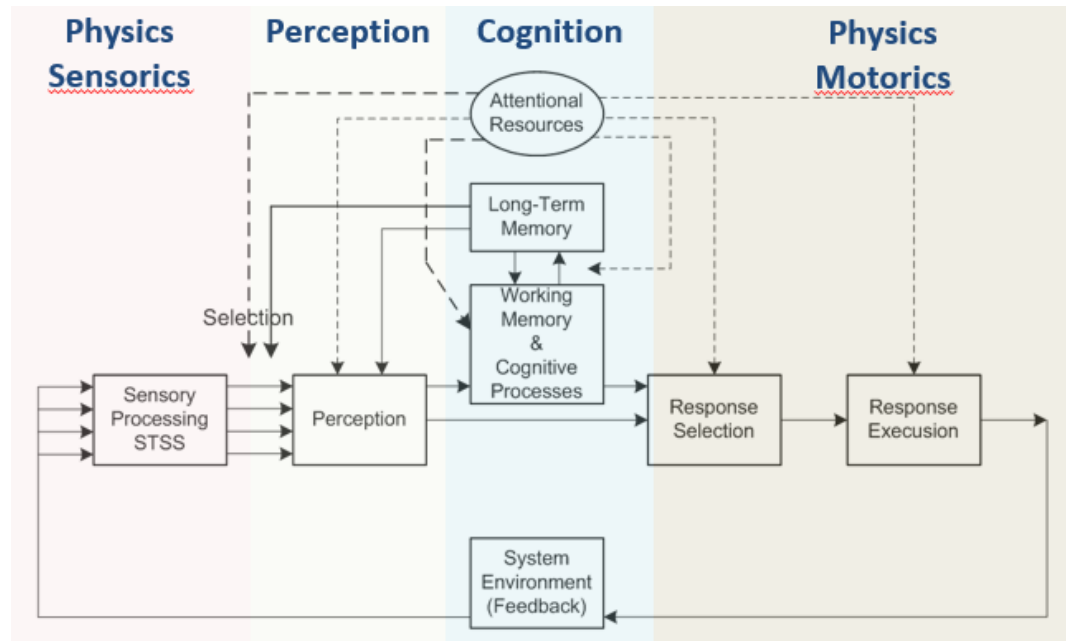
<http://www.cs.ox.ac.uk/people/michael.wooldridge/pubs/imas/videos/part1/>



<http://micro.seas.harvard.edu/research.html>

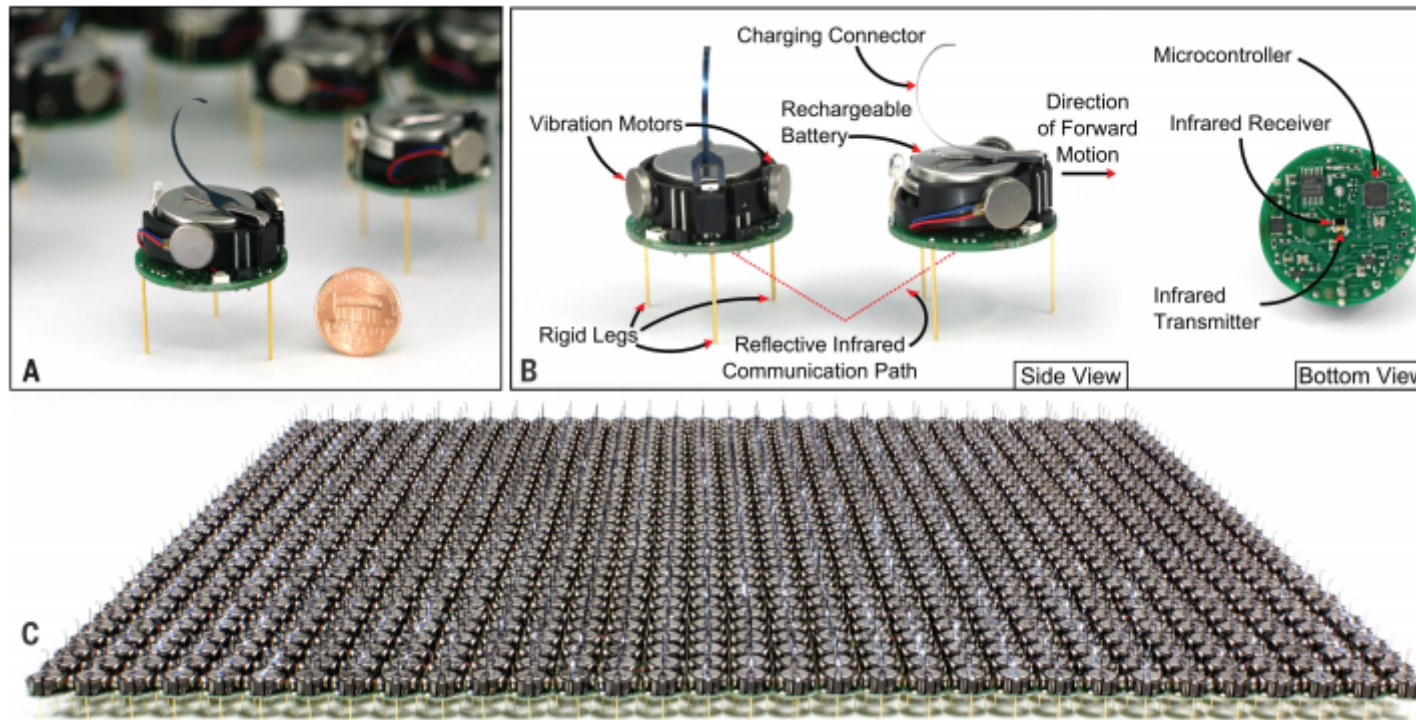
- Connection → computing as interaction of things
- Ubiquity → embedded computing at low cost
- Delegation → fully autonomous vehicles
- Intelligence → human problem solving
- Human-oriented abstractions → human learning

Perception > Decision > Action



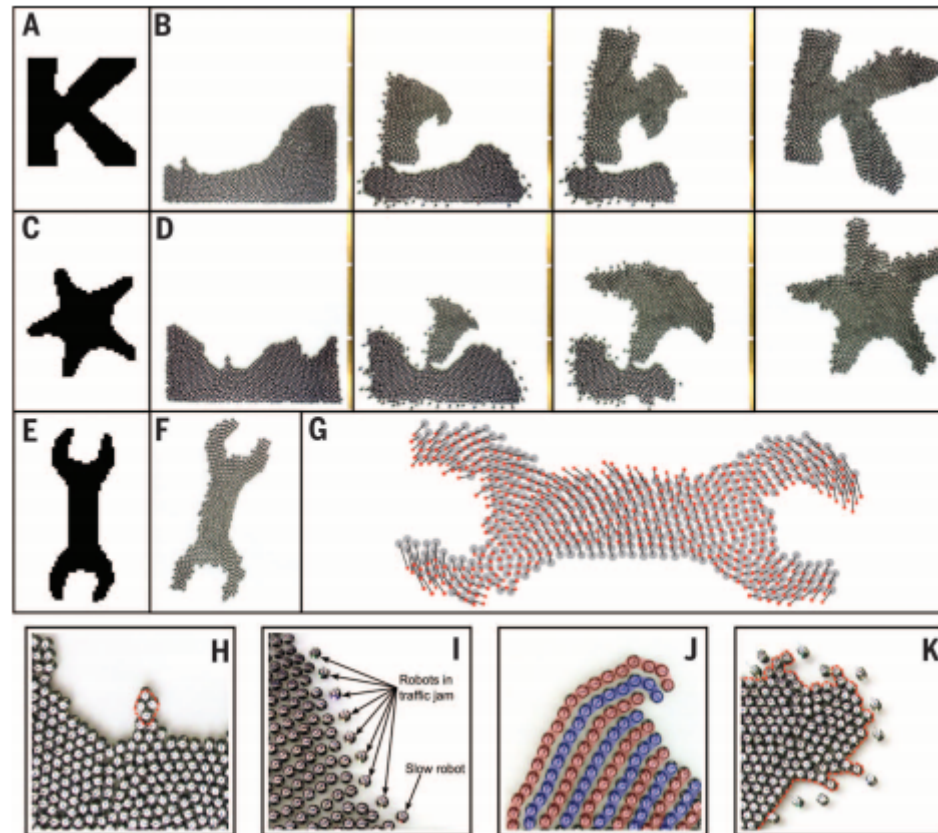
- Agent:= computer system which is able to perform autonomous actions in a certain environment to meet delegated goals
 - The agent has to decide WHAT action to perform
 - The agent has to decide WHEN to perform it

Social ability in agents is interacting with other agents via cooperation, coordination, negotiation

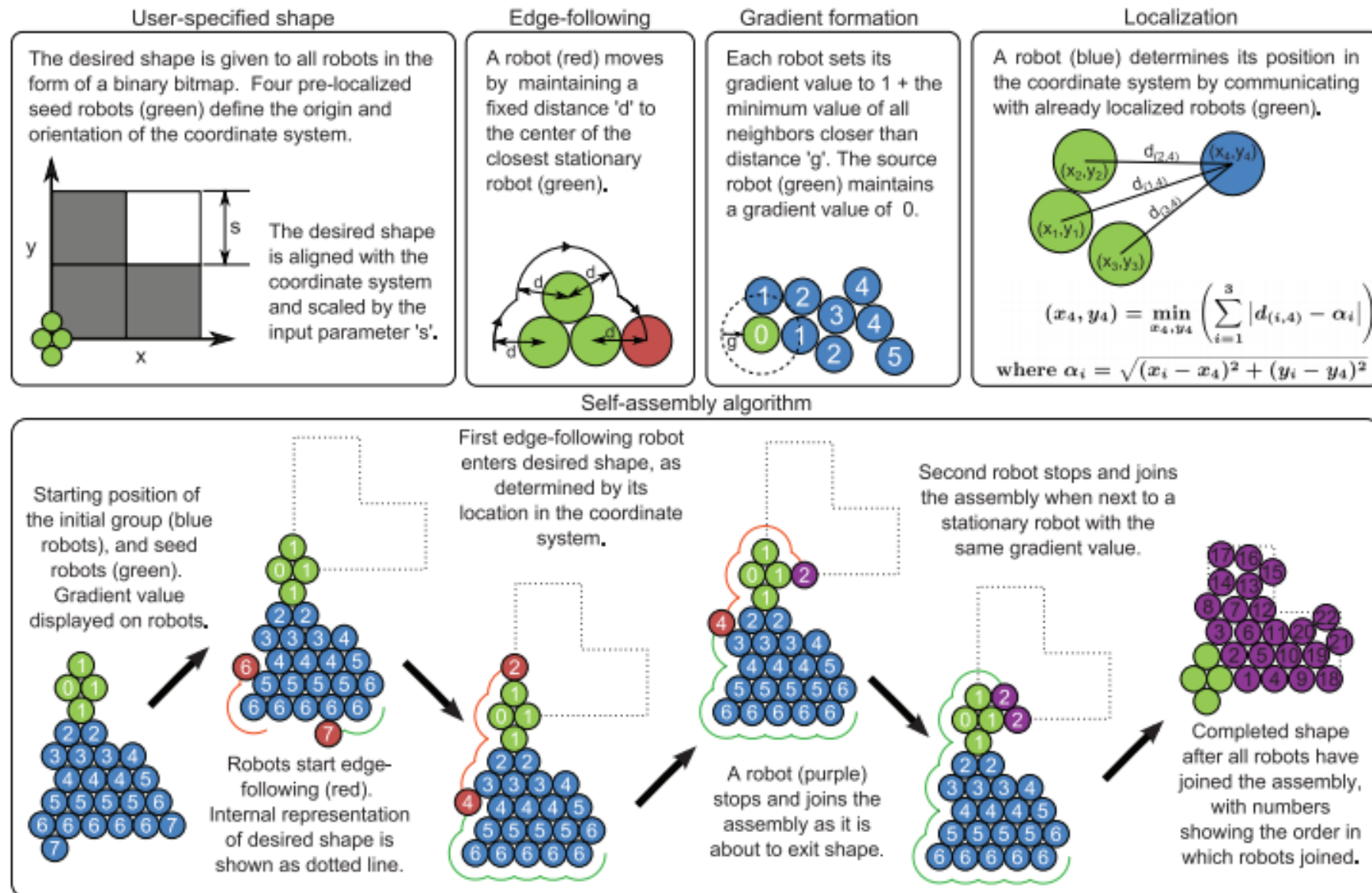


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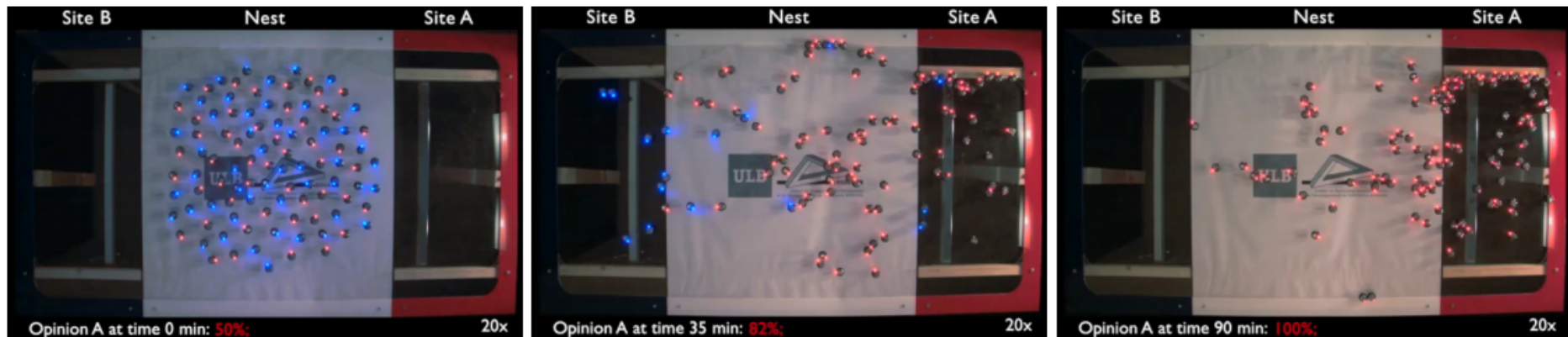
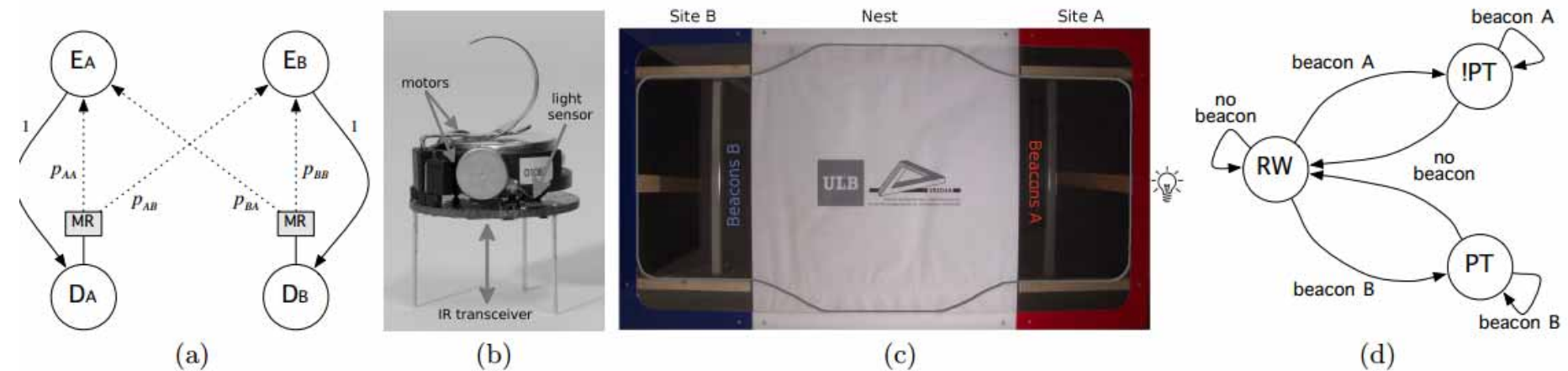
Social ability in agents is interacting with other agents via cooperation, coordination, negotiation



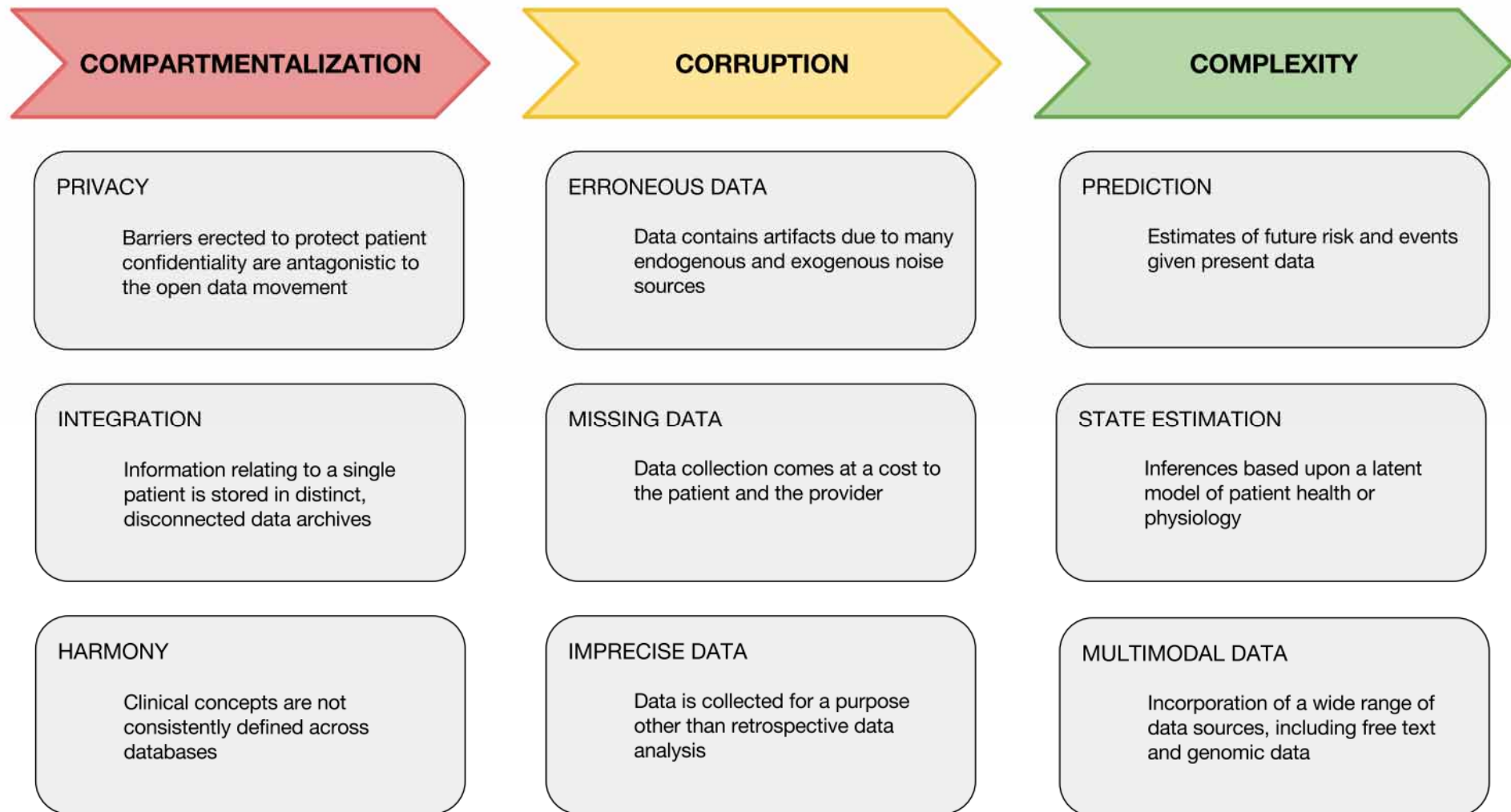
Rubenstein, M., Cornejo, A. & Nagpal, R. 2014. Programmable self-assembly in a thousand-robot swarm. *Science*, 345, (6198), 795-799, doi:10.1126/science.1254295



Rubenstein, M., Cornejo, A. & Nagpal, R. 2014. Programmable self-assembly in a thousand-robot swarm. Science, 345, (6198), 795-799, doi:10.1126/science.1254295



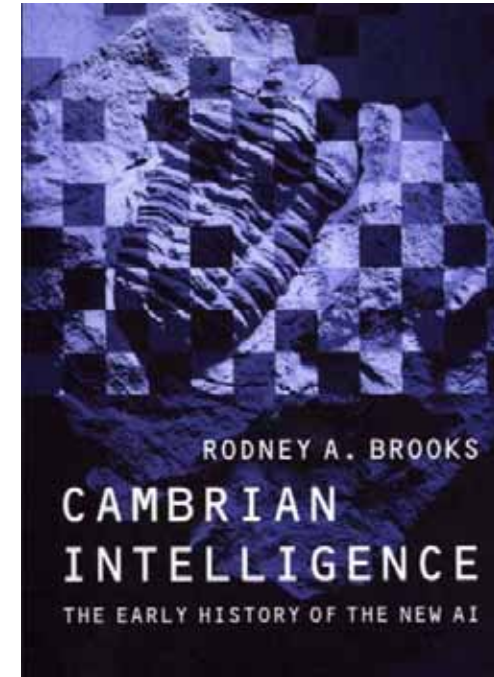
Valentini, G., Hamann, H. & Dorigo, M. Efficient decision-making in a self-organizing robot swarm: On the speed versus accuracy trade-off. Proceedings of the 2015 International Conference on Autonomous Agents and Multiagent Systems, 2015. International Foundation for Autonomous Agents and Multiagent Systems, 1305-1314.



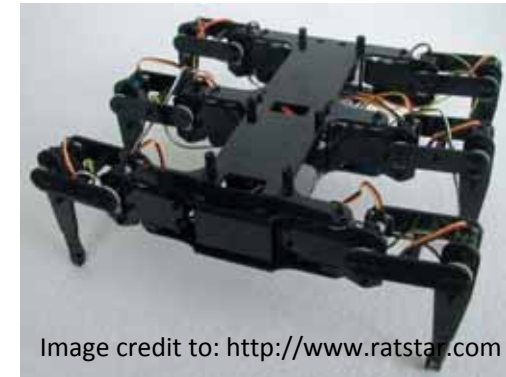
Johnson, A. E., Ghassemi, M. M., Nemati, S., Niehaus, K. E., Clifton, D. A. & Clifford, G. D. 2016. Machine learning and decision support in critical care. Proceedings of the IEEE, 104, (2), 444-466, doi:10.1109/JPROC.2015.2501978.

- **Agent design:** How do we build agents that are capable of independent, autonomous action in order to successfully carry out the tasks that we delegate to them?
- **Society Design:** How do we build agents that are capable of interacting (cooperating, coordinating, negotiating) with other agents – and humans - in order to successfully carry out the tasks that we delegate to them, particularly when the other agents cannot be assumed to share the same interests/goals?
- **Agents as a paradigm** for software engineering: Software engineers have derived a progressively better understanding of the characteristics of complexity in software. It is now widely recognised that interaction is probably the most important single characteristic of complex software
- **Agents as a tool** for understanding human societies: Multiagent systems provide a novel new tool for simulating societies, which may help shed some light on various kinds of social processes.
- **Agents are the achievable bit of the AI project:** The aim of Artificial Intelligence as a field is to produce general human-level intelligence. This requires a very high level of performance in lots of areas: Vision, Natural language understanding/generation, Reasoning
- Building an agent that can perform well on a narrowly defined task in a specific environment is much easier (though not easy)

- 1. Intelligent behaviour can be generated without explicit representations of the kind that symbolic AI proposes.
- 2. Intelligent behaviour can be generated without explicit abstract reasoning of the kind that symbolic AI proposes.
- 3. Intelligence is an emergent property of certain complex systems.
- 1. Situatedness and embodiment: ‘Real’ intelligence is situated in the world, not in disembodied systems such as theorem provers or expert systems.
- 2. Intelligence and emergence: ‘Intelligent’ behaviour arises as a result of an agent’s interaction with its environment. Also, intelligence is ‘in the eye of the beholder’; it is not an innate, isolated property.



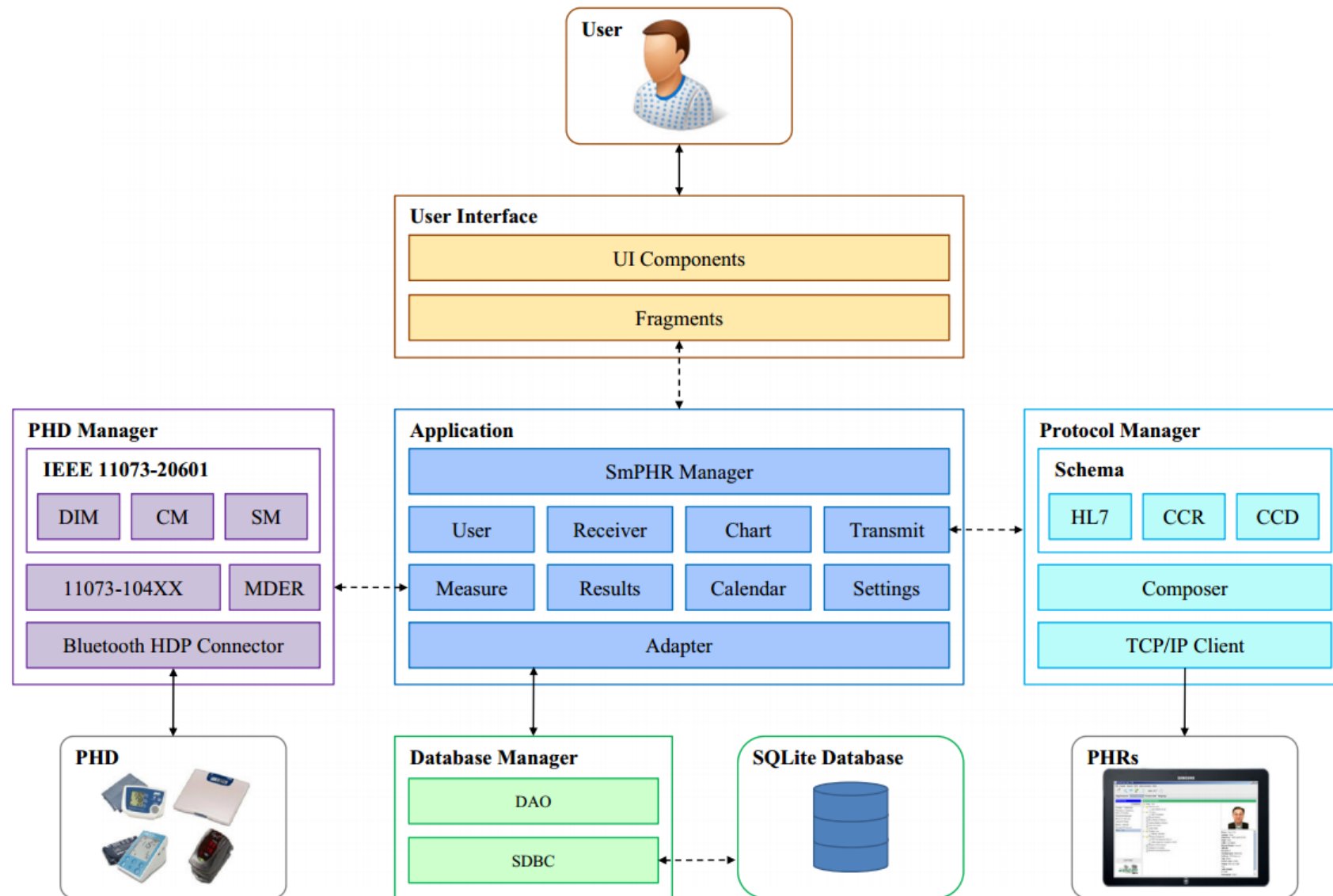
i-Robot company



- A subsumption architecture is a hierarchy of task-accomplishing behaviours.
 - Each behaviour is a simple rule-like structure.
 - Each behaviour 'competes' with others to exercise control over the agent.
- Lower layers represent more primitive kinds of behaviour, (such as avoiding obstacles), and have precedence over layers further up the hierarchy.
- The resulting systems are, in terms of the amount of computation they do, extremely simple.
- Some of the robots do tasks that would be impressive if they were accomplished by symbolic AI systems

Maes, P. 1993. Modeling adaptive autonomous agents. *Artificial life*, 1, (1_2), 135-162.

03 Applications of Multi-Agent Systems in Health Informatics

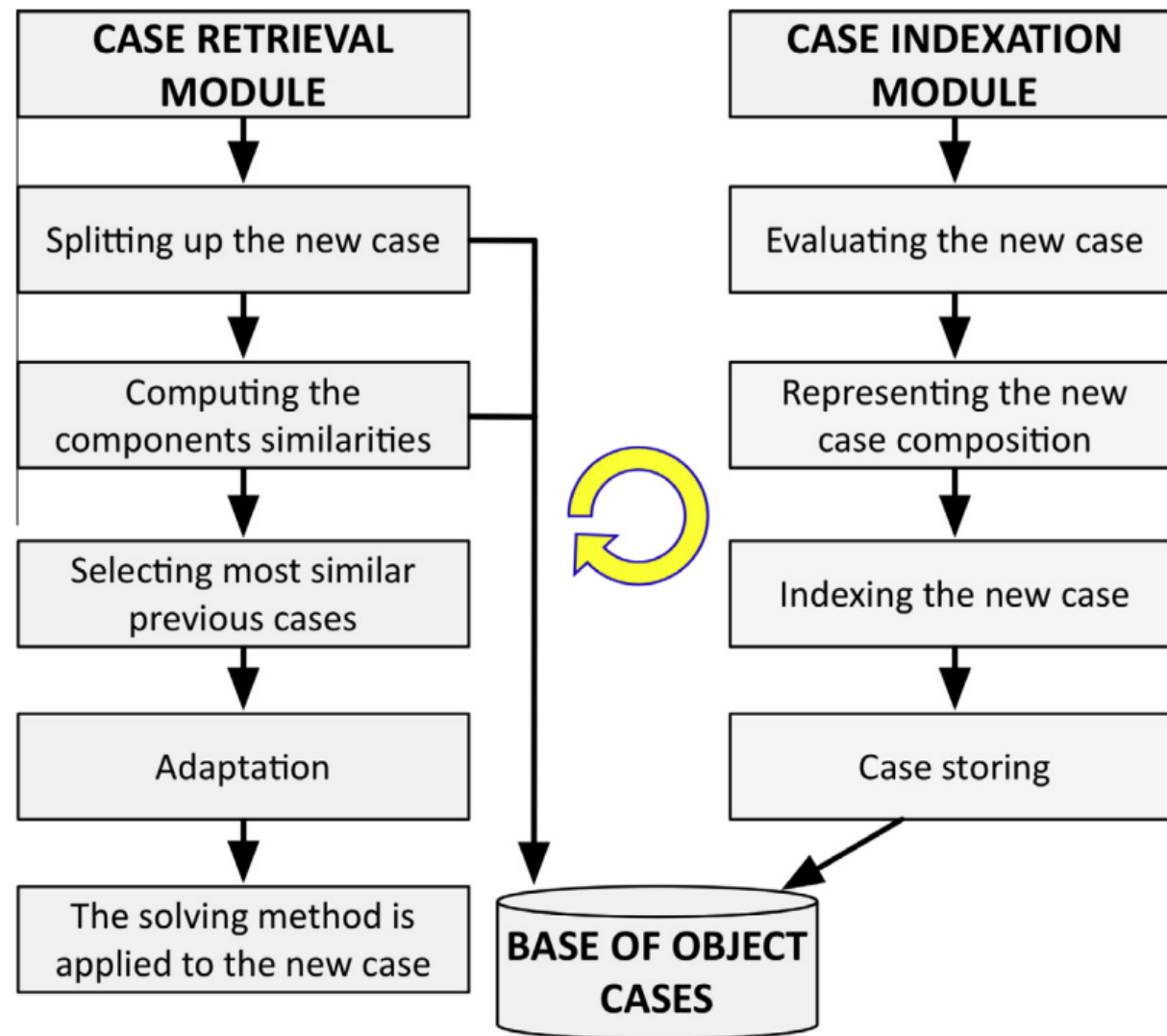


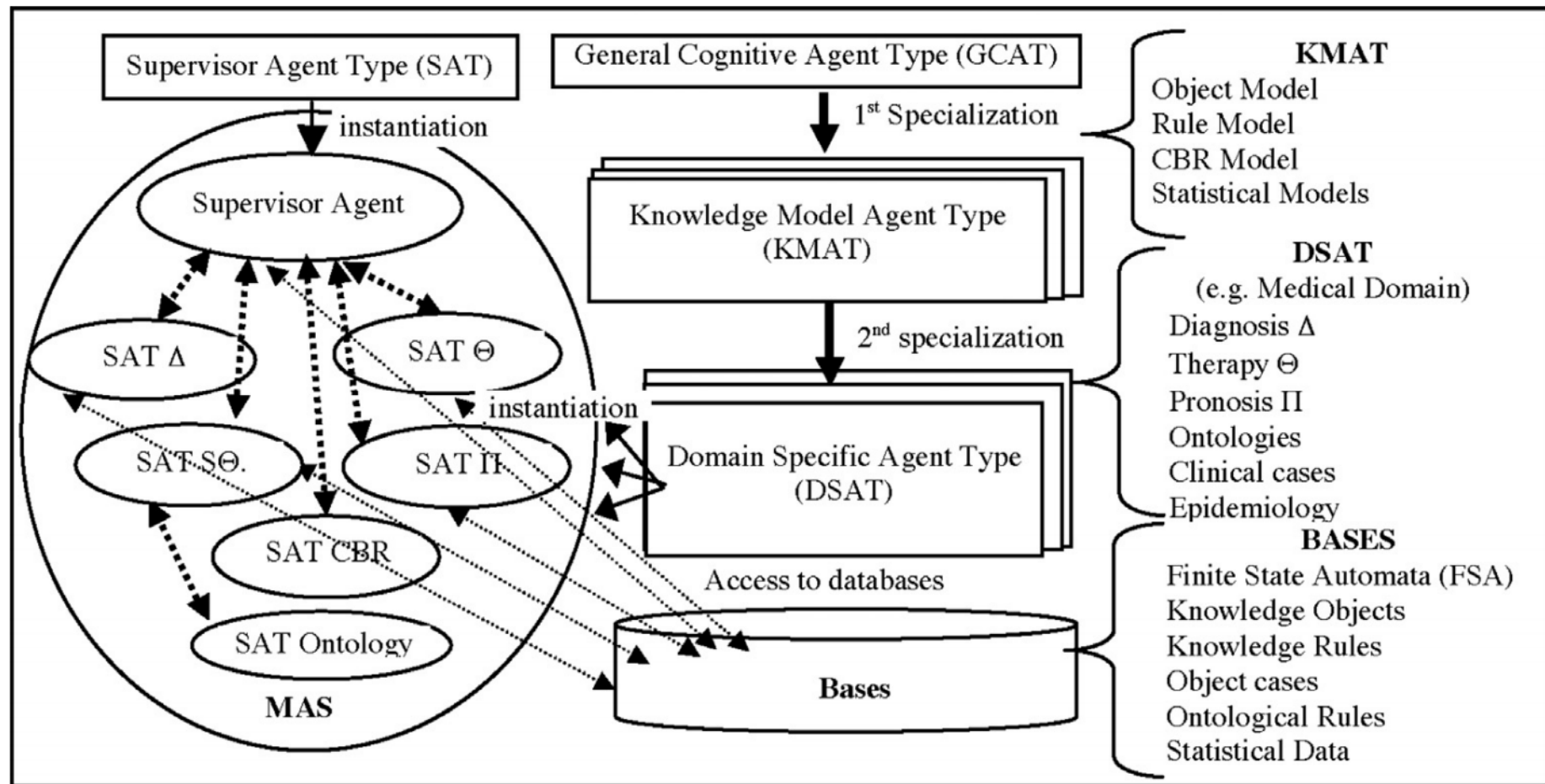
Park, H. S., Cho, H. & Kim, H. S. 2015. Development of a Multi-Agent m-Health Application Based on Various Protocols for Chronic Disease Self-Management. Journal of Medical Systems, 40, 1, 1-14, doi:10.1007/s10916-015-0401-5.

Park, H. S., Cho, H. & Kim, H. S. 2015. Development of a Multi-Agent m-Health Application Based on Various Protocols for Chronic Disease Self-Management. Journal of Medical Systems, 40, 1, 1-14, doi:10.1007/s10916-015-0401-5.

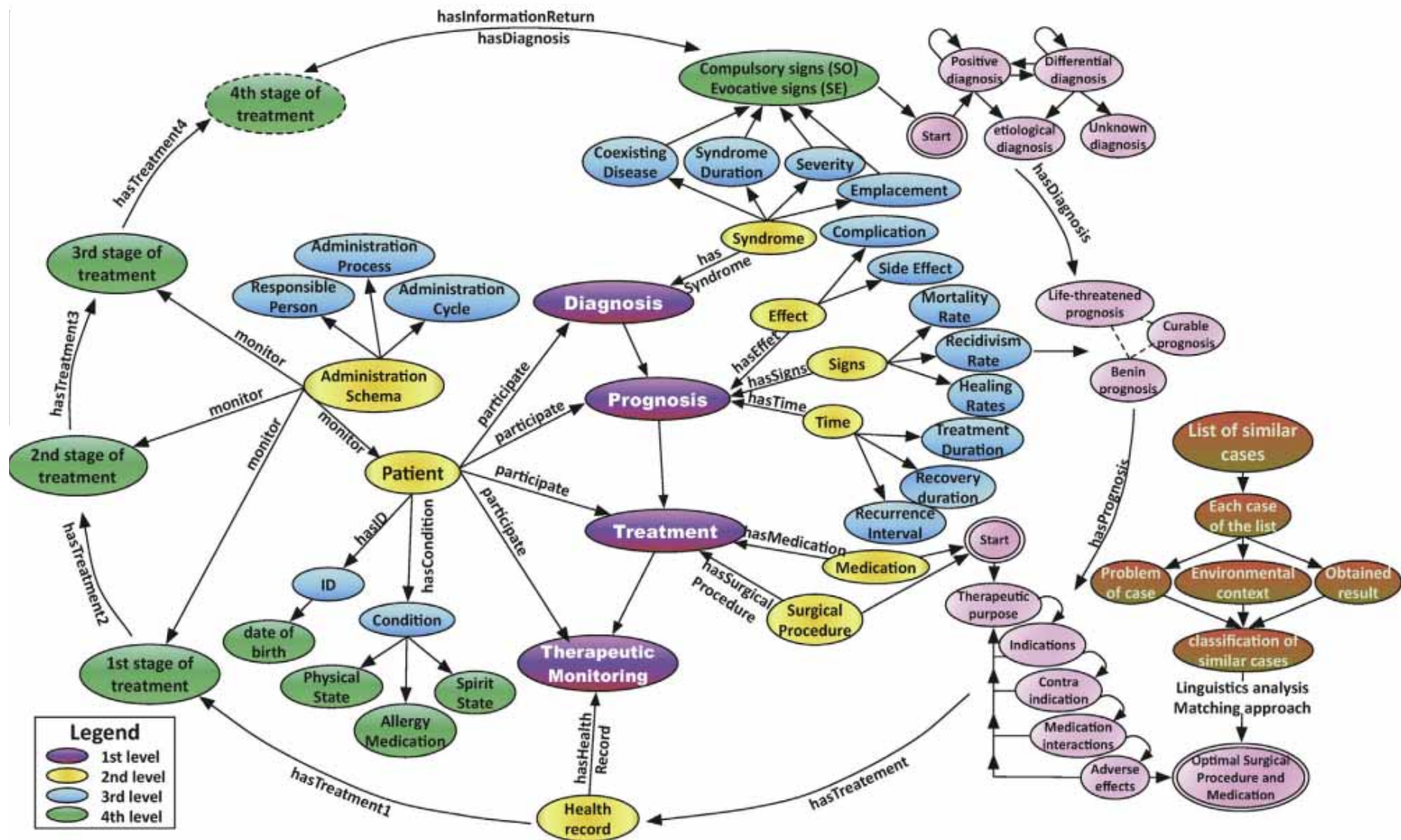


Shen, Y., Colloc, J., Jacquet-Andrieu, A. & Lei, K. 2015. Emerging medical informatics with case-based reasoning for aiding clinical decision in multi-agent system. Journal of biomedical informatics, 56, 307-317, doi:10.1016/j.jbi.2015.06.012.

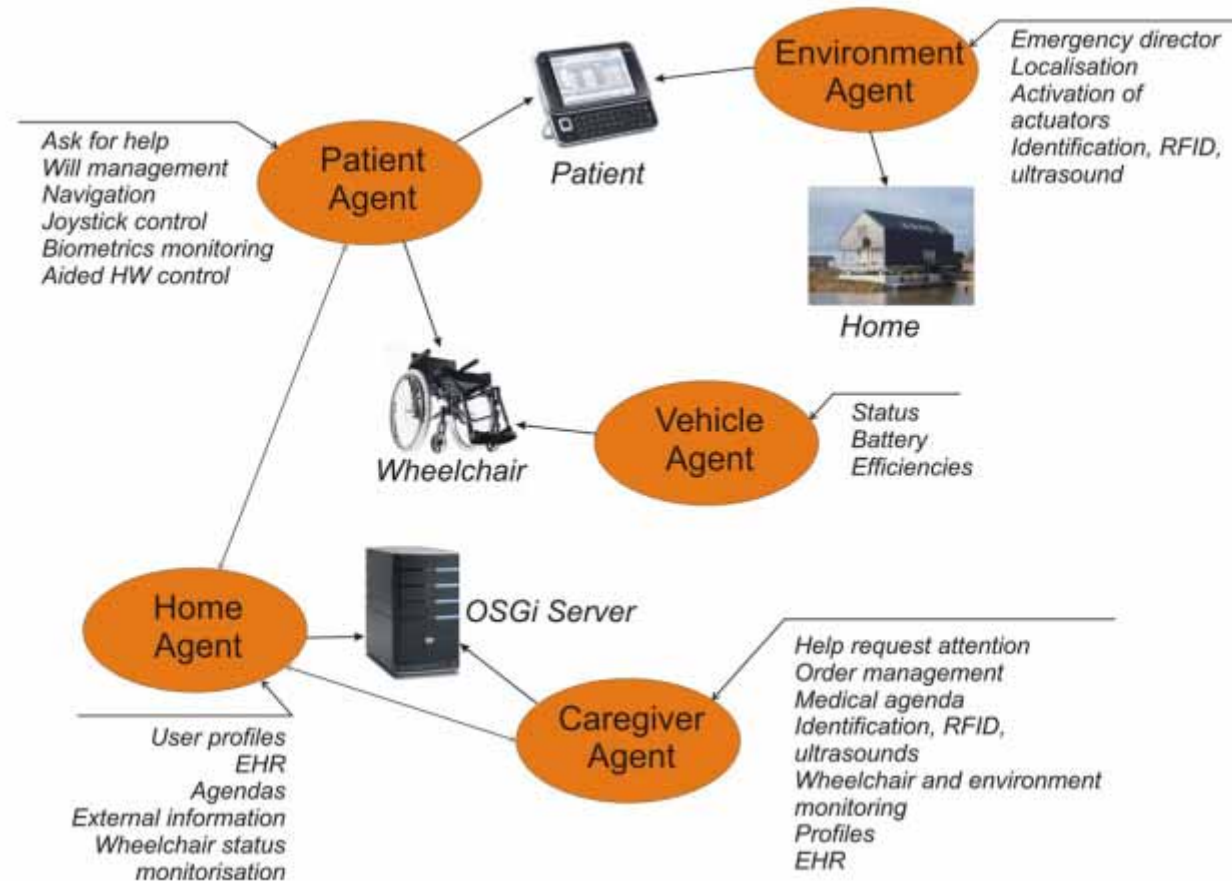




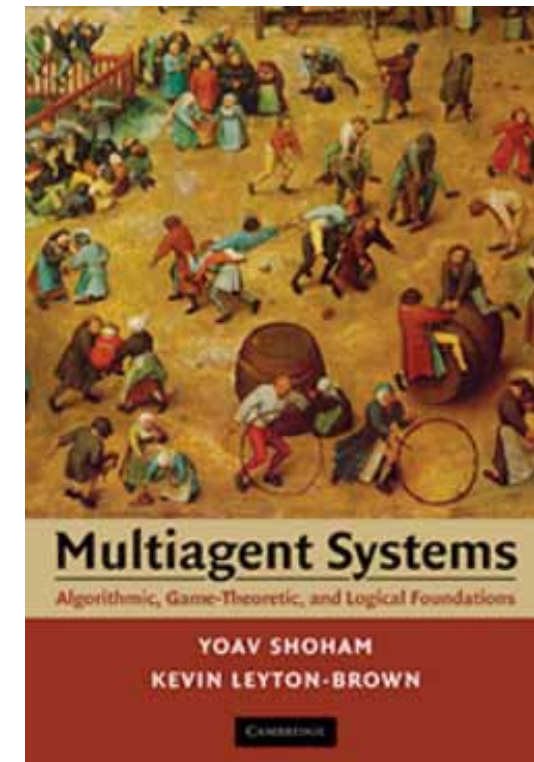
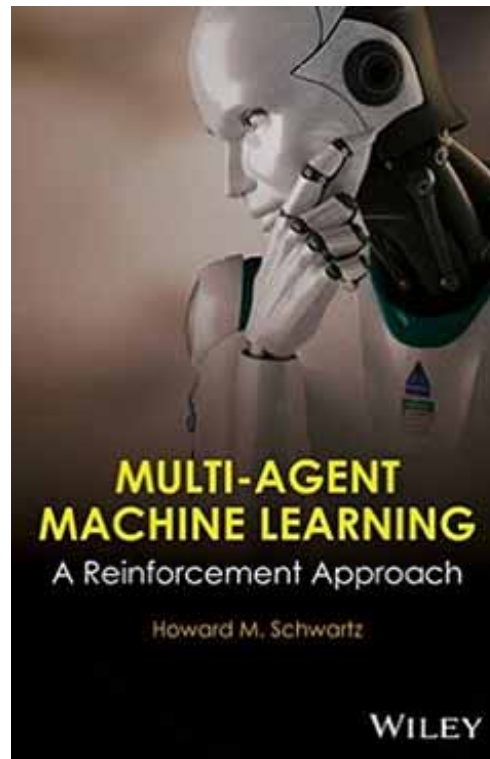
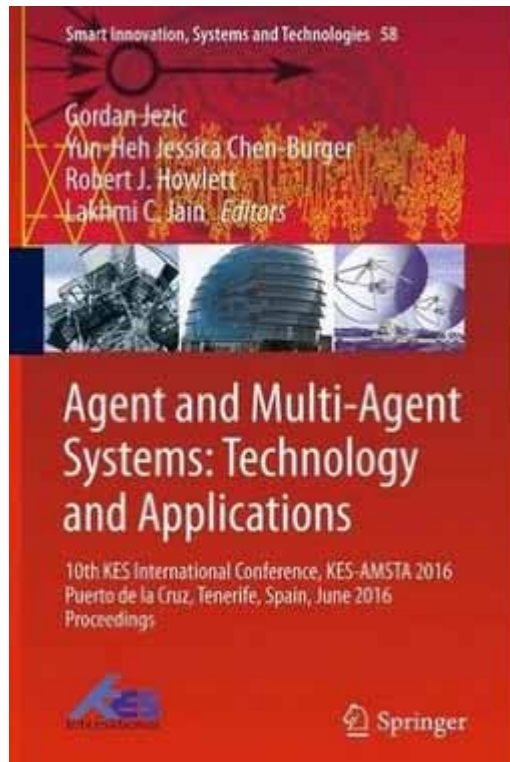
Shen, Y., Colloc, J., Jacquet-Andrieu, A. & Lei, K. 2015. Emerging medical informatics with case-based reasoning for aiding clinical decision in multi-agent system. Journal of biomedical informatics, 56, 307-317, doi:10.1016/j.jbi.2015.06.012.



Shen, Y., Colloc, J., Jacquet-Andrieu, A. & Lei, K. 2015. Emerging medical informatics with case-based reasoning for aiding clinical decision in multi-agent system. *Journal of biomedical informatics*, 56, 307-317, doi:10.1016/j.jbi.2015.06.012.

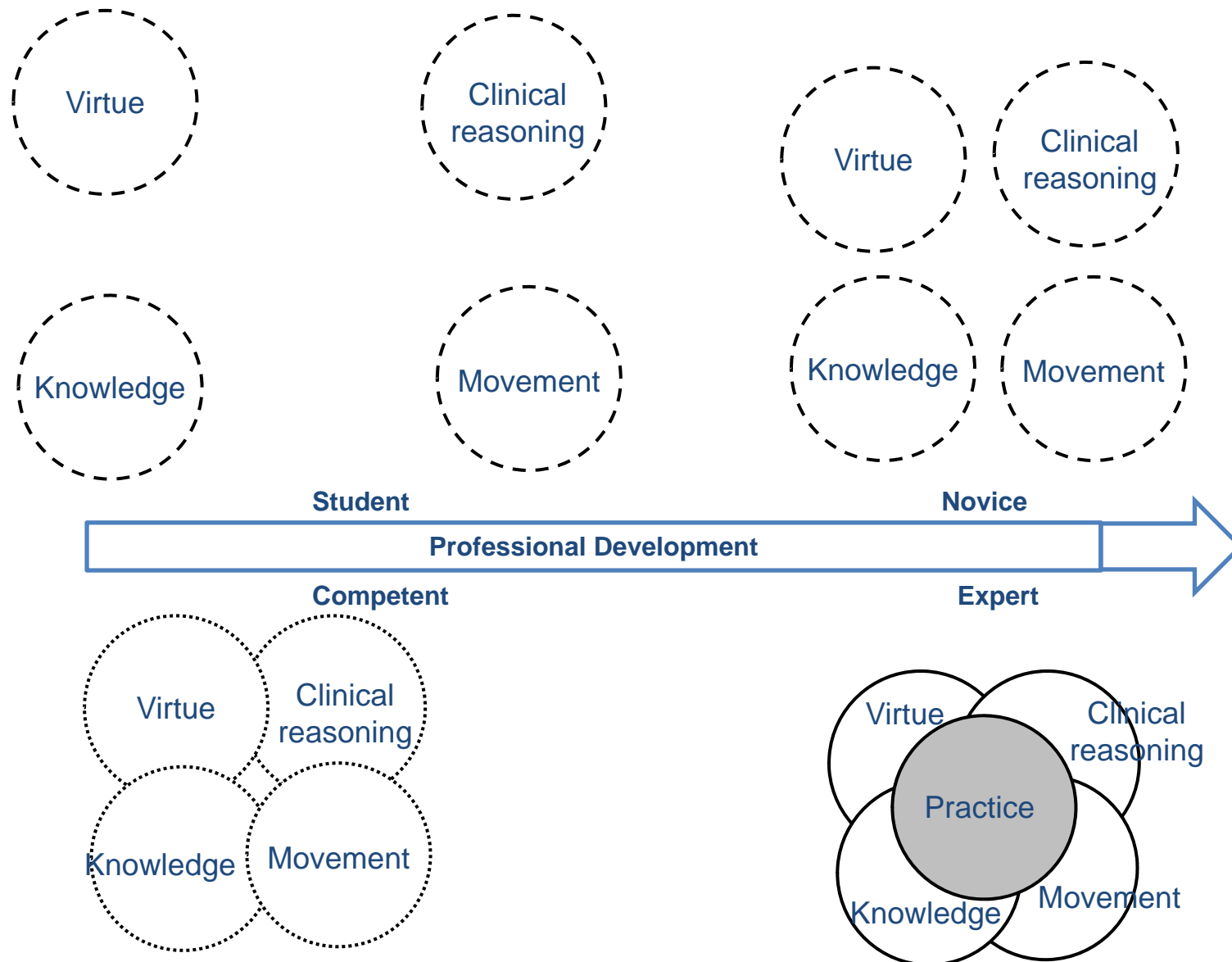


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04 Remember: Medical Decision Making as a Search Problem



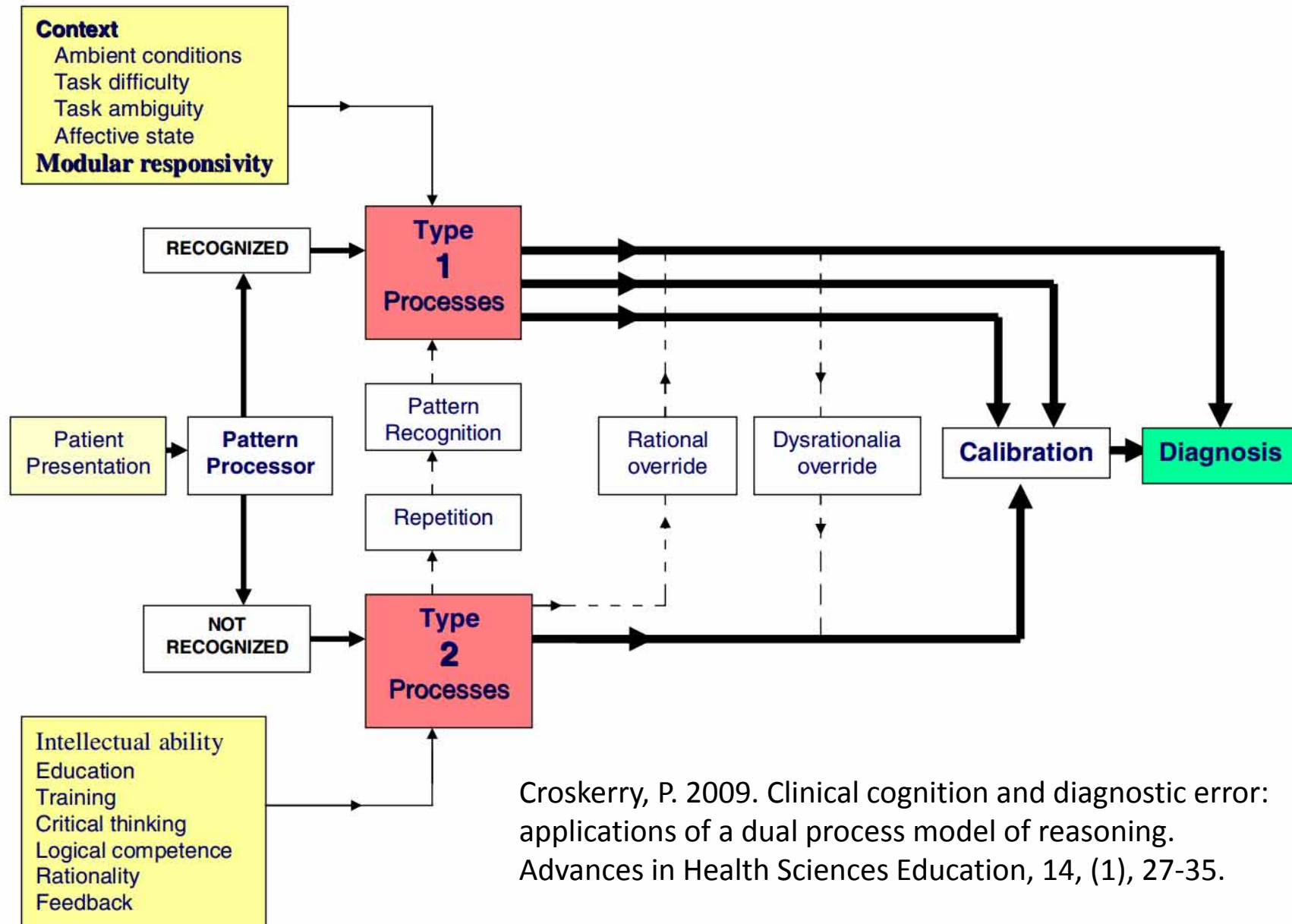


Resnik, L. & Jensen, G. M. 2003. Using clinical outcomes to explore the theory of expert practice in physical therapy. *Physical Therapy*, 83, (12), 1090-1106.

Characteristic	Type 1 Heuristic Intuitive	Type 2 Systematic Analytic
Cognitive Style	Heuristic associative (experience-based) Inductive reasoning	Bounded rationality (Hypothetico-deductive) Normative reasoning
Cost (high/low)	Low	
Automaticity(high/low)		Low
Rate (fast/slow)		Low
Reliability (high/low)	Low	
Errors (high/low)		Low
Effort (high/low)	Low	
Predictive Power (high/low)	Low	
Emotional Component		Low
Scientific Rigor (high/low)	Low	
Context (high/low)		Low
Cognitive Awareness	Low	

Characteristic	Type 1 Heuristic Intuitive	Type 2 Systematic Analytic
Cognitive Style	Heuristic associative (experience-based) Inductive reasoning	Bounded rationality (Hypothetico-deductive) Normative reasoning
Cost	Low	High
Automaticity	High	Low
Rate	Fast	Slow
Reliability	Low	High
Errors	High	Low
Effort	Low	High
Predictive Power	Low	High
Emotional Component	High	Low
Scientific Rigor	Low	High
Context	High	Low
Cognitive Awareness	Low	High

Croskerry, P. 2009. Clinical cognition and diagnostic error: applications of a dual process model of reasoning. *Advances in Health Sciences Education*, 14, (1), 27-35.



Croskerry, P. 2009. Clinical cognition and diagnostic error: applications of a dual process model of reasoning. *Advances in Health Sciences Education*, 14, (1), 27-35.

Most (if not all) medical decisions can be formulated as a search in a huge search space [1]

**Medical Decision Making is
searching for an optimal (“good”*)
solution within a search space**

***) Attention in clinical practice:**

“Good intentions are the opposite of good”

in German: “Gut gemeint ist das Gegenteil von gut”

[1] Pena-Reyes, C. A. & Sipper, M. 2000. Evolutionary computation in medicine: an overview. Artificial Intelligence in Medicine, 19, (1), 1-23.

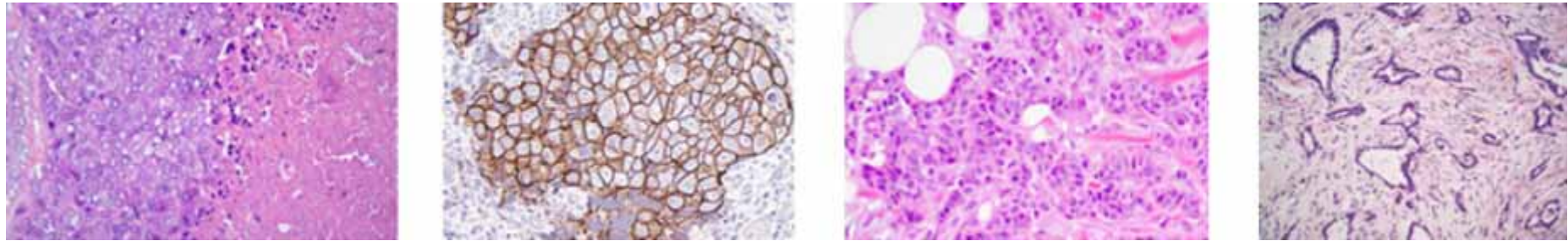
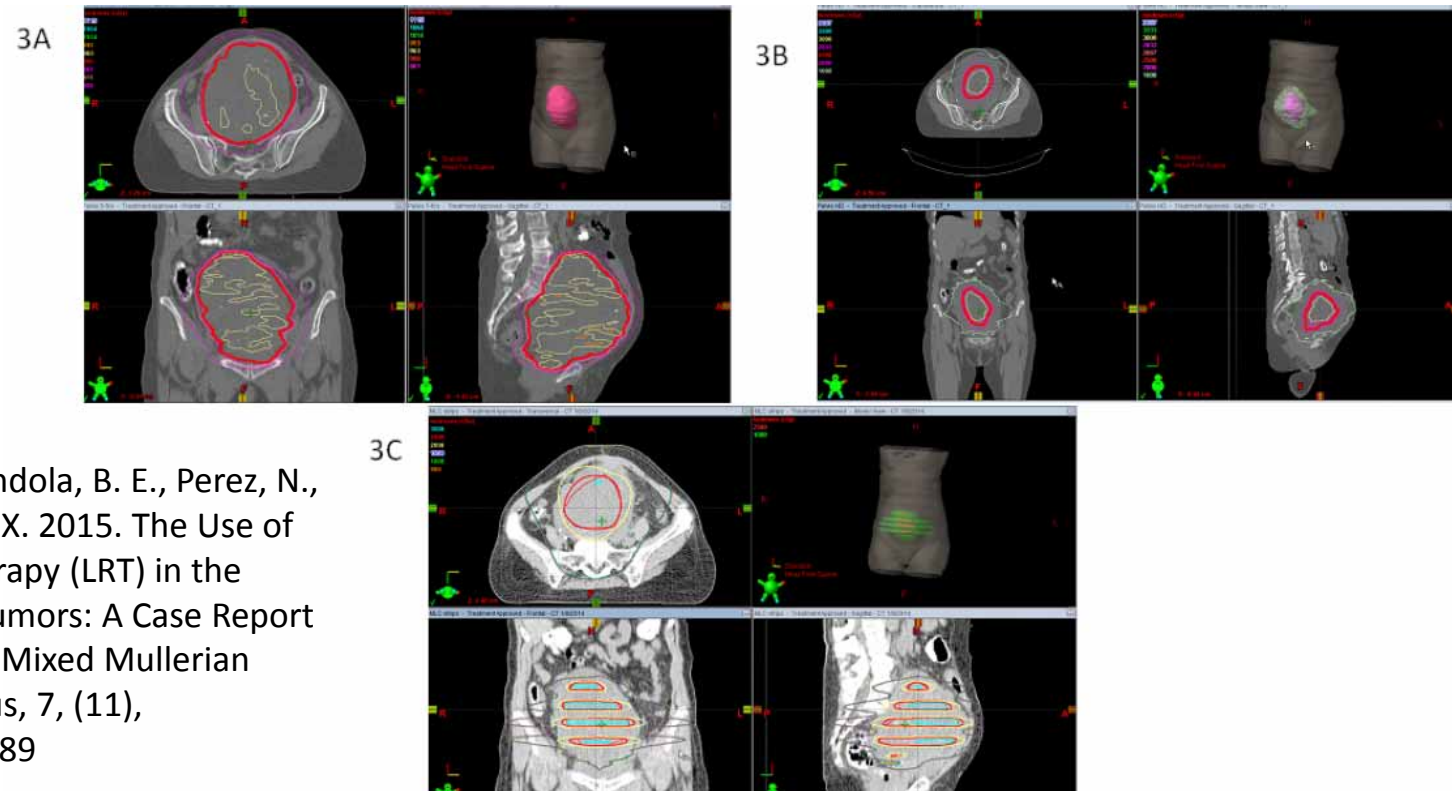


Image Source: <https://blogforbreastcancer.wordpress.com/2015/06/30/biopsy-basics-prediction-prognostics-pathology/>

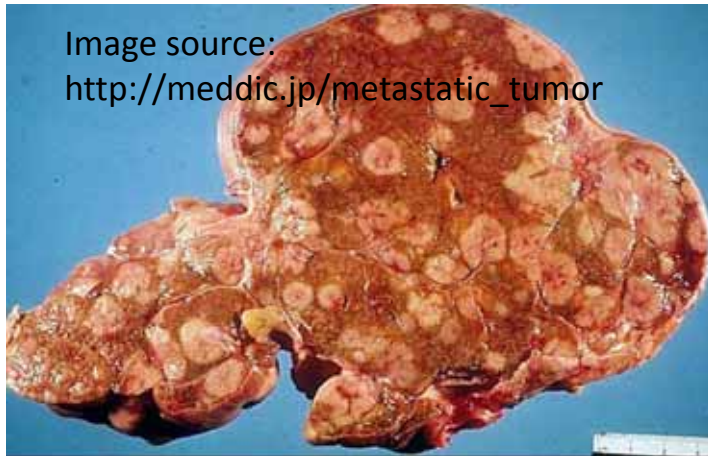
- Example 1: a pathologist analyzing biopsies to decide whether they are malignant or not.
- The pathologist is searching in the space of all possible cell features for a set of features permitting to provide a clear diagnosis

Pena-Reyes, C. A. & Sipper, M. 1999. A fuzzy-genetic approach to breast cancer diagnosis. *Artificial intelligence in medicine*, 17, (2), 131-155.



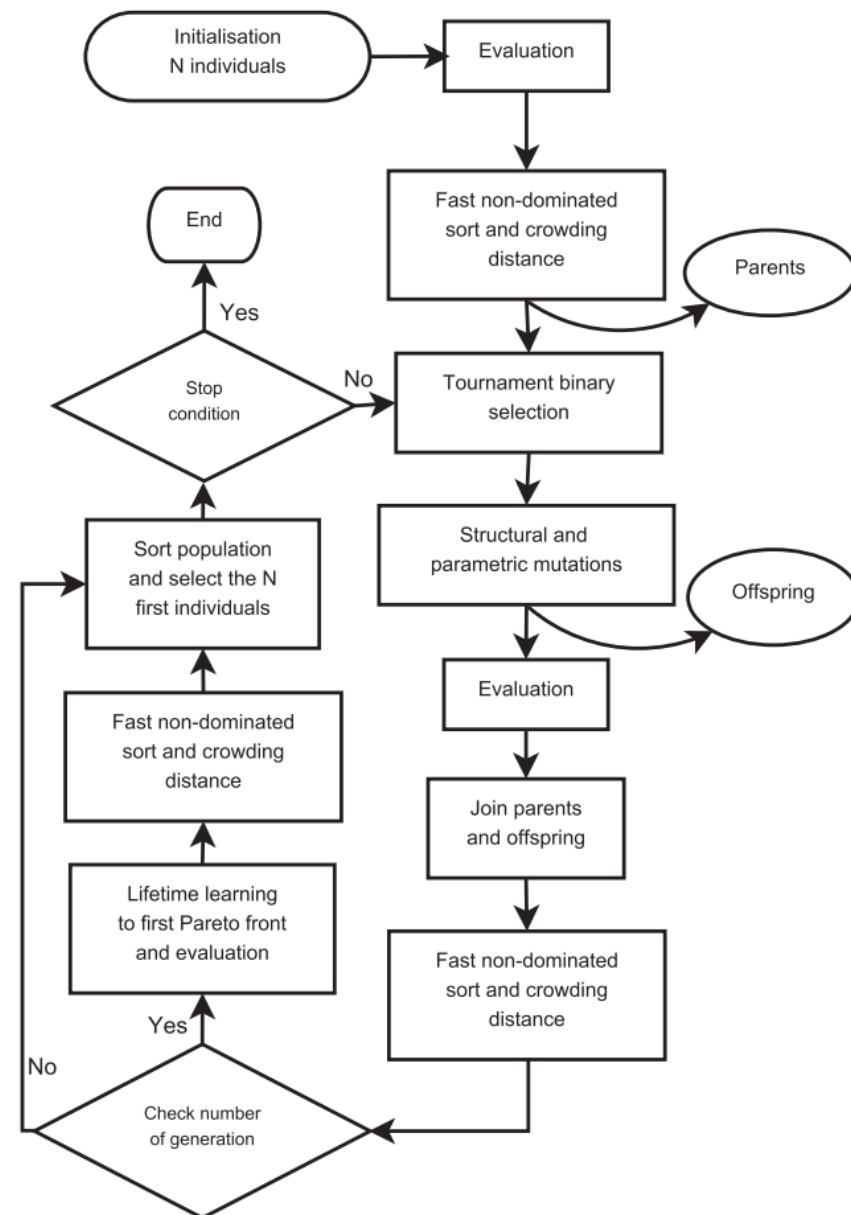
Suarez, J. M. B., Amendola, B. E., Perez, N., Amendola, M. & Wu, X. 2015. The Use of Lattice Radiation Therapy (LRT) in the Treatment of Bulky Tumors: A Case Report of a Large Metastatic Mixed Mullerian Ovarian Tumor. Cureus, 7, (11), doi:10.7759/cureus.389

- Example 2: A radiologist planning a sequence of radiation doses is searching for the best treatment in the space of all possible treatments



The optimal allocation of organs in liver transplantation is a problem that can be resolved using machine-learning techniques. Classical methods of allocation included the assignment of an organ to the first patient on the waiting list without taking into account the characteristics of the donor and/or recipient.

Cruz-Ramírez, M., Hervás-Martínez, C., Fernandez, J. C., Briceno, J. & De La Mata, M. 2013. Predicting patient survival after liver transplantation using evolutionary multi-objective artificial neural networks. *Artificial intelligence in medicine*, 58, (1), 37-49, doi:doi:10.1016/j.artmed.2013.02.004.



05 Gamification for testing interactive Machine Learning

Science is to test crazy ideas – Engineering is to put these ideas into Business
A. Holzinger

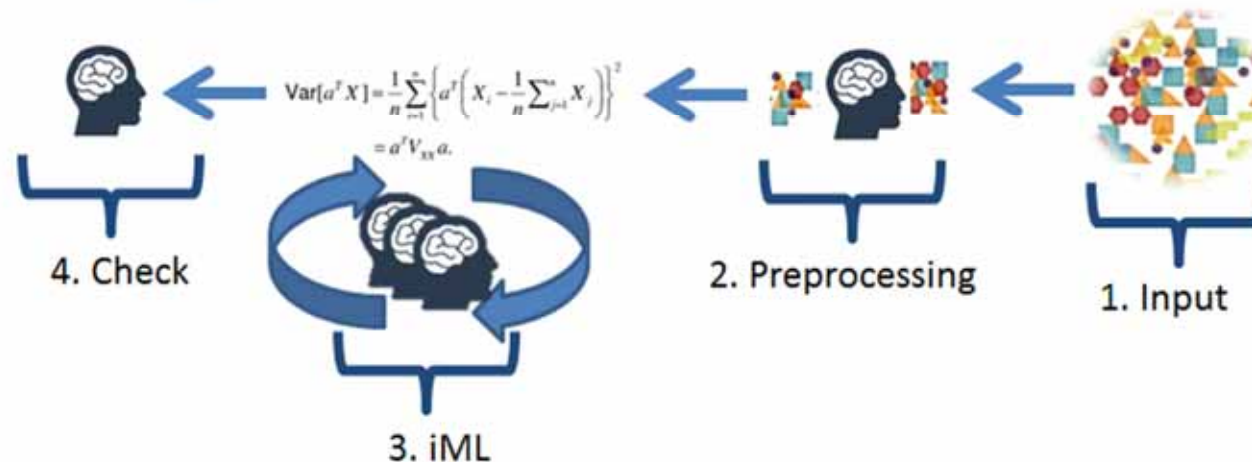
Central question: What if we could solve hard computational problems just by playing games?

Idea: increasing the performance of Machine Learning algorithms by human interaction in form of playing simple games

Advantages:

- Trivial - no need to understand technical background (the simpler the better)
- Reaching large number of people
- Enjoyable and control-able motivator
- Fits well to **federated learning** approach

Interactive Machine Learning: Human is seen as an agent involved in the actual learning phase, step-by-step influencing measures such as distance, cost functions ...



Holzinger, A. 2016. Interactive Machine Learning for Health Informatics: When do we need the human-in-the-loop? *Brain Informatics*, 3, (2), 119-131, doi:10.1007/s40708-016-0042-6.

Holzinger, A. 2016. Interactive Machine Learning (iML). *Informatik Spektrum*, 39, (1), 64-68, doi:10.1007/s00287-015-0941-6.

Holzinger, A., Plass, M. & Kickmeier-Rust, M. D. Interactive Machine Learning (iML): a challenge for Game-based approaches. In: Guyon, I., Viegas, E., Escalera, S., Hamner, B. & Kegl, B., eds. *Challenges in Machine Learning: Gaming and Education*, 2016 Barcelona. NIPS Workshops.

WEEKLY GAMING HOURS – OVERALL GAMING TIME

IN A TYPICAL WEEK, HOW MANY HOURS OF YOUR LEISURE TIME DO YOU PERSONALLY SPEND ON EACH OF THE FOLLOWING?

- Prefer Physical
- Prefer Digital

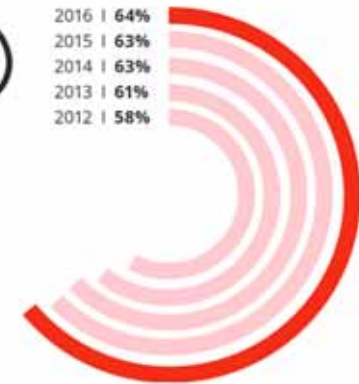


PERCENTAGE OF GAMERS

AMONG GENERAL POPULATION (AGED 13+)



2016	64%
2015	63%
2014	63%
2013	61%
2012	58%



Source: US Games 360 Report: 2017 - Nielsen -
<http://www.nielsen.com/us/en/insights/reports/2017/us-games-360-report-2017.html>

- adding video game elements in a non gaming context ...
- has been used in health, education, solving of computational problems, etc.
- e.g.: Mira rehab games - motivating people to get better



Brauner, P., Holzinger, A. & Ziefle, M. 2015. Ubiquitous computing at its best: Serious exercise games for older adults in ambient assisted living environments European Alliance on Innvoation (EAI) Endorsed Transactions: Pervasive Games, 1, (4), 1-12, doi:<http://dx.doi.org/10.4108/sg.1.4.e3>.

- Reduce dimensions of complex structures, to find an input format for the ML algorithm
 - example: a protein to points in 2D
 - more important example: Protein Folding process to *Traveling Salesman Problem (TSP)*

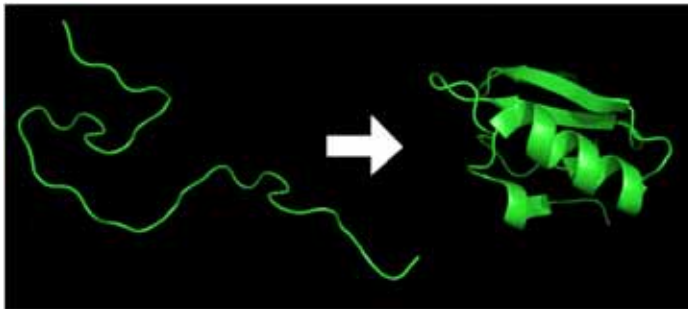
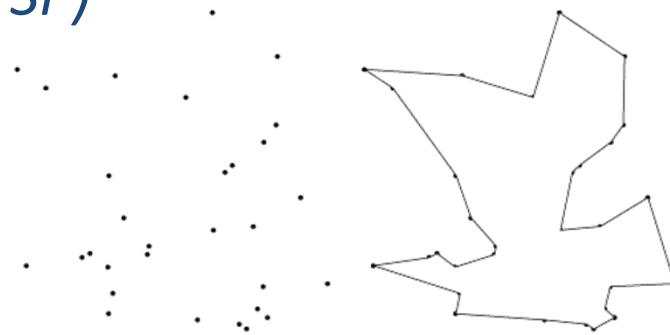


Illustration of the process of protein folding. Chymotrypsin inhibitor 2 from pdb file 1LW6.



TSP from <http://mathworld.wolfram.com/TravelingSalesmanProblem.html>
29.05.2017

- Proteins -> chain of amino acids
- basis of “how biology gets things done”
- Protein folding – extremely important for health
- proteins fold into special shapes to carry out particular functions
- misfolding: diseases, ... cancer, Alzheimer's, etc.
- Understanding protein folding = understanding diseases = helping develop new drugs = meaningful input for our iML algorithm

Theoretical background - PP - TSP

- find the shortest tour in a graph
- NP hard problem

our approach for solving TSP: **ACO (Ant colony optimization)** with iML elements.

Theoretical background - iML - Ants

- every ant deposits a certain amount of pheromones on a trail
- ants prefer trails with high pheromone values
- ants, who choose a short path return earlier to the nest (= more pheromones on path) and following ants will decide to choose this particular path more likely.

Theoretical background - iML - ACO basics

- A simple ant algorithm consists of:
 - **a state transition rule**
this rule takes a distance and pheromone measure and decides the possibility to choose an edge in the graph
 - **a pheromone updating rule**
this rule updates the pheromones according to the “traffic” on particular edges (usually after every iteration)

Theoretical background - iML - ACO basics

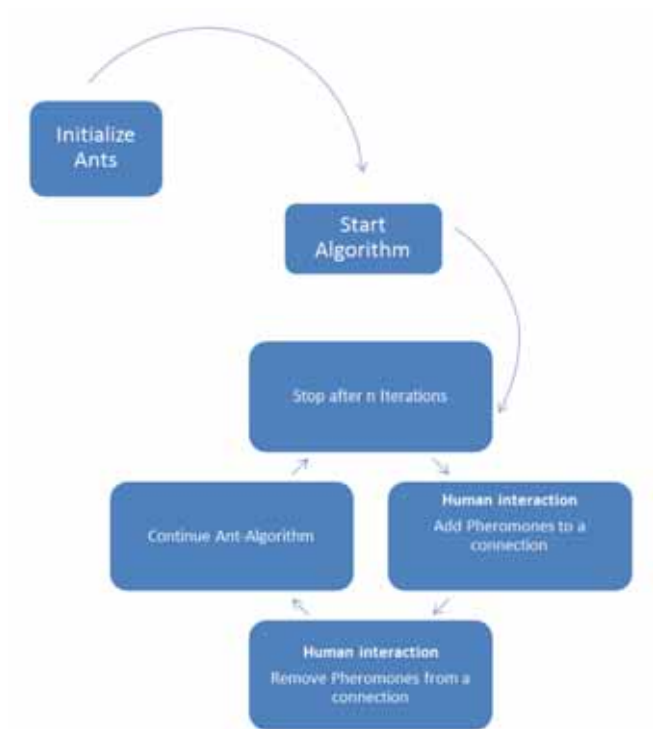
Pseudocode:

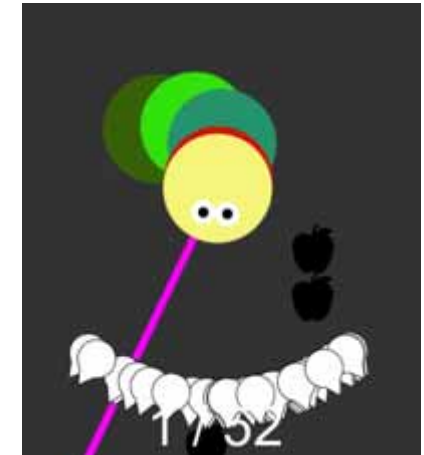
Algorithm 1 AS algorithm pseudocode

```
1: Initialize trail
2: while stopping criteria not satisfied do
3:   position each ant in starting position
4:   repeat
5:     for each ant do
6:       choose next node by state transition rule
7:     end for
8:   until every ant completed the tour
9:   perform global pheromone updating rule
10: end while
```

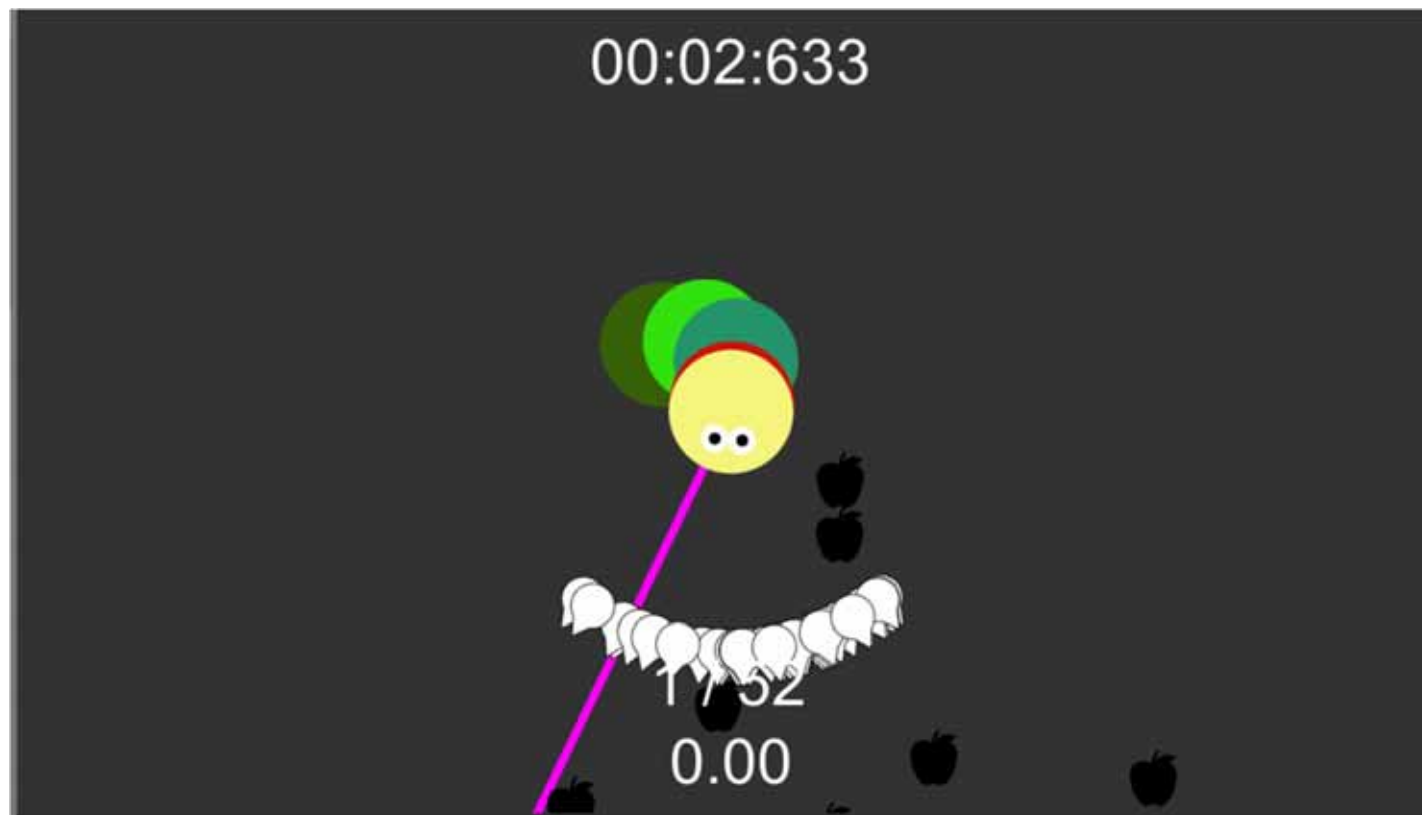
Theoretical background - iML - ACO interactive

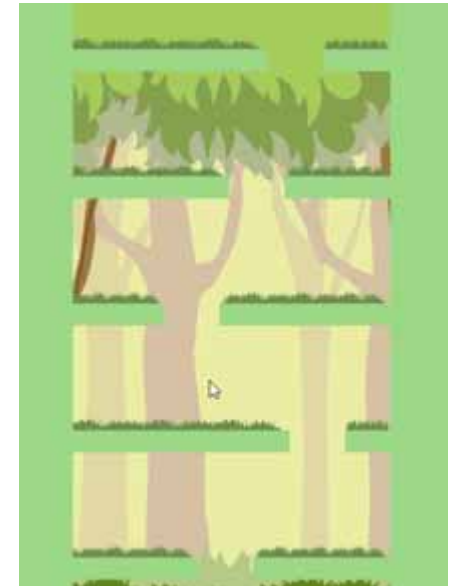
- We made the algorithm interactive
- There is a possibility to stop the algorithm during and after an iteration and change some values





- Goal: eat all apples as fast as possible
- distribution of apples = TSP
- In the background:
- suggestion to choose certain apples by ant algorithm (not necessary - human vs. machine)
- consideration of your choices





- Goal: Move as far down as possible
- you need to choose between 2 directions = 2 edges in the TSP
- suggestion system not implemented yet



- possible extensions of games:
- High-scores (online and local) – extremely motivating [1]
- UI improvements
- competition elements including levels, achievements, multiplayer, ...
- please check the Games (URLs on the Website)
- and send your comments via e-Mail

[1] Ebner, M. & Holzinger, A. 2007. Successful implementation of user-centered game based learning in higher education: An example from civil engineering. Computers and Education, 49, (3), 873-890, doi:10.1016/j.compedu.2005.11.026.

Conclusion



<https://www.youtube.com/watch?v=2HMPRXstSvQ>

- Standard (monkey work) –
yes ... let the algorithm do it 😊
- The gained time can be spent for increasing
quality – focus to research and/or complex
tasks
- Still there will be computational hard problems
where a human expert can bring in experience,
expertise knowledge, intuition
- **Most of all: Black box approaches can not
explain WHY a decision has been made**



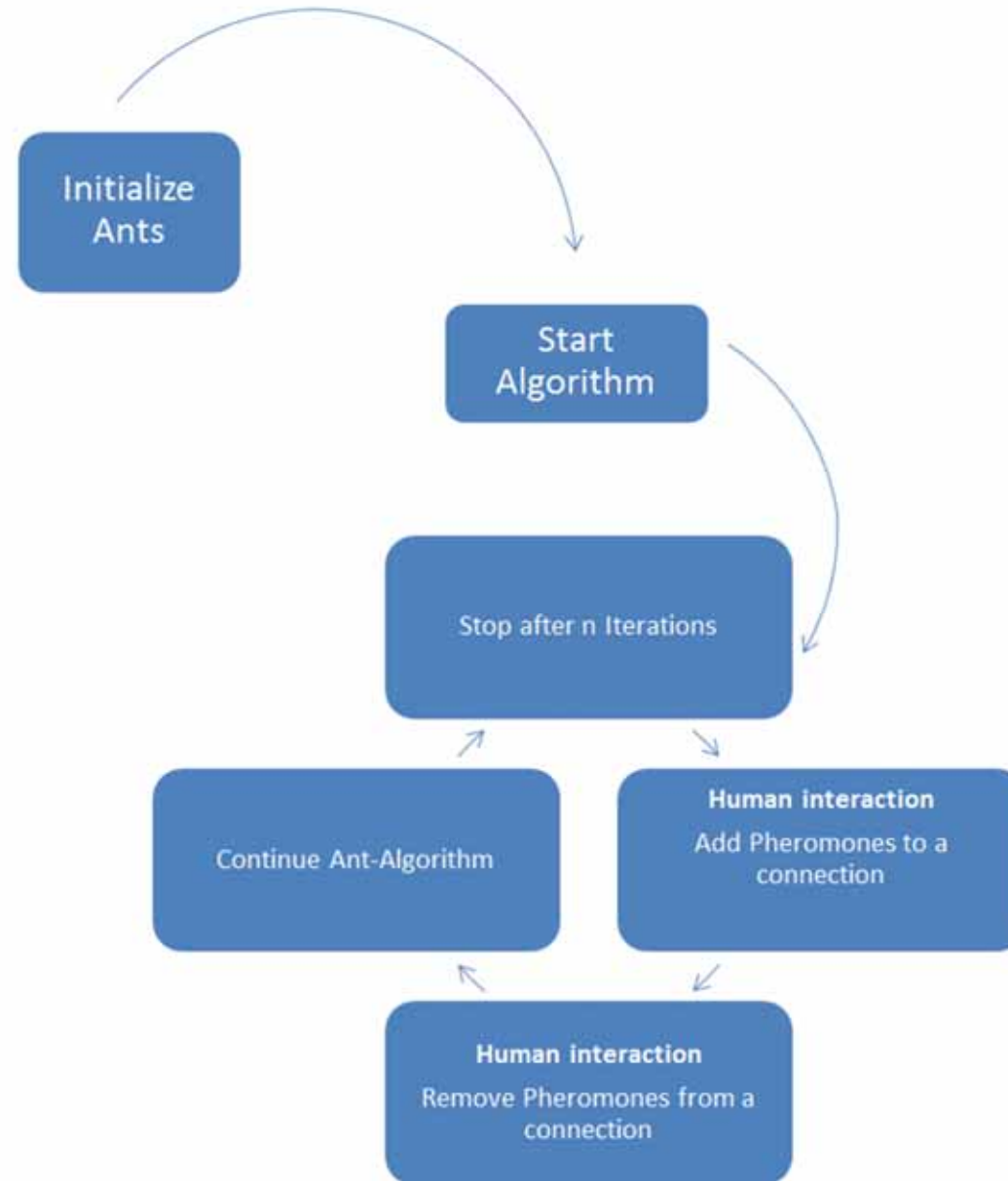
Thank you!

Questions

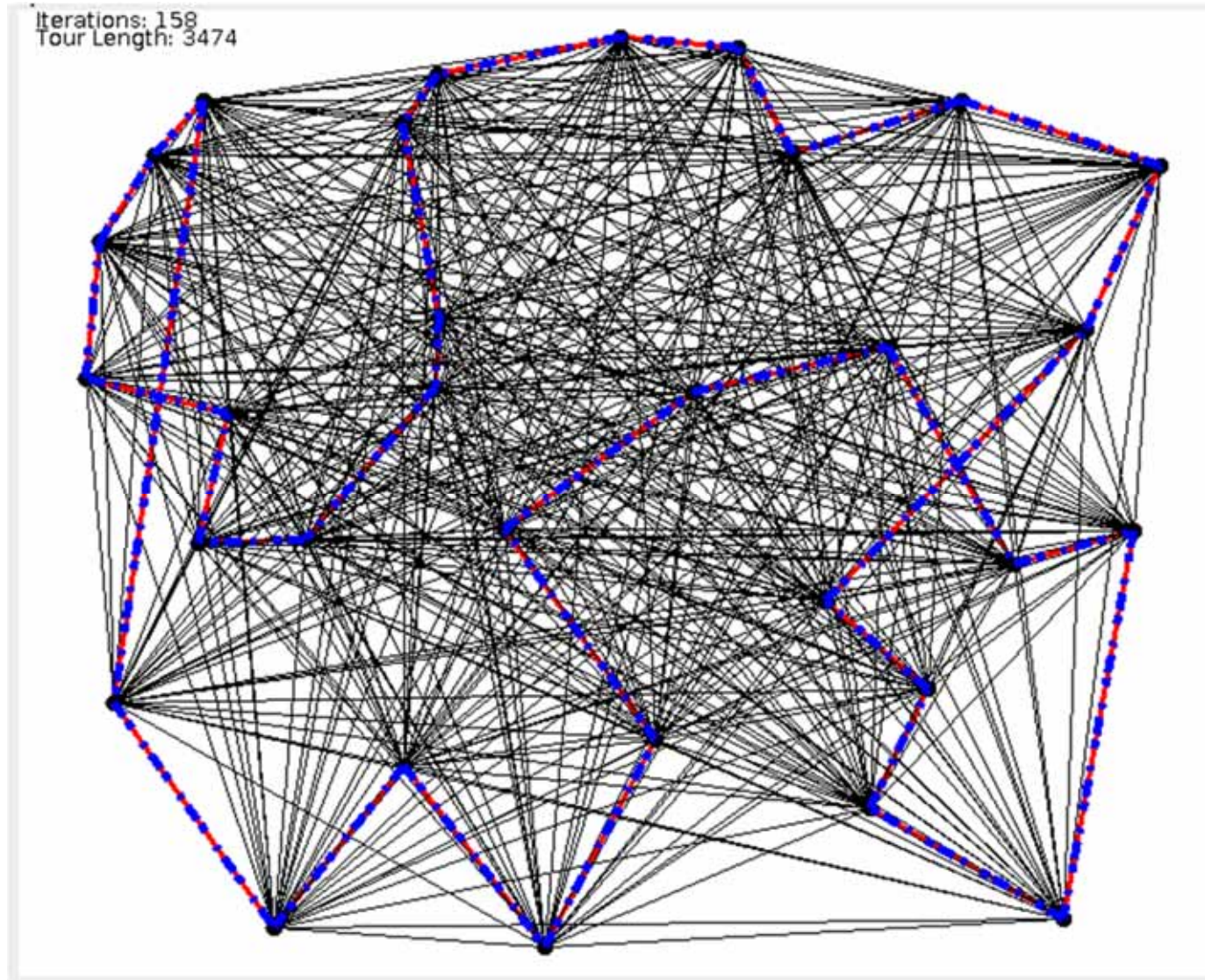
- 1=our daily life is decision making! The metaphor “estimate how far you can jump” – shall demonstrate that uncertainty matters – particular in clinical medical decisions!
- 2= The Bayesian brain – our brain as Bayesian statistical inference machine: i.e. when we perceive our physical world, make a decision, and take an action: we are always uncertainties – Bayesian networks help to understand how our brain works;
- 3= Travelling salesman problem – NP-hard – here the human-in-the-loop can help as we will see in the next lecture
- 4= Modeling or system identification problems – typical in machine learning – problem in aML is that all these are black-box approaches and iML fosters a glass-box approach for direct interaction with the algorithm itself
- 5=shows again the complexity of natural-language and the context-dependency!
- 6=In graph theory, an isomorphism of graphs G and H is a bijection between the vertex sets of G and H Find the matches -> graph matching -> very important in proteins -> subgraph isomorphism -> NP hard
- 7=grch. Stokhos (“aim”) -> stochastic – in medicine we are constantly confronted with random variables over time. It is the counterpart to deterministic processes;
- 8= Image right: Starburst galaxy, Messier 82 (M82) in the center of milky way (with Hubble telescope); Left: Cluster of benign microcalcifications
- 9= The famous “Ötzi” – the radiologists needed 10 years to discover the arrow in the chest of the prehistoric man. Example for decision making
- 10= The grand challenge is in data integration, to fuse the heterogeneous data sets, sampled from very diverse sources and time-dependend data collected over time; this also needs temporal models; 3 Billion USD per year are spend alone in the US for health (320 Mill Inhabitants);

- What is the general idea of evolutionary algorithms?
- What is the difference between CI, EC, and GA?
- Why are EC relevant for health informatics?
- What are the main differences in the ideas of Lamarck, Darwin, Baldwin, and Mendel?
- Please explain the general scheme of an evolutionary algorithm and explain the components!
- Sketch the pseudocode of a fitness function!

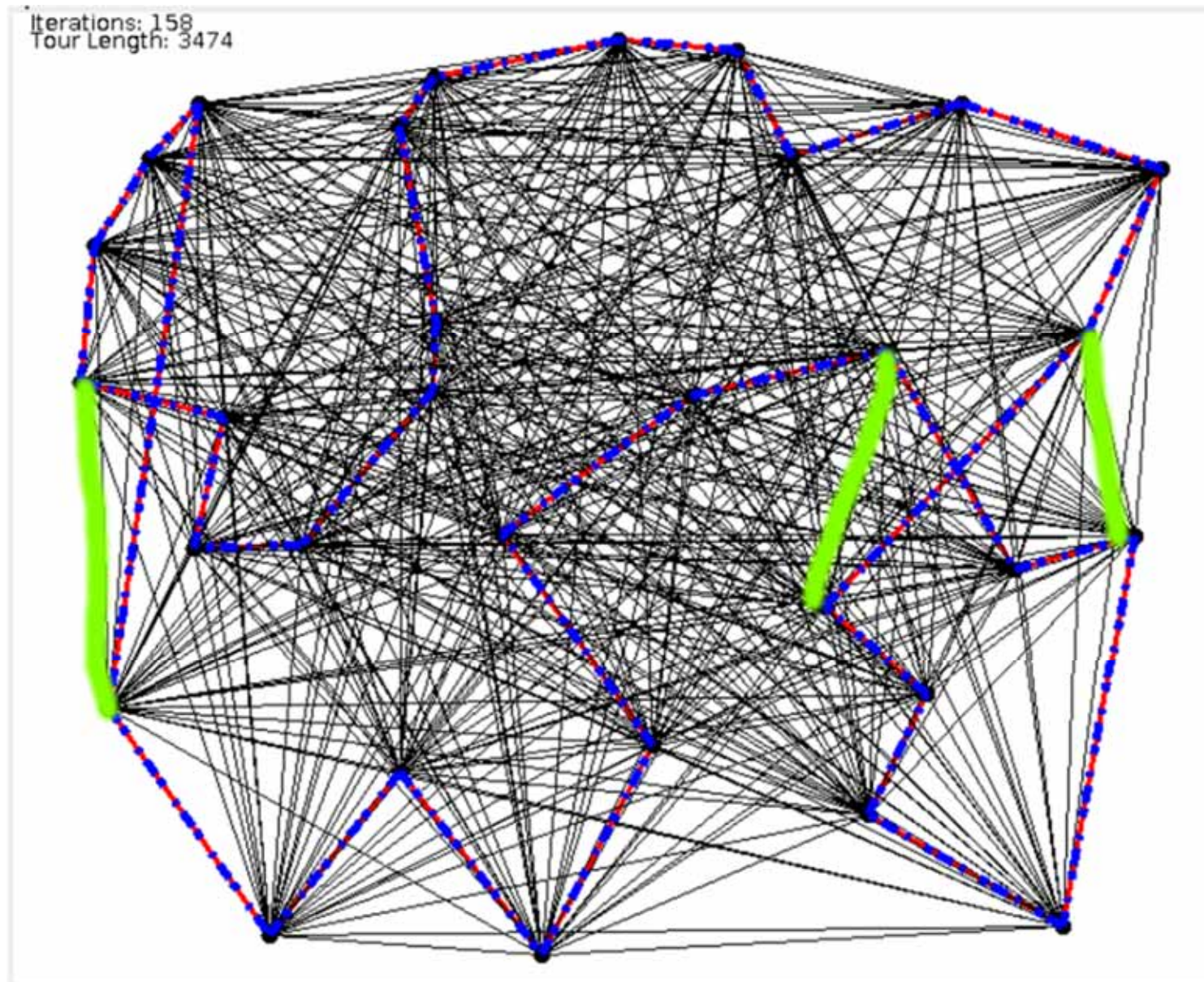
Appendix



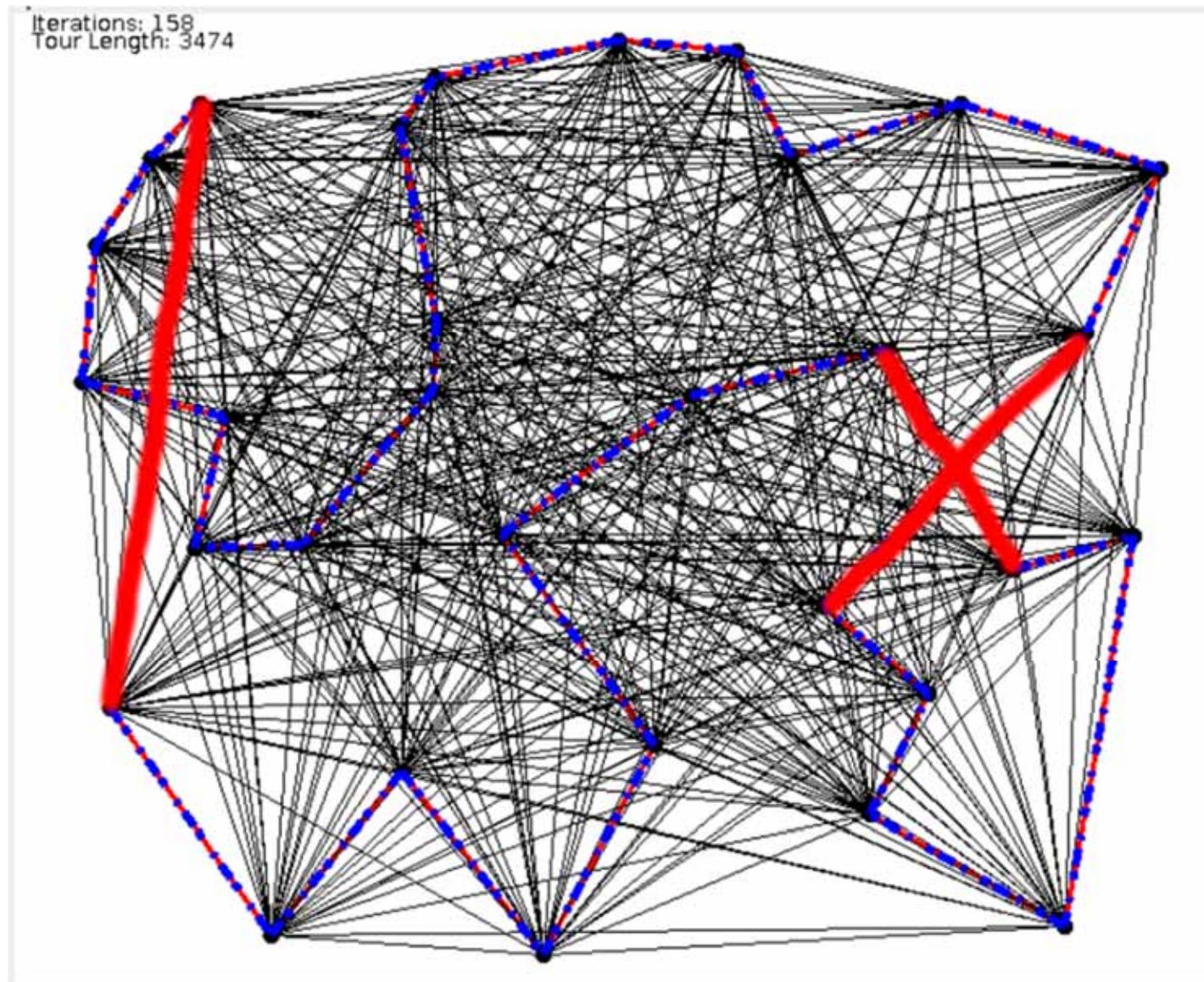
Bring in the Human



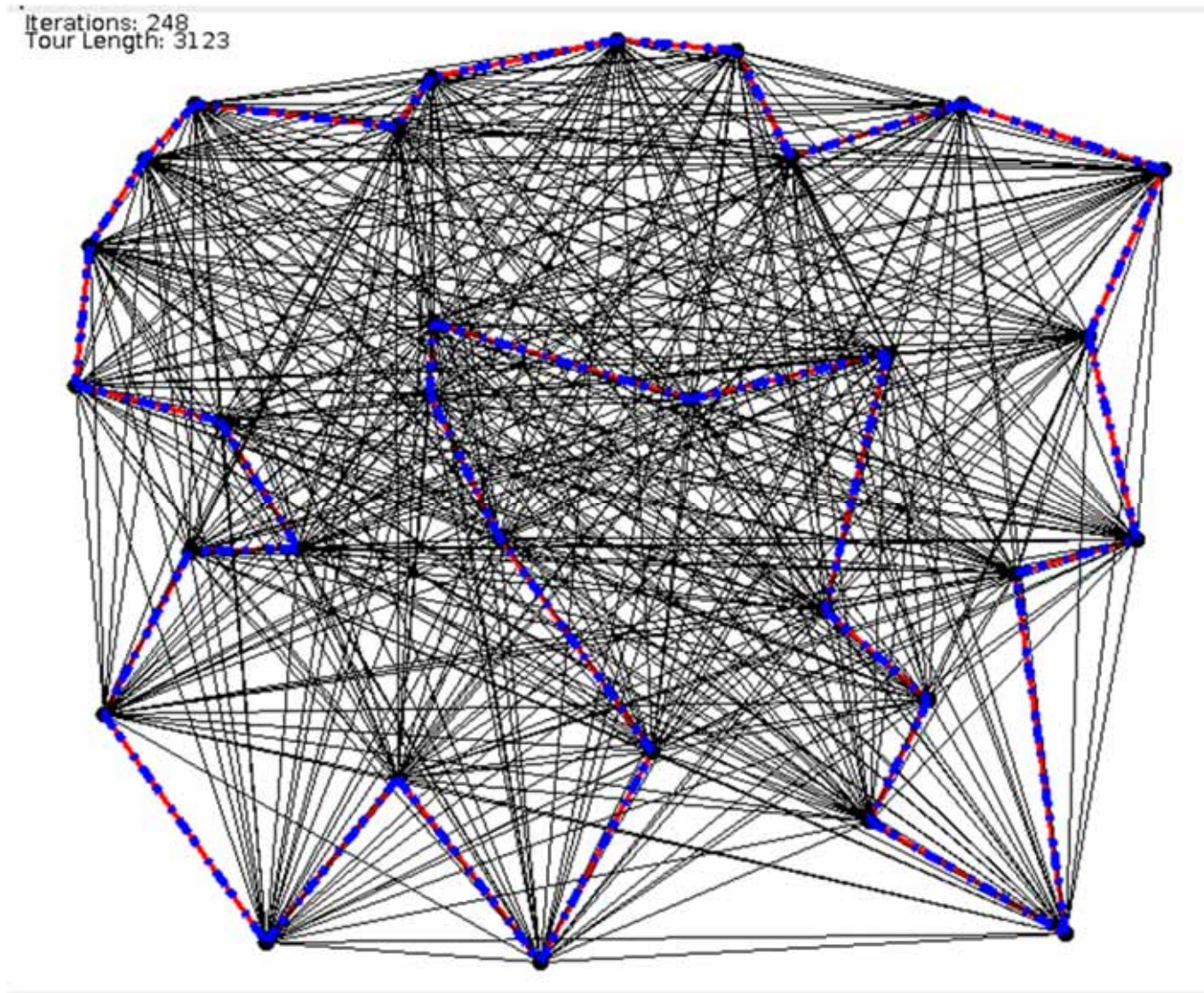
Add Pheromones



Remove Pheromones



Result:



- Please explain the five mainstreams in ML!
- Why is it generally not easy to solve problems in health informatics?
- What is the model of a computational agent?
- Why is protein folding a hard problem?
- Explain why the study of human learning and machine learning can benefit from each other?
- What is a Pheromon and how does it work?
- In which areas are humans better than computers?
- What is the human kernel experiment?
- Why is simulated annealing interesting?
- Explain the Ant Colony Algorithm via pseudo code!
- Why should we study natural computing?

Appendix



“The contagion spread rapidly and before its progress could be arrested, sixteen persons were affected of which two died. Of these sixteen, eight were under my care. On this occasion I used for the first time the affusion of cold water in the manner described by Dr. Wright. It was first tried in two cases ... [then] employed in five other cases. It was repeated daily, and of these seven patients, the whole recovered.”

Currie (1798)

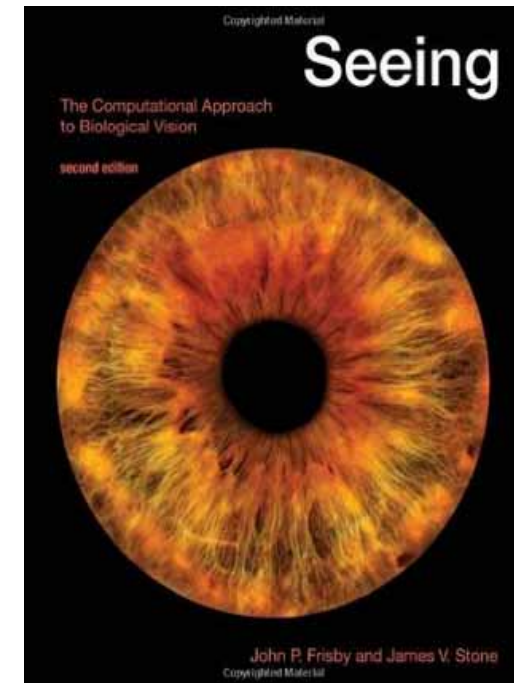
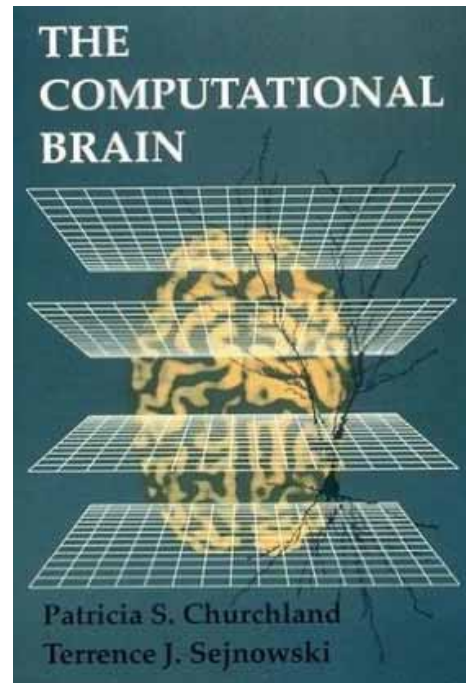
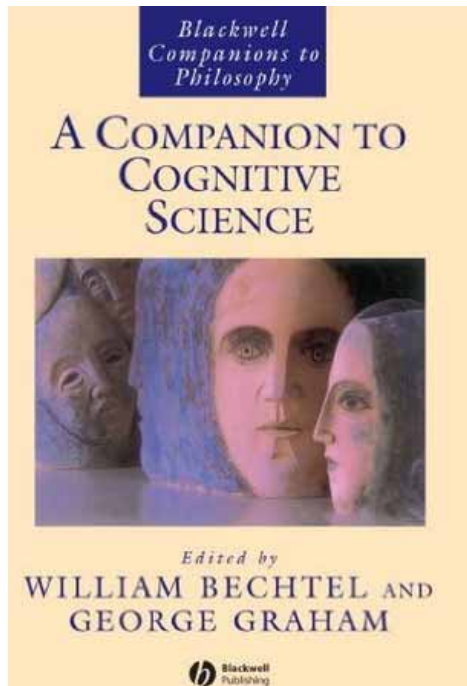
Medical Reports on, the Effects of Water, Cold and Warm, as a Remedy in Fevers and Febrile Diseases

[illegible]

- Testing of novel Evolutionary algorithms:
 - Intelligent Water Drops
 - Bacteria Foraging Search
 - ...

- EVOLKNO crowdsourcing platform to implement and test new algorithms:
 - Open Source data for Researchers to test algorithms
 - Evaluate quality, reusability and efficiency of algorithms

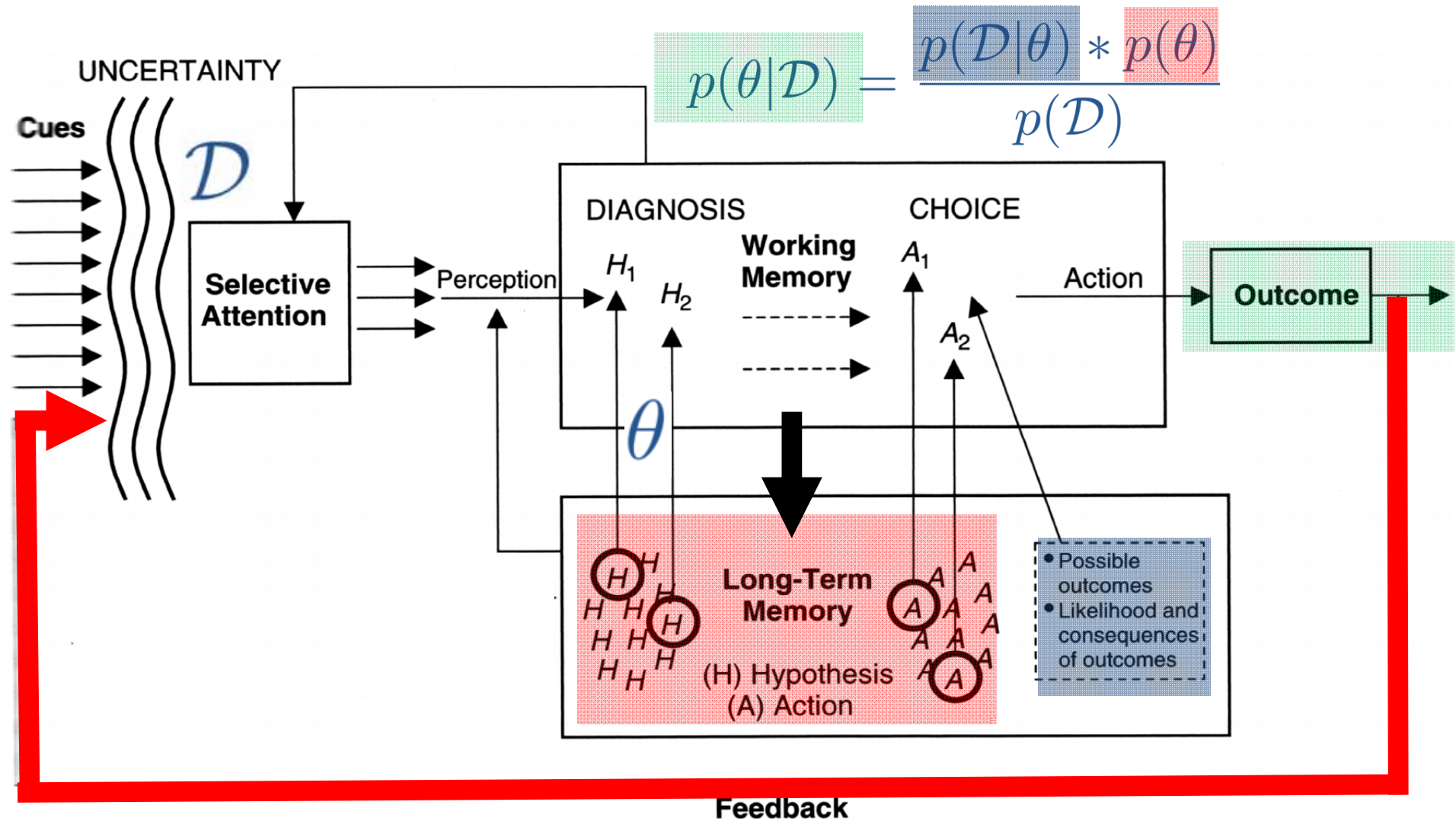
[16] Holzinger, K., Palade, V., Rabadan, R., & Holzinger, A. (2014). Darwin or lamarck? future challenges in evolutionary algorithms for knowledge discovery and data mining. In Interactive Knowledge Discovery and Data Mining in Biomedical Informatics (pp. 35-56). Springer Berlin Heidelberg.



- 1 = This is a **chromosome** – in computation we call it a sequence of **information objects**. Each cell of any living creature has blueprints in the form of this chromosomes, which are strings of DNA and blocks of DNA, called ‘genes’, are responsible for the manifestation of traits, such as eye color, beard, etc.; Building blocks for chromosomes are proteins.
- 2 = This is a typical **naïve Bayes classifier**: An example E is classified to the class with the maximum posterior probability; wnb = weighted naïve Bayes, V denotes the classification given by the wnb, and is the weight of the attribute; The naïve Bayes classifier combines this model with a decision rule. One common rule is to pick the hypothesis that is most probable; this is known as the maximum a posteriori or MAP decision rule.
- 3= This is the famous finding of Charles **Darwin: tree** of life. Darwin used the tree-structure in the context of his theory of evolution: Populations of individuals compete for limited resources; a fitness function is associated with each individual, which quantifies ability to survive; Parent populations reproduce to form offspring populations; and the traits of offspring are a combination of the traits of parents.

- 4=This is the experiment by Mnih et al (2015) “Google Deepmind”: Human-level control through deep reinforcement learning, before the GO hype. They applied a deep network for playing an **Atari-Game**.
- 5=The **classification** experiment by Josh Tenenbaum, where he asks the question: How does the human mind get so much from so little?
- 6=Amazingly fascinating **big numbers**: We have 10^{80} elementary particles in the universe, multiplied by 10^{40} time steps since the big bang, we have 10^{120} possible computations in the universe – an amazing large number – BUT (big but!): one DNA molecule carries genetic information of the DNA with $3 \cdot 10^9$ base pairs having $4^{3 \cdot 10^9}$ combinations – which is a far larger number !!
- 7= **Distance measures**, Euclidean, Manhattan, Maximum; very important for similarity measures of vectors. The Manhattan distance is the simple sum of the horizontal and vertical components, whereas the diagonal distance might be computed by applying the Pythagorean theorem.





Wickens, C. D. (1984) *Engineering psychology and human performance*.
Columbus (OH), Charles Merrill, Altered by Holzinger, A. (2017)