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Integrated Processes for Modelling & Simulation Health Care Systems

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CSO dwh GmbH – Simulation Services and Technical Solutions, Vienna

dexhelpp

Decision Support for Health Policy and Planning

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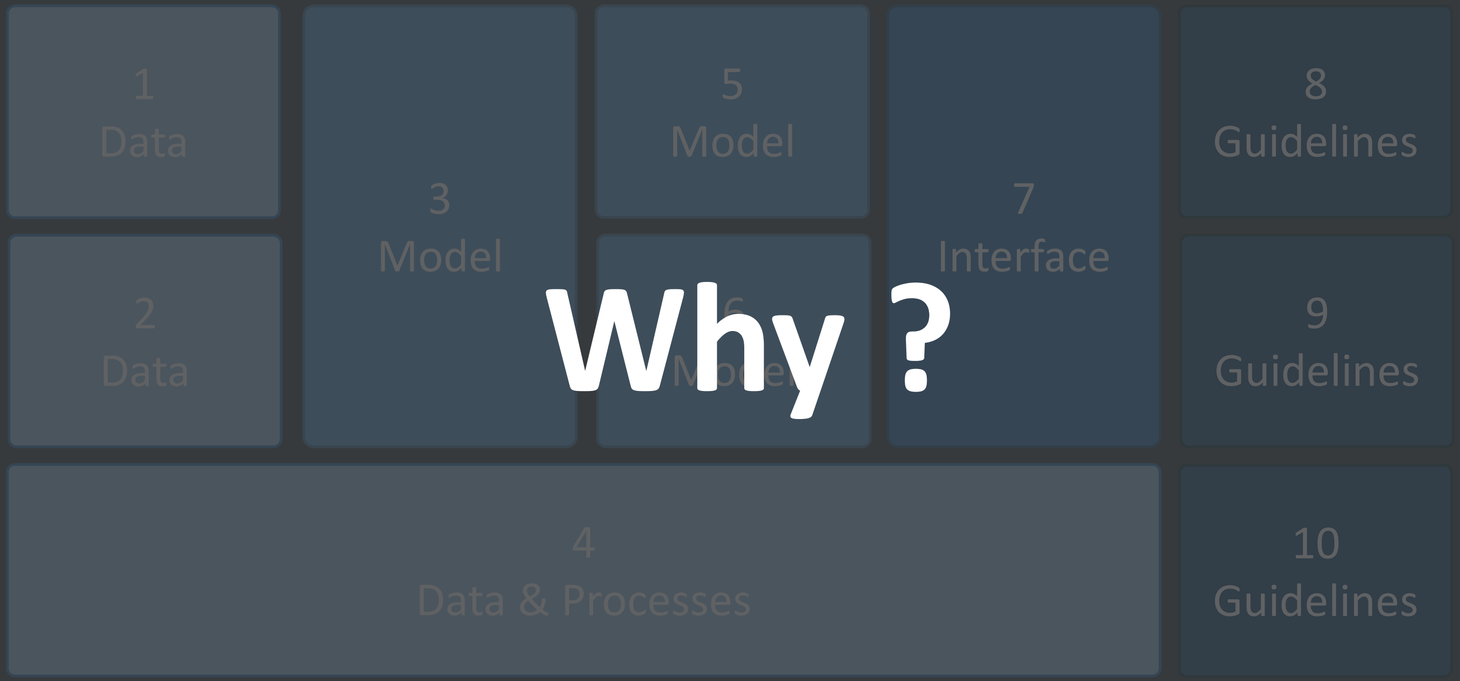
10 Concepts to Integrate

Why?

-> Dynamics & Complexity
-> Economics
-> Big Data

How?

-> 4th Paradigm
-> Modelling Dynamics
-> Data vs. Models
-> Processes



Integrated Processes for Modelling & Simulation

Man schützt das Klima am besten, indem man kinderlos bleibt, 58,6 Tonnen CO_2 pro Jahr lassen sich so einsparen, heißt es. So ein Unsinn!
by Gregor Walter-Drop, DIE ZEIT, 21. März 2019, Nr. 13/2019

Strange Decision Support

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“We recommend four widely applicable high-impact (i.e. low emissions) actions with the potential to contribute to systemic change and substantially reduce annual personal emissions: having one fewer child (an average for developed countries of 58.6 tonnes CO_2-equivalent (tCO_2e) emission reductions per year), living car-free (2.4 tCO_2e saved per year), avoiding airplane travel (1.6 tCO_2e saved per roundtrip transatlantic flight) and eating a plant-based diet (0.8 tCO_2e saved per year). “

Seth Wynes and Kimberly A Nicholas 2017 Environ. Res. Lett. 12 074024

Kritik: „…Modellannahmen gehen von falschen Annahmen aus, stellen Fakten absurd zusammen um auf die Ergebnisse zu kommen“

The Seven Tools of Causal Inference, with Reflections on Machine Learning
by Judea Pearl, Communications of the ACM, March 2019, Vol. 62 No. 3, Pages 54-60, 10.1145/3241036

Causal Inference refl. ML

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„...Machine learning researchers have noted current systems lack the ability to recognize or react to new circumstances they have not been specifically programmed or trained for.... „

„...Another obstacle is "explainability," or that "machine learning models remain mostly black boxes" unable to explain the reasons behind their predictions or recommendations, thus eroding users' trust..."

Classification of causal information in terms of the kind of questions each class is capable of answering:

Level (Symbol)	Typical Activity	Typical Questions	Examples
1. Association $P(y\|x)$	Seeing	What is? How would seeing *X* change my belief inY?	What does a symptom tell me about a disease? What does a survey tell us about the election results?
2. Intervention $P(y\|do(x), z)$	Doing, Intervening	What if? What if I do *X*?	What if I take aspirin, will my headache be cured? What if we ban cigarettes?
3. Counterfactuals $P(y_x\|x', y')$	Imagining, Retrospection	Why? Was it *X* that caused *Y*? What if I had acted differently?	Was it the aspirin that stopped my headache? Would Kennedy be alive had Oswald not shot him? What if I had not been smoking the past two years?

Economics Example Health Systems

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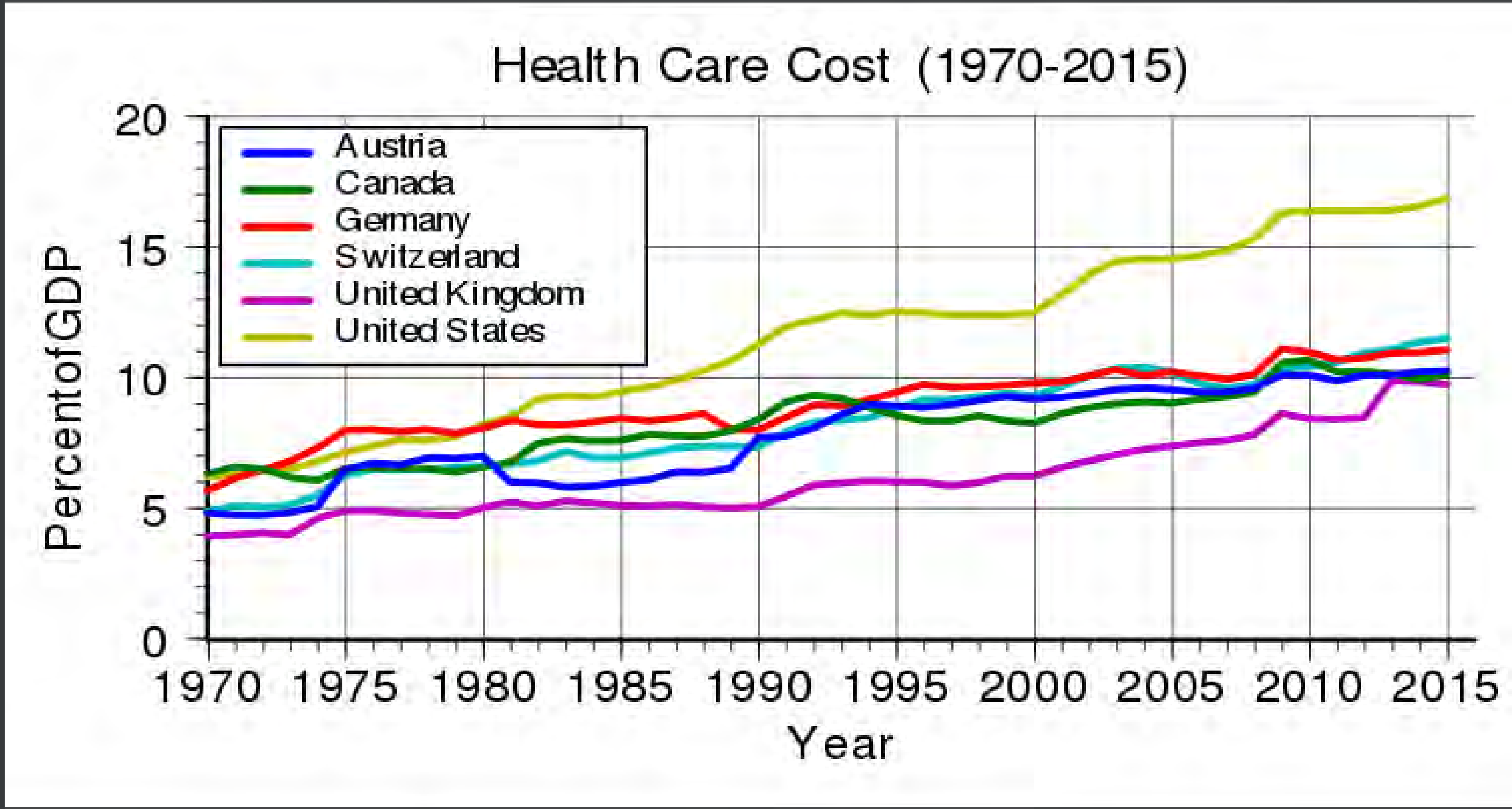
Dissociation of Prooved Benefit of Costs for Medical Care

Pharma-ceutical	Application	Discovery	Costs € (Patient/Year)	Effects (Survival)
Insulin	Typ 1 Diabetes	1920	500	Decades
Statins	Cardiology	1990	5.000	Years
Monoclonal Antibodies	Onkology	2000	50.000	Month/Weeks
Encyme Alternation	Metabolism	2010	500.000	???

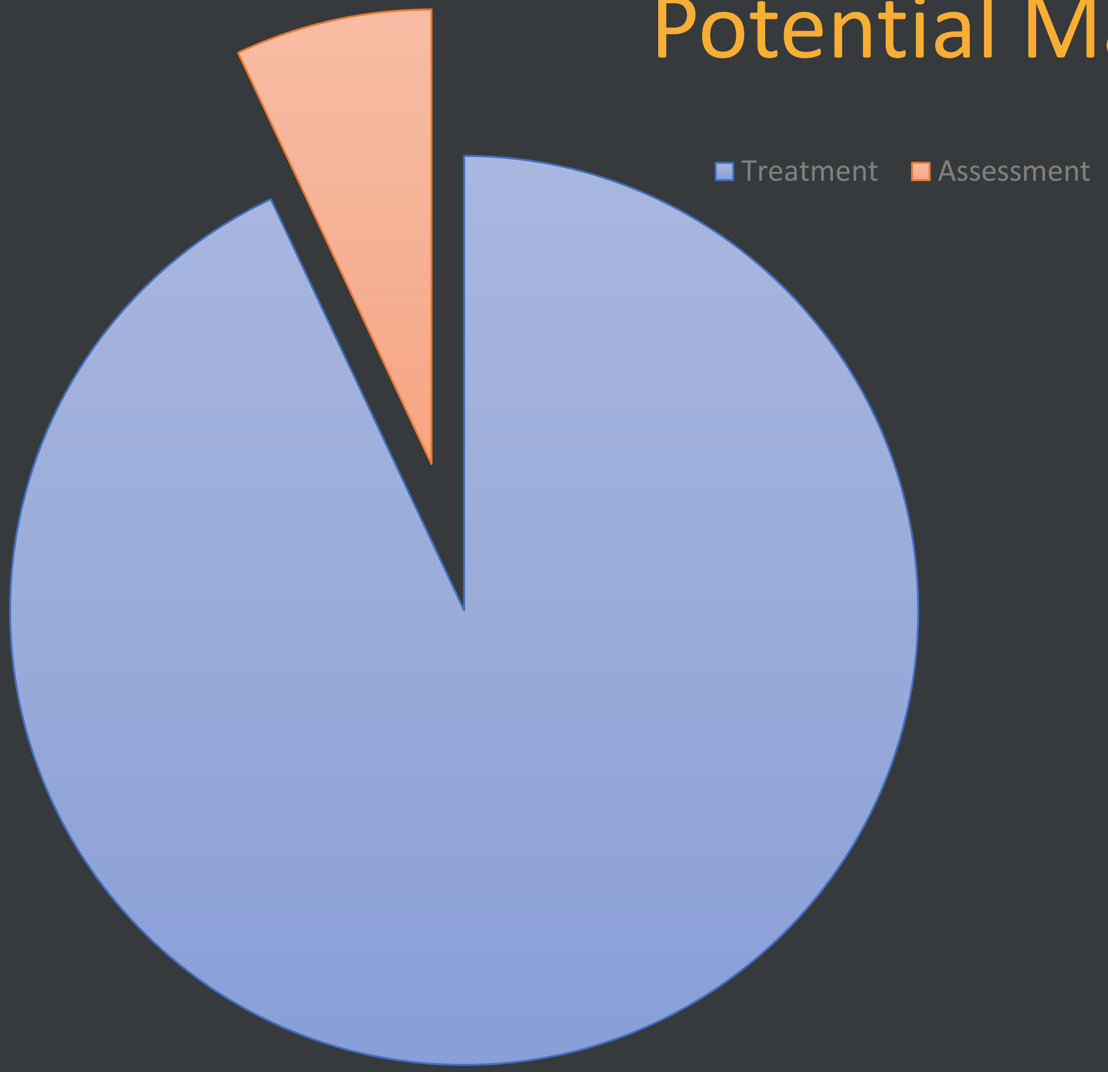
Source: C. Wild, Ludwig Boltzmann Institute for Health Technology Assessment, Vienna

Economics Example Health Systems



https://en.wikipedia.org/wiki/Healthcare_in_Austria

Health Care Assessment of Interventions
Potential Market



Austria – 2-3 Billion €
UK – 13-20 Billion €
Germany – 17-27 Billion €

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Development vs. Measuring

Advanced Treatment
New Medication
Cutting Edge Technology
Innovative Diagnosis
Fair Distribution of Health Services
Disease Prevention

Dealing with Increasing Costs
Estimating Reachable Outcomes
Measuring of Adherence
Managing # of Patients
Developing Registers
Benchmarking Interventions

Economical Need

Combination of Methods

Complex & Dynamic Processes

Increasing & Complex Data

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Integrated Processes for Modelling & Simulation

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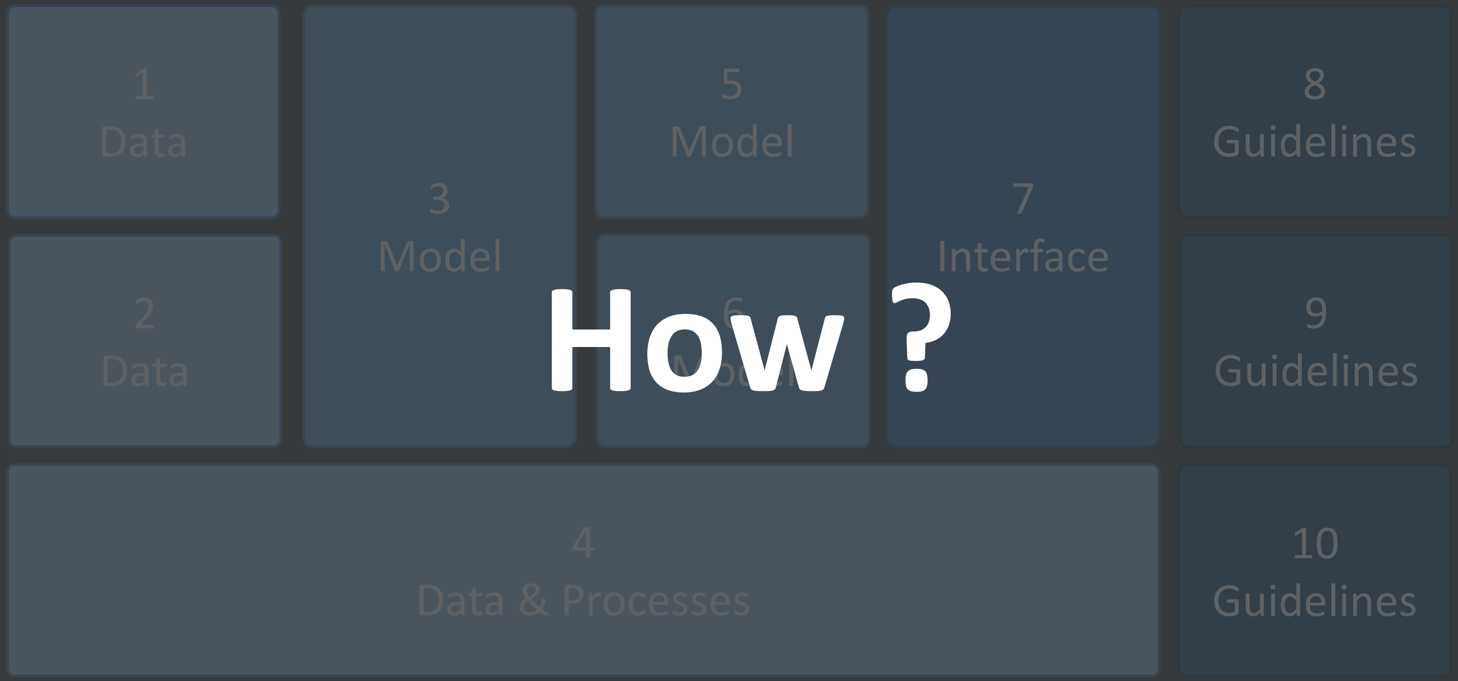

How ?

Integrated Processes for Modelling & Simulation

Data Driven System Simulation

10 Concepts to Integrate:
Implementing Future Simulation Models, including Data Processes

https://www.eurosim.info/tcs/tc-ddss/

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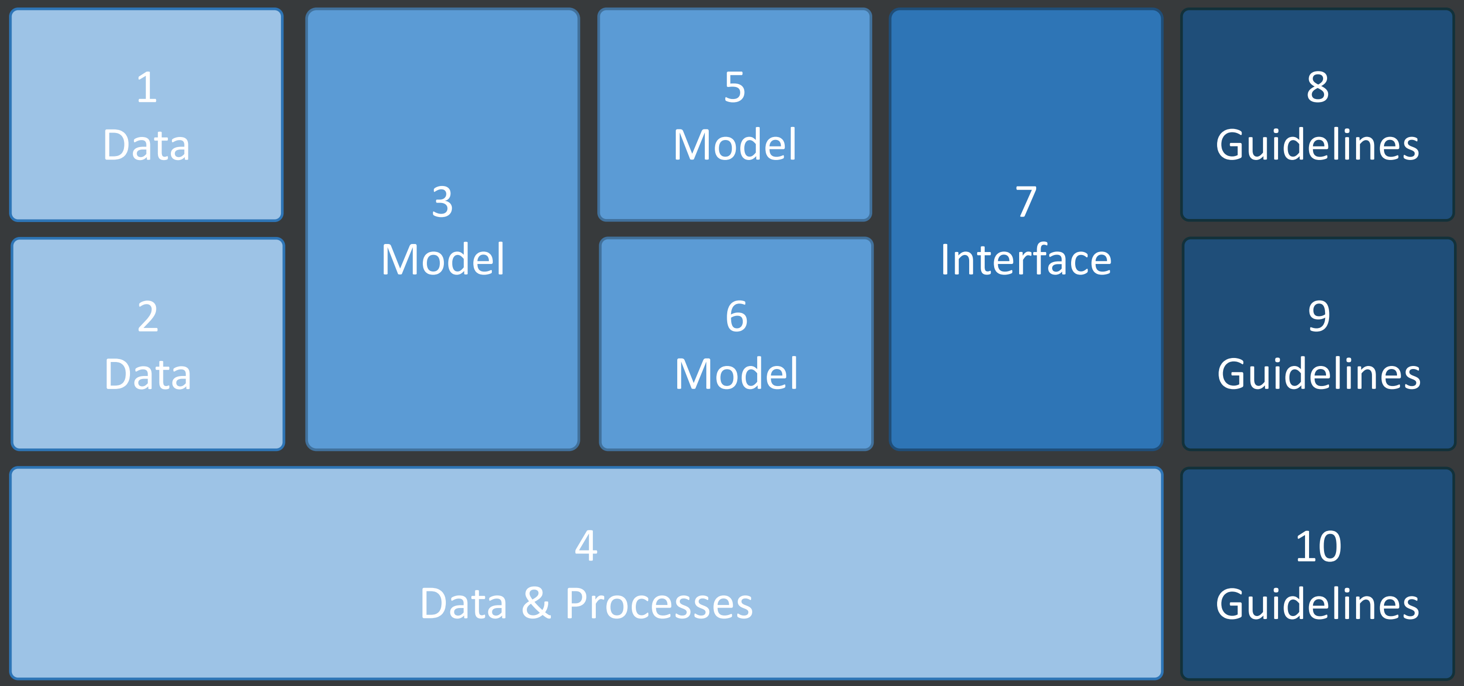

Integrated Processes for Modelling & Simulation

The Fourth Paradigm by Jim Gray (Microsoft)

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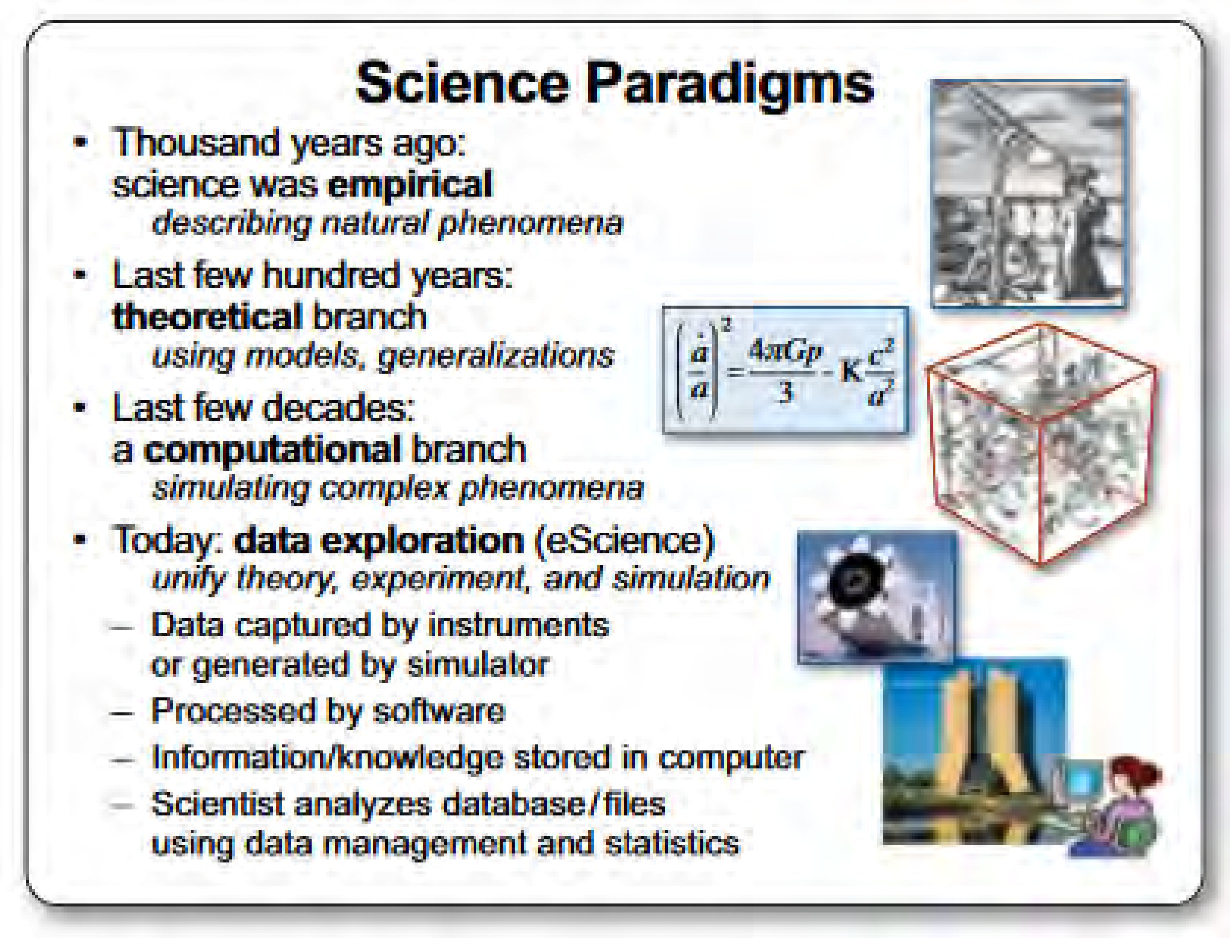

Hey, T., Tansley, S. & Tolle, K. (eds.) (2009). The Fourth Paradigm: Data-Intensive Scientific Discovery. Redmond, Washington: Microsoft Research.

Describe
↓
Model
↓
Simulate
↑↓
Explore Data

Modelling Dynamics

10 Concepts to Integrate

Why?

-> Dynamics & Complexity
-> Economics
-> Big Data

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-> Modelling Dynamics
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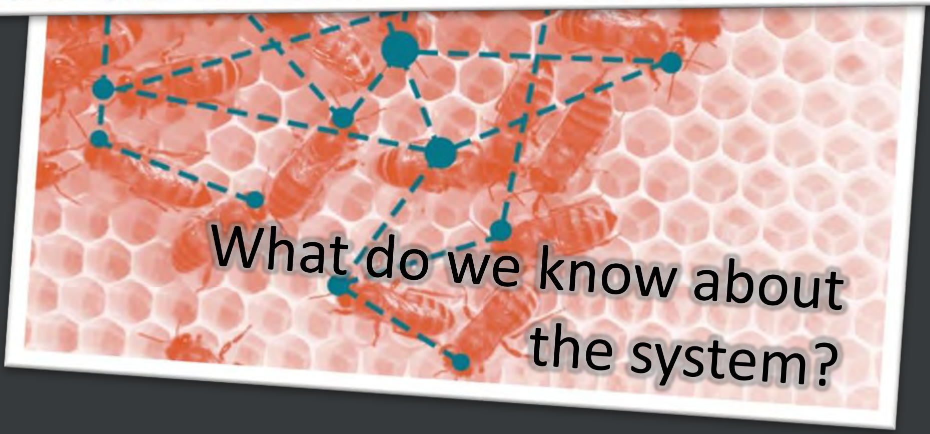
-> Processes

Which Questions are to be answered?

Which Data Ressources are available?

Which Systems & Processes are described ?



N. Popper:"Comparative Modelling and Simulation, A Concept for Modular Modelling and Hybrid Simulation of Complex Systems", PhD Thesis

Modelling Dynamics

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Structures & Knowledge

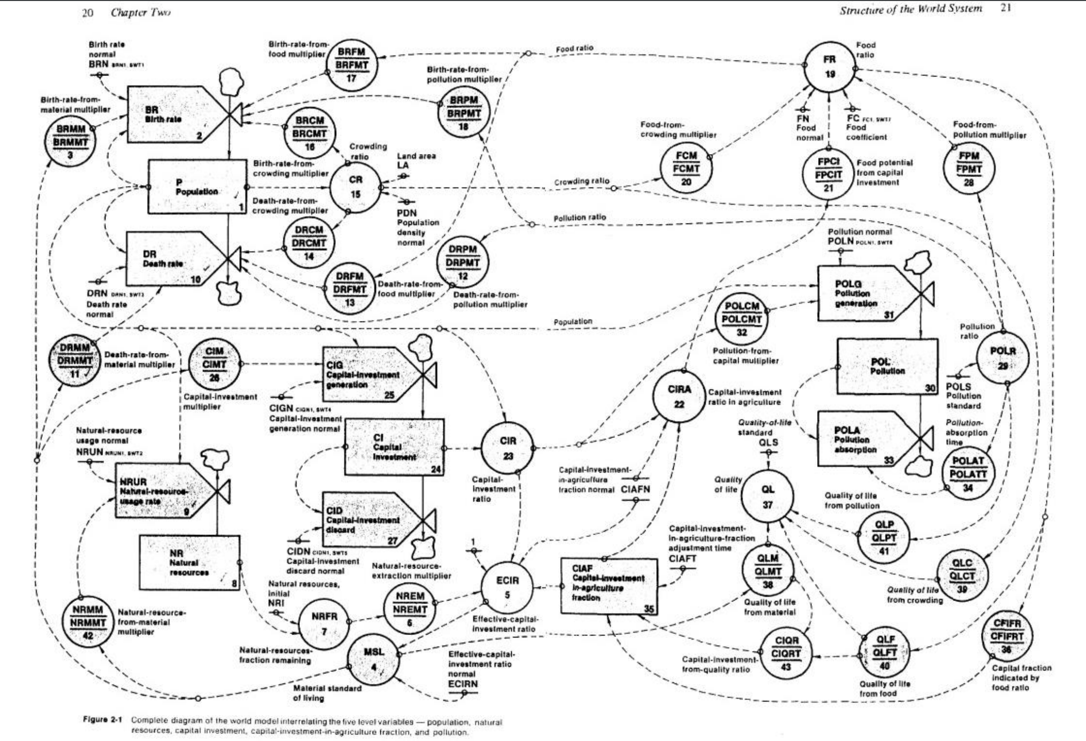

Figure 2-1 Complete diagram of the world model interrelating the five level variables — population, natural resources, capital investment, capital-investment-in-agriculture fraction, and pollution.

Forrester, Jay W., World Dynamics. 1973 second ed. 1971, Waltham, MA: Pegasus Communications. P. 144, Reproduced by permission of Jay W. Forrester.

Data vs. Models
in Health System Research

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10 Concepts to Integrate

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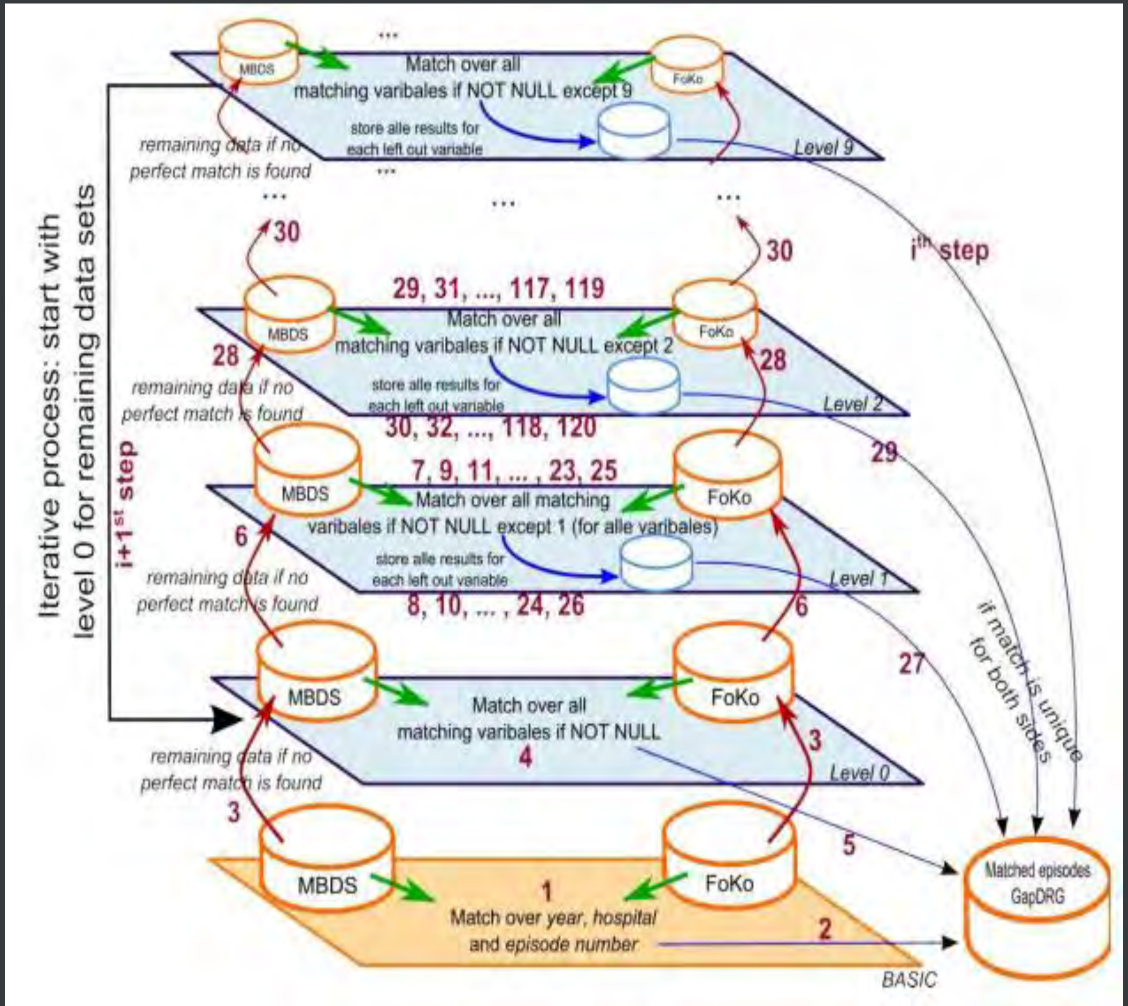
Big Data Sets



Structures & Knowledge

Modelling and Simulation Processes

10 Concepts to Integrate

Why?

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-> Big Data

How?

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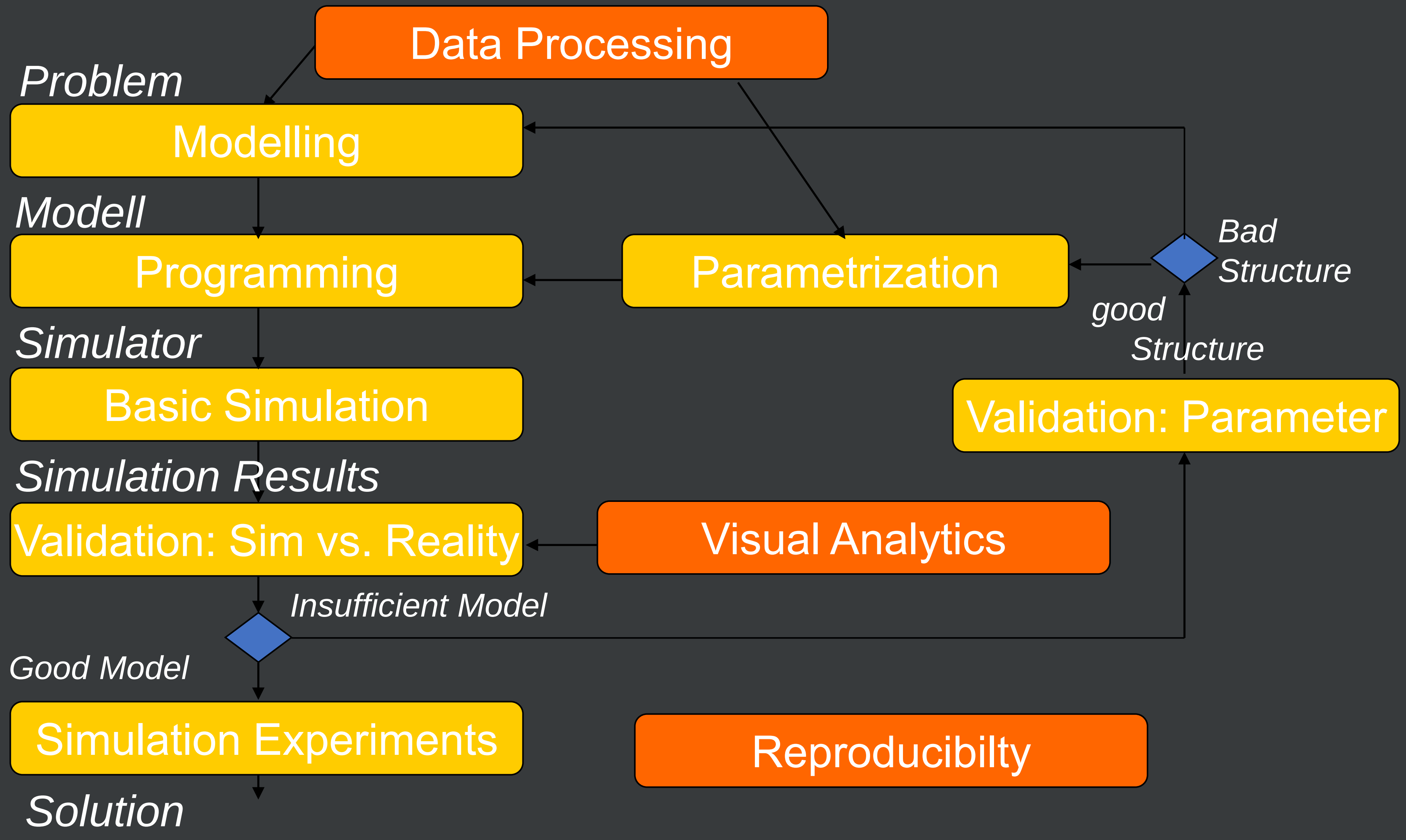
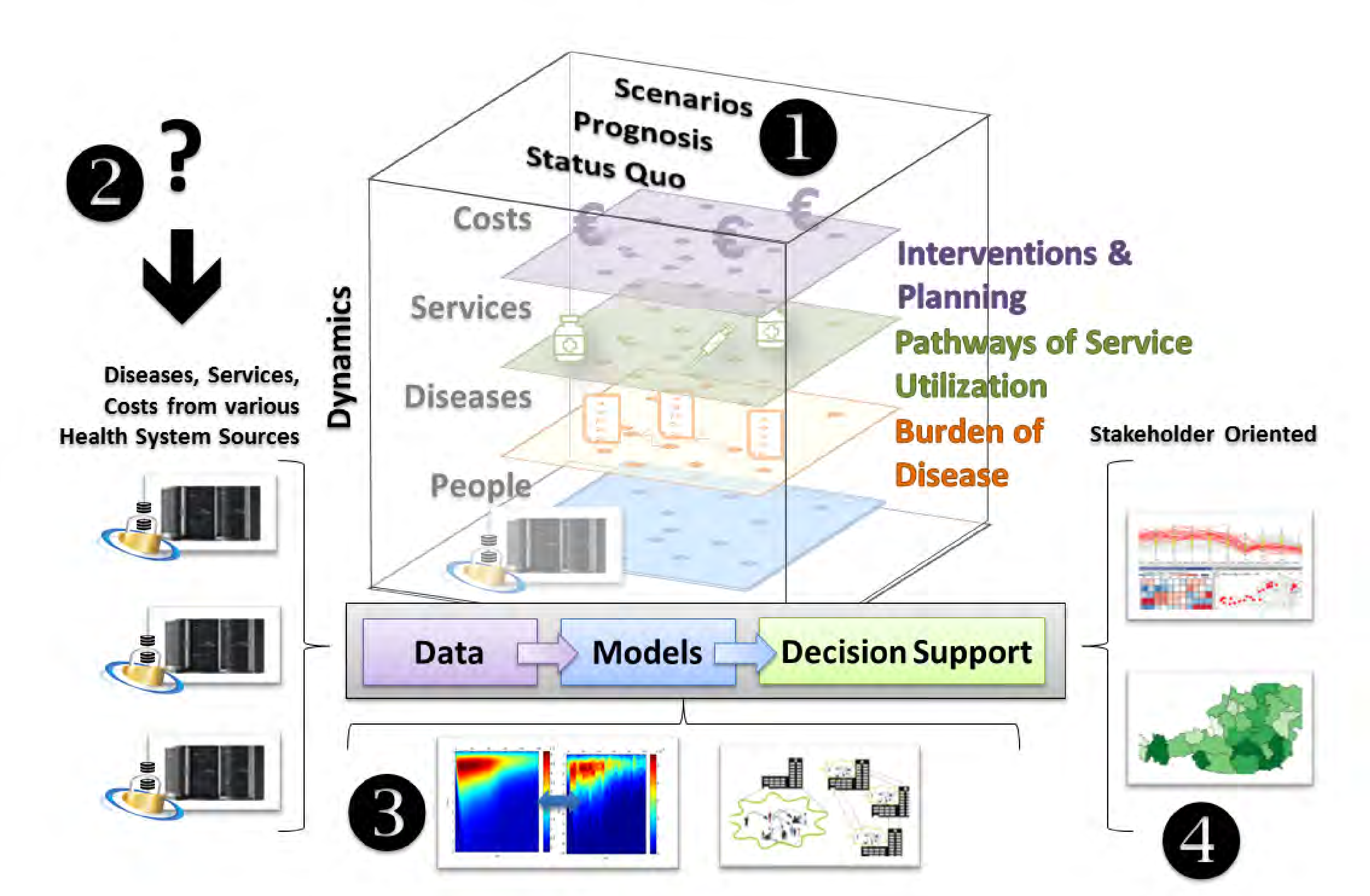


Example Health System: DEXHELPP

DEXHELPP

Decision Support for Health Policy and Planning: Methods, Models and Technologies based on existing health care data



10 Concepts to Integrate

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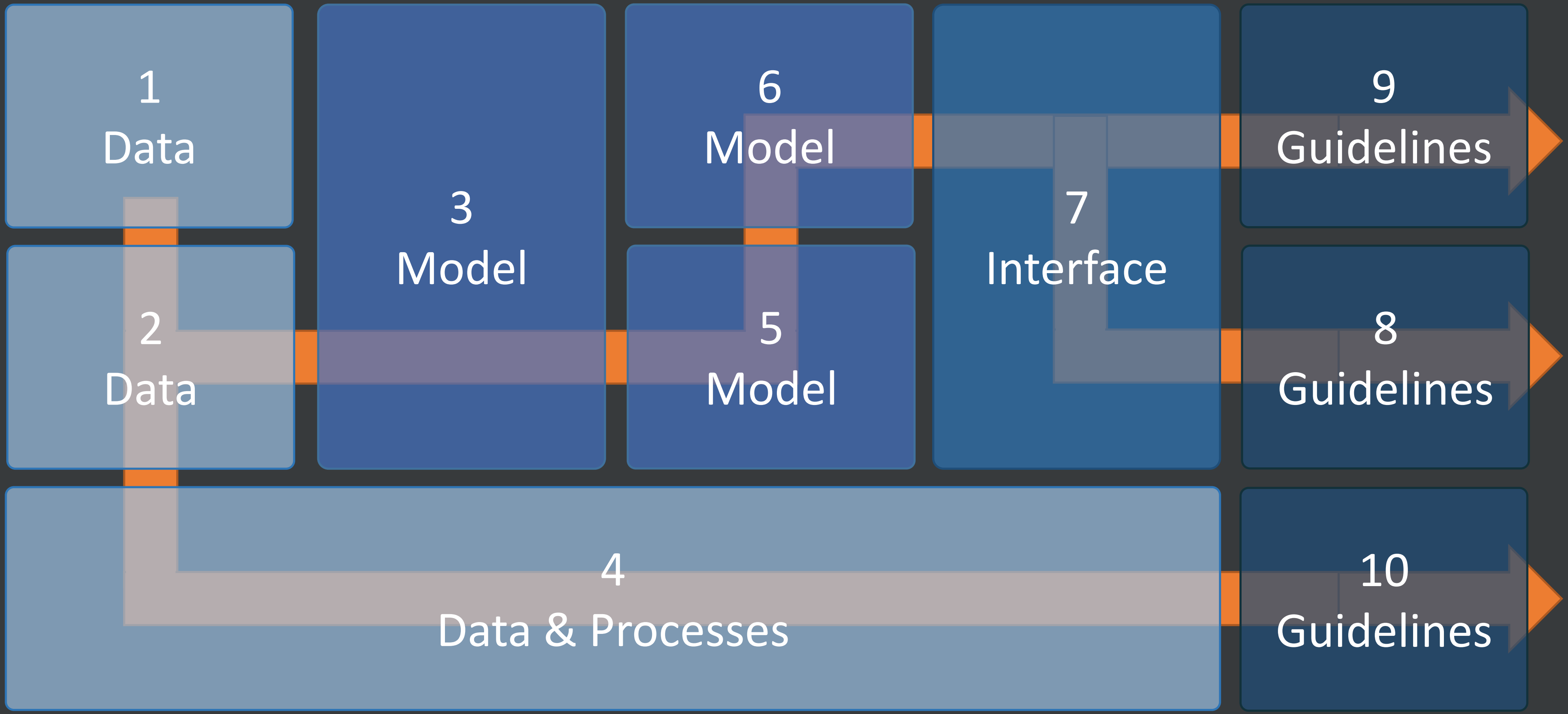
10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data
3. Modular & Efficient Solutions
4. Reproducible Processes
5. Different Methods for Different Questions (Complexity)
6. Comparability of Results
7. Make it Understandable
8. Open and Independent Solutions
9. Priority for Data Security and Stake Holder Interests
10. Broad Applications (Health System, Energy, Industry, Energy, Mobility, Infra-structure)



Concept 1

10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data

Problems of Collected Data

- Biased Collection of Data e.g. Sensor Data or Reimbursement Data is available
- Pre-processing at Various Stakeholders
- Privacy Demands

METHOD: Explorative Visual Computing – Visual Analytics and Statistics

Interactive Dashboards

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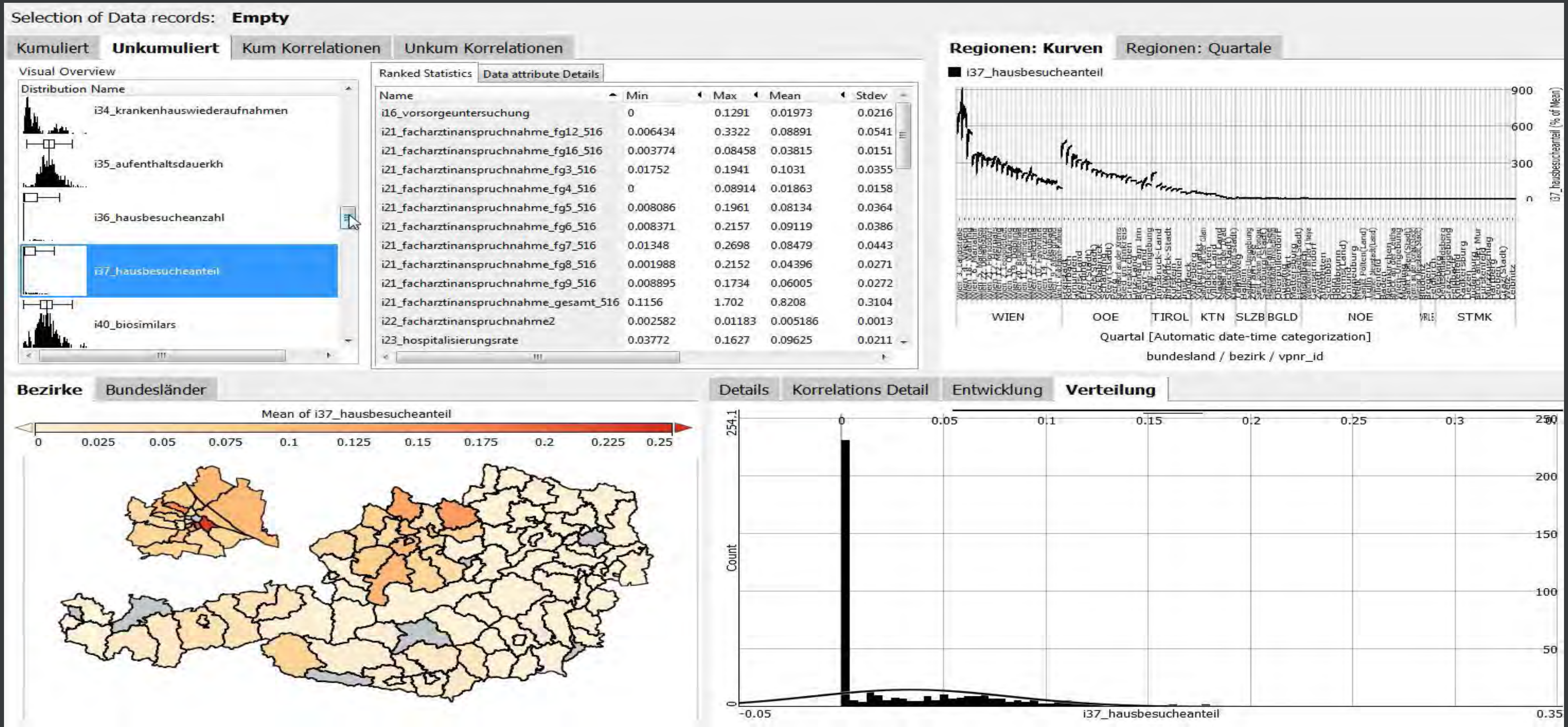
10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data



H. Piringer, M. Gyimesi et al: Stroke Analyse und Modellierung, DEXHELPP

Data on Stroke Treatment

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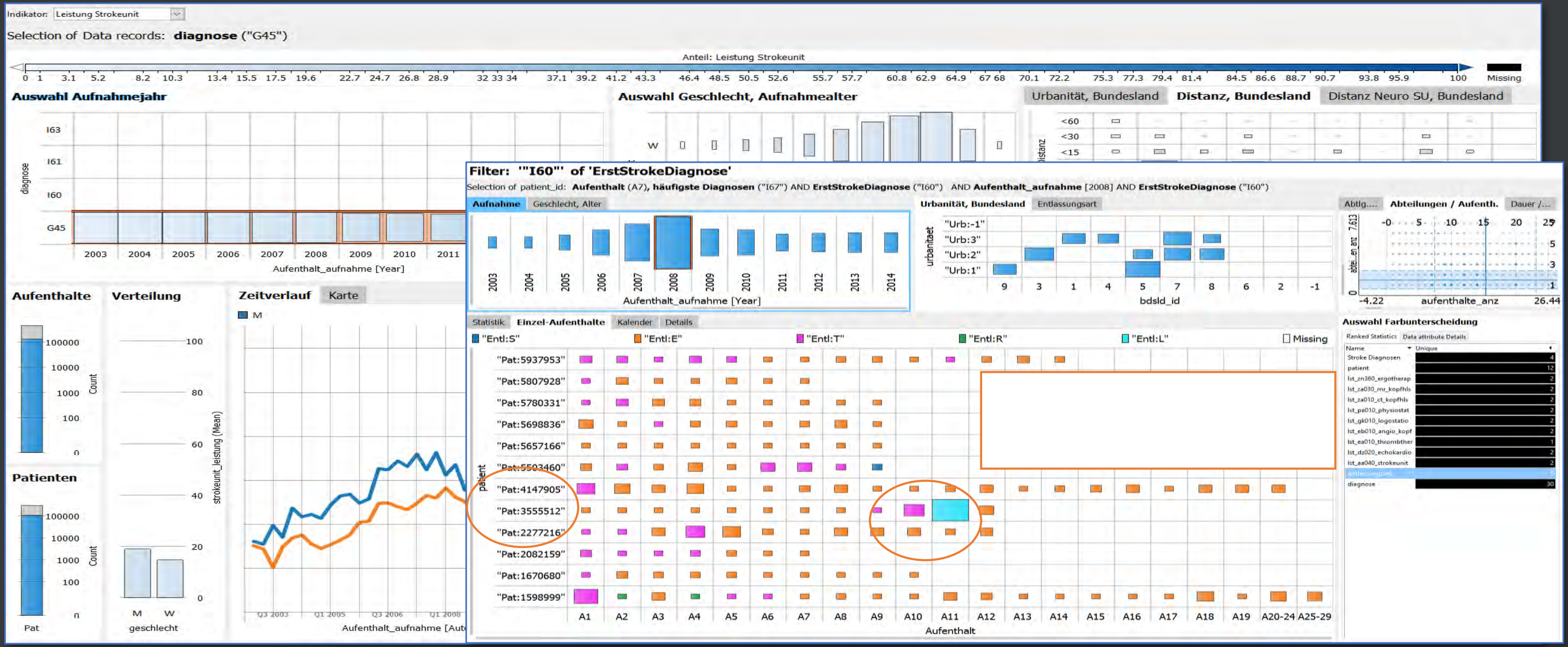
10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data

Applied to: Data and Trend analysis of stroke treatment

- Percentage of patients being treated in stroke units
- Inspection of patient histories for outlier detection and hypothesis generation



H. Piringer, M. Gyimesi et al: Stroke Analyse und Modellierung, DEXHELPP

Concept 2

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10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data

Integration of Different Data Sets

- Pre-processing at Various Stakeholders
- Unstructured and Different Structures
- Privacy Demands

METHOD: Data Processes (Integration & Linkage) & Modelling Tools (Parametrization & Calibration)

Data Levels

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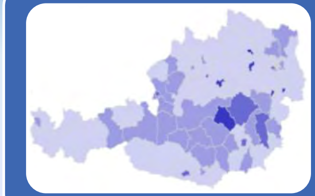
10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data



Austrian Health System Data

Provincial Data

Clinical Data

OMICS
(excluded at the moment)

DEXHELPP

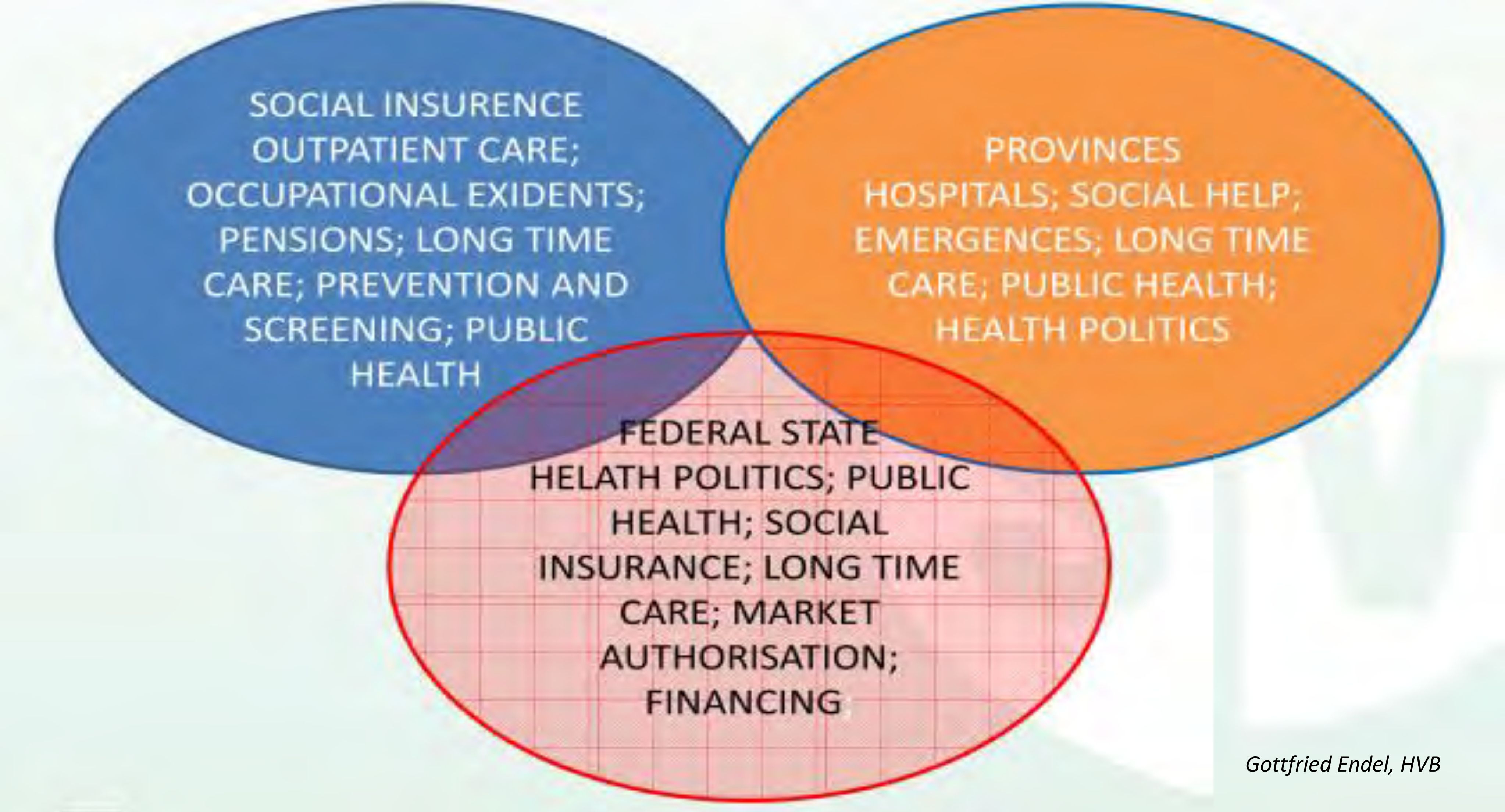
DEXHELPP
2018 PLUS

DEXHELPP
FUTURE

Health System Austria
3 Areas

10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data

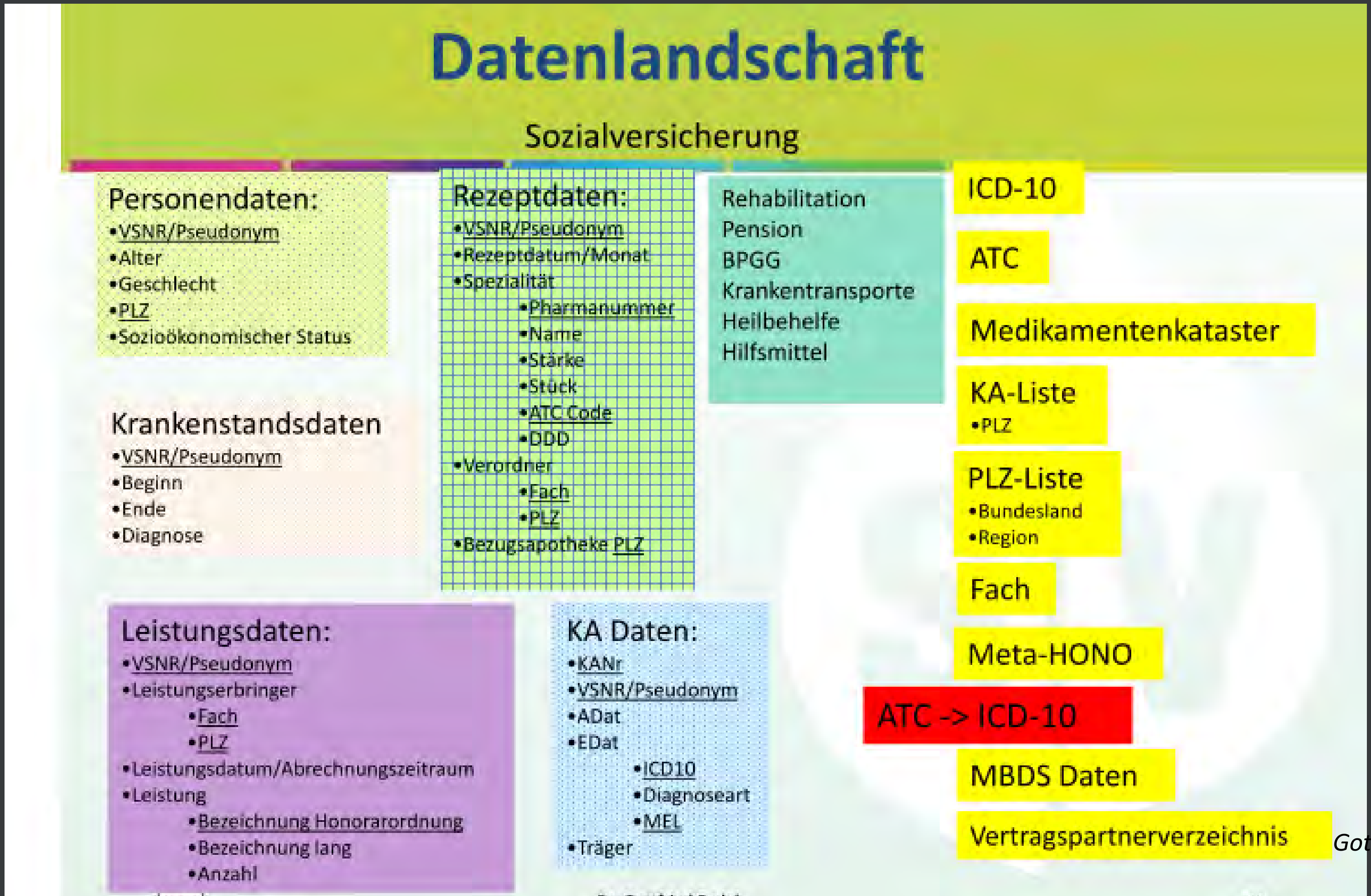


Gottfried Endel, HVB

Data Social Insurancess

10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data

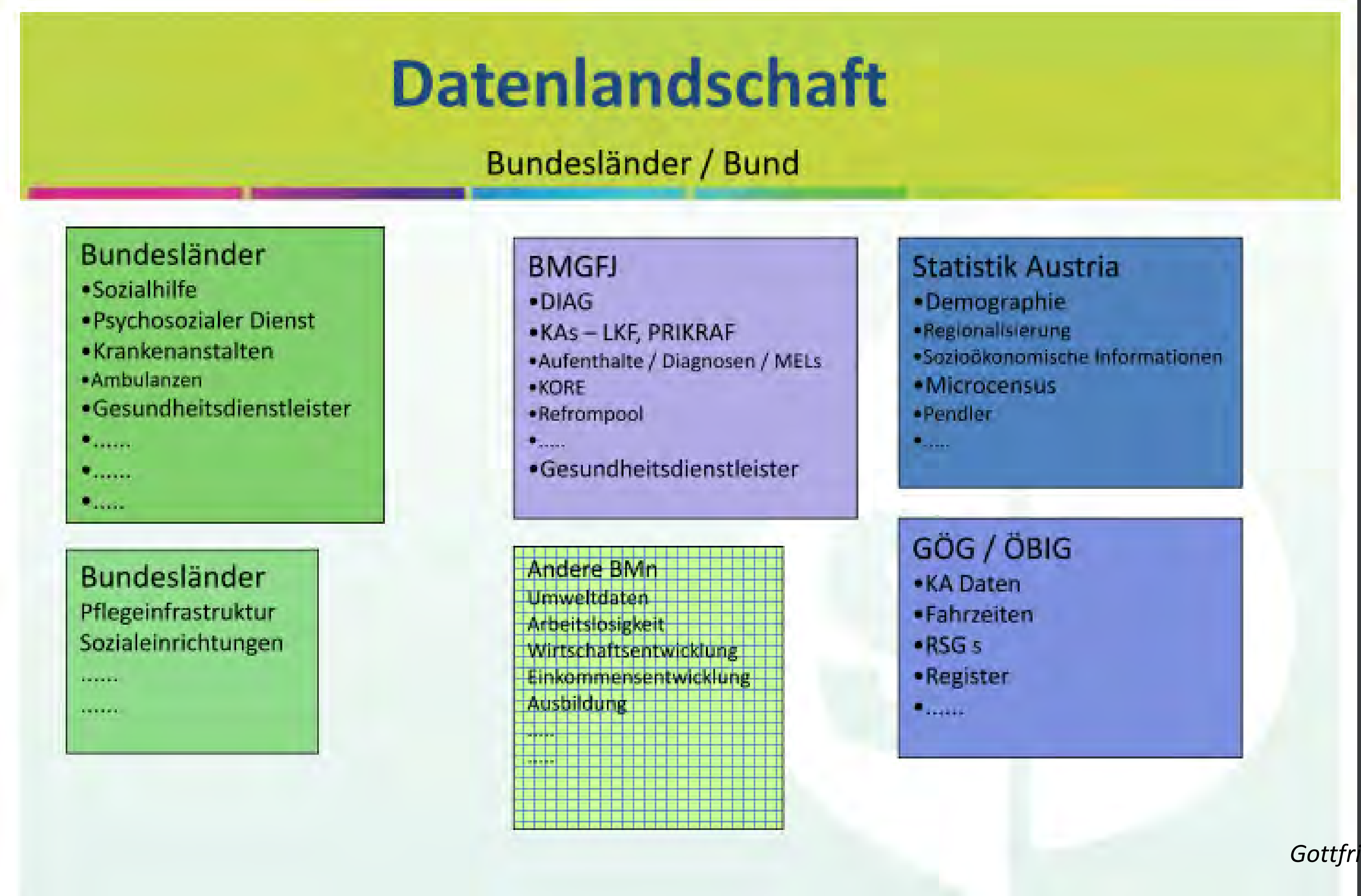


Gottfried Endel, HVB

Data Provinces & Austria

10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data



Gottfried Endel, HVB

Data Processing DEXHELPP until now….

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10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
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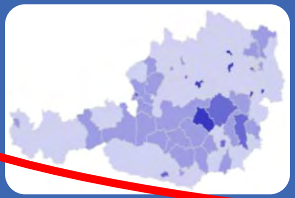

Austrian Health System Data

Provincial Data

Clinical Data

Hospitals/Inpatients
Phycisians /Outpatients

OMICS
(excluded at the moment)

$\sum$

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Diagnosis

Treatment

- Therapy
- Medication

Accounting

Example Record Linkage

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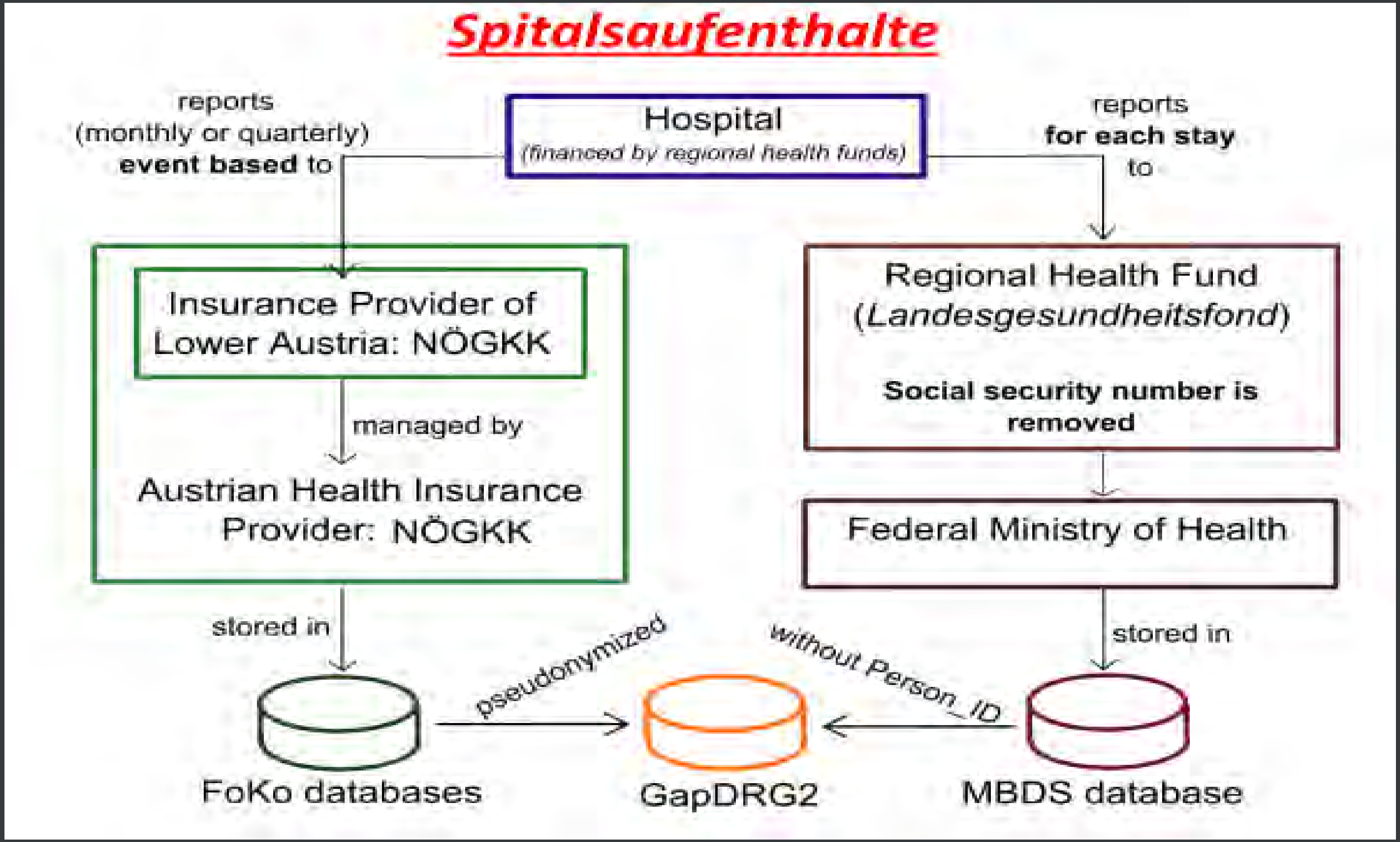
10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data



Example Record Linkage

10 Concepts to Integrate

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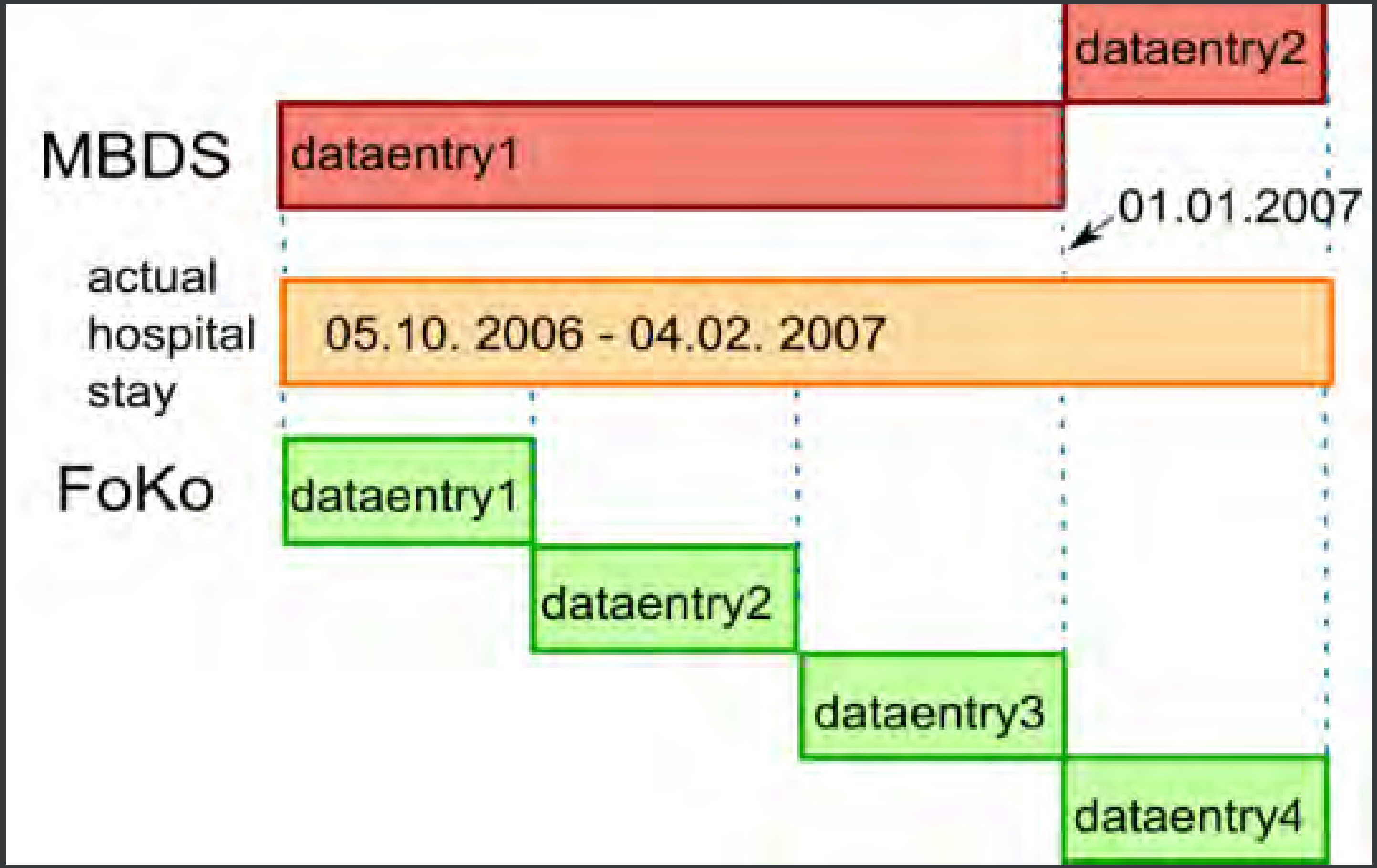
2. Potential to Integrate Missing Data



B. Glock, F. Endel et al: Challenges and Results with the Record Linkage of Austrian Health Insurance Data of Different Sources, Informatics for Health Conference 2017 (24 – 26. April, Manchester, UK)

Example Record Linkage

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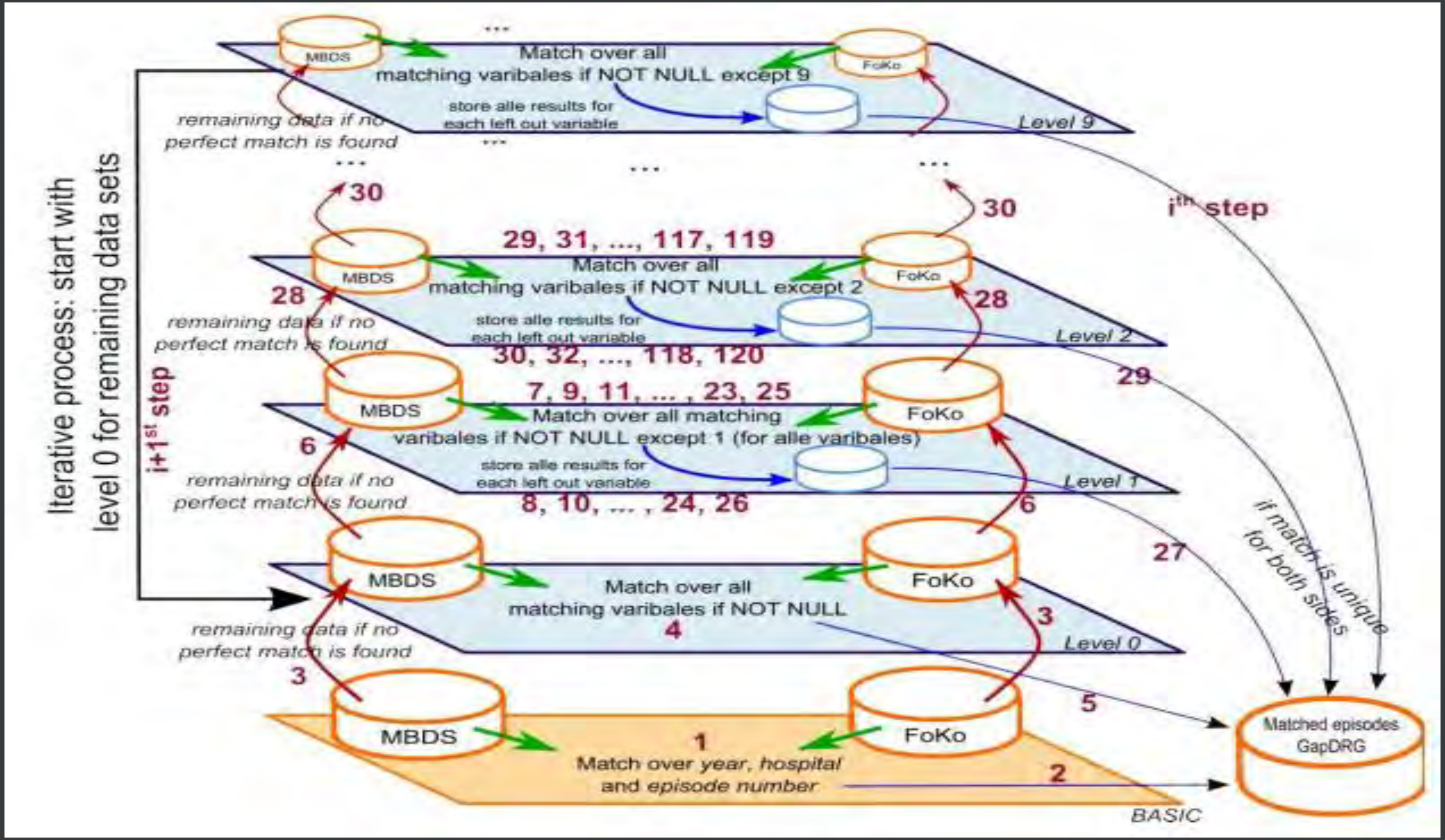
10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data



Concept 3

10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data
3. Modular & Efficient Solutions

Modular Concepts for Models

- We can find wrong Data
- We can change wrong Data …
- …even over time and when integrated
- We need transparent, “simple” Models

METHOD: Modular Models, Coupling of Models

Virtual Population

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10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
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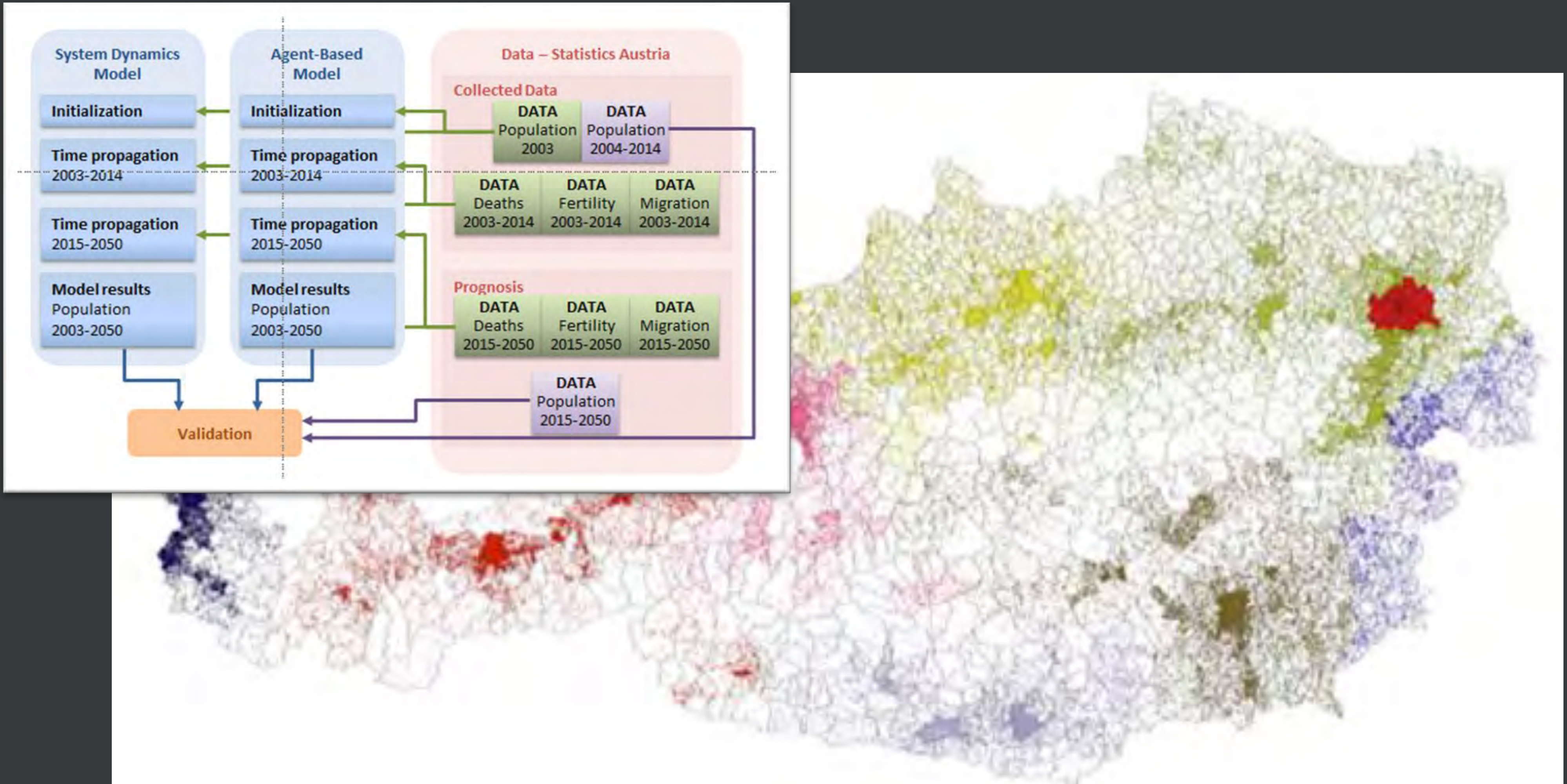
3. Modular & Efficient Solutions



M. Bicher, F. Miksch, B. Jahn, et al: DEXHELPP GEPOC, Generic Population Concept, DEXHELPP Report

Social Network Layers

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10 Concepts to Integrate

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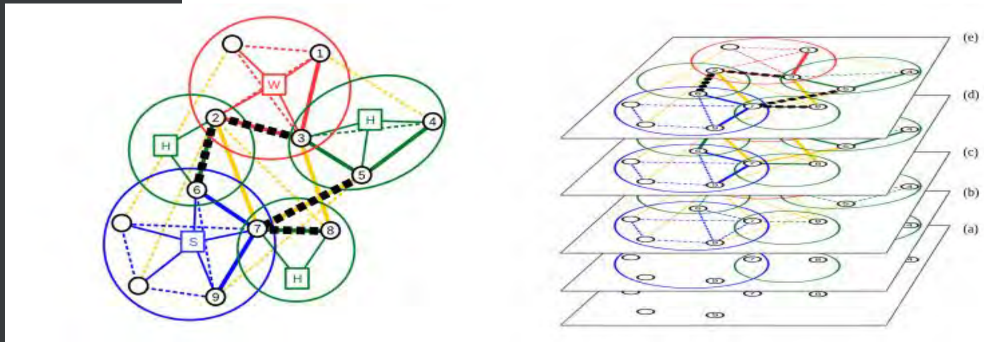
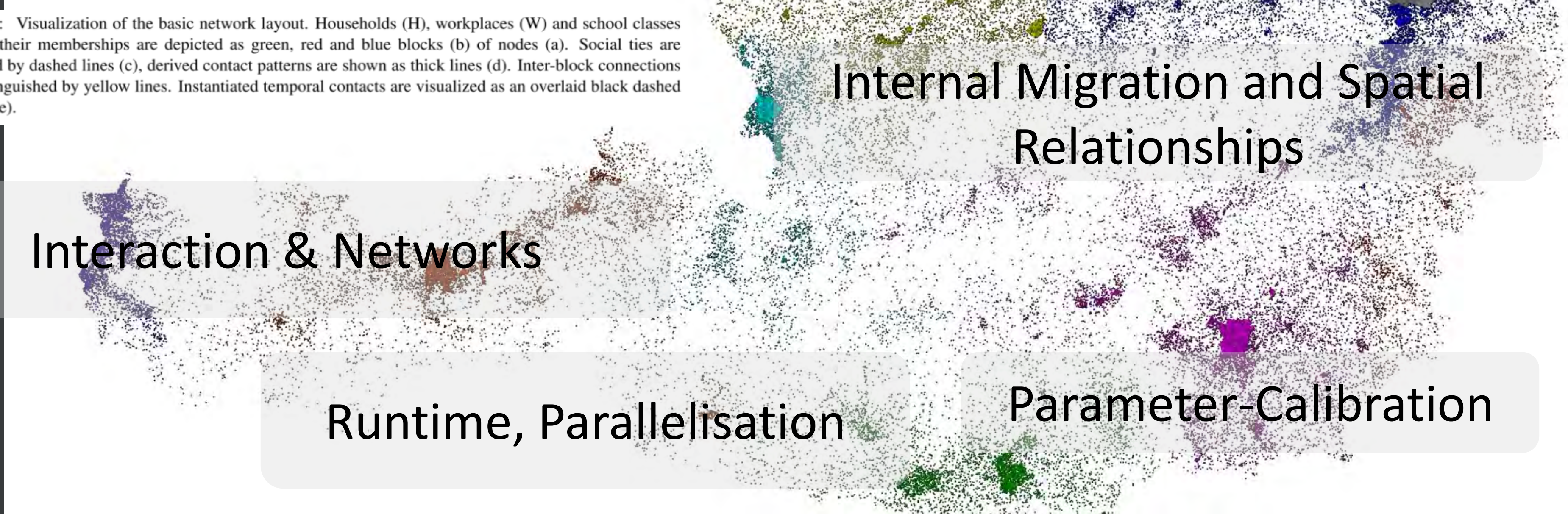
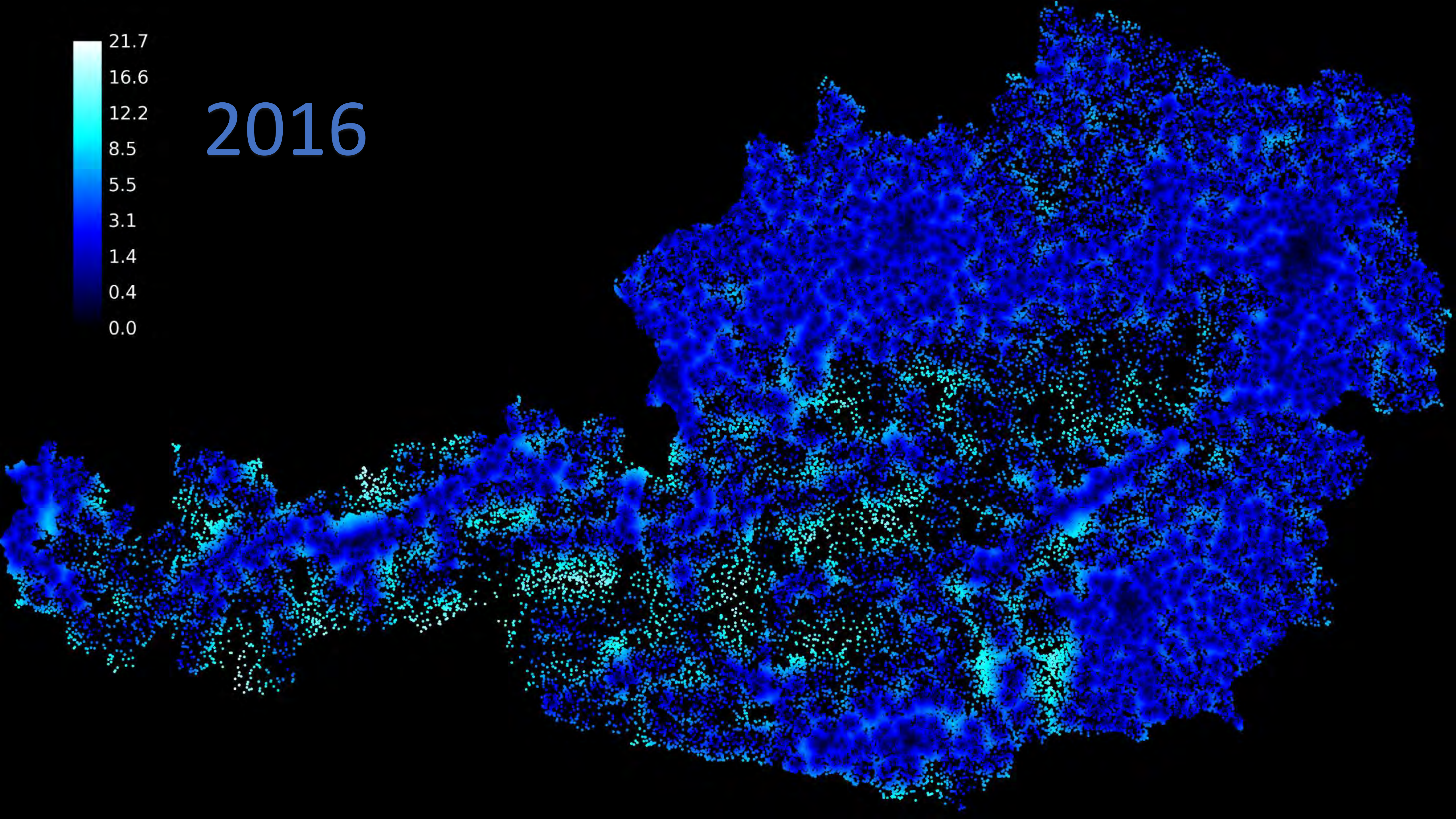


Figure 1: Visualization of the basic network layout. Households (H), workplaces (W) and school classes (S) and their memberships are depicted as green, red and blue blocks (b) of nodes (a). Social ties are indicated by dashed lines (c), derived contact patterns are shown as thick lines (d). Inter-block connections are distinguished by yellow lines. Instantiated temporal contacts are visualized as an overlaid black dashed pattern (e).

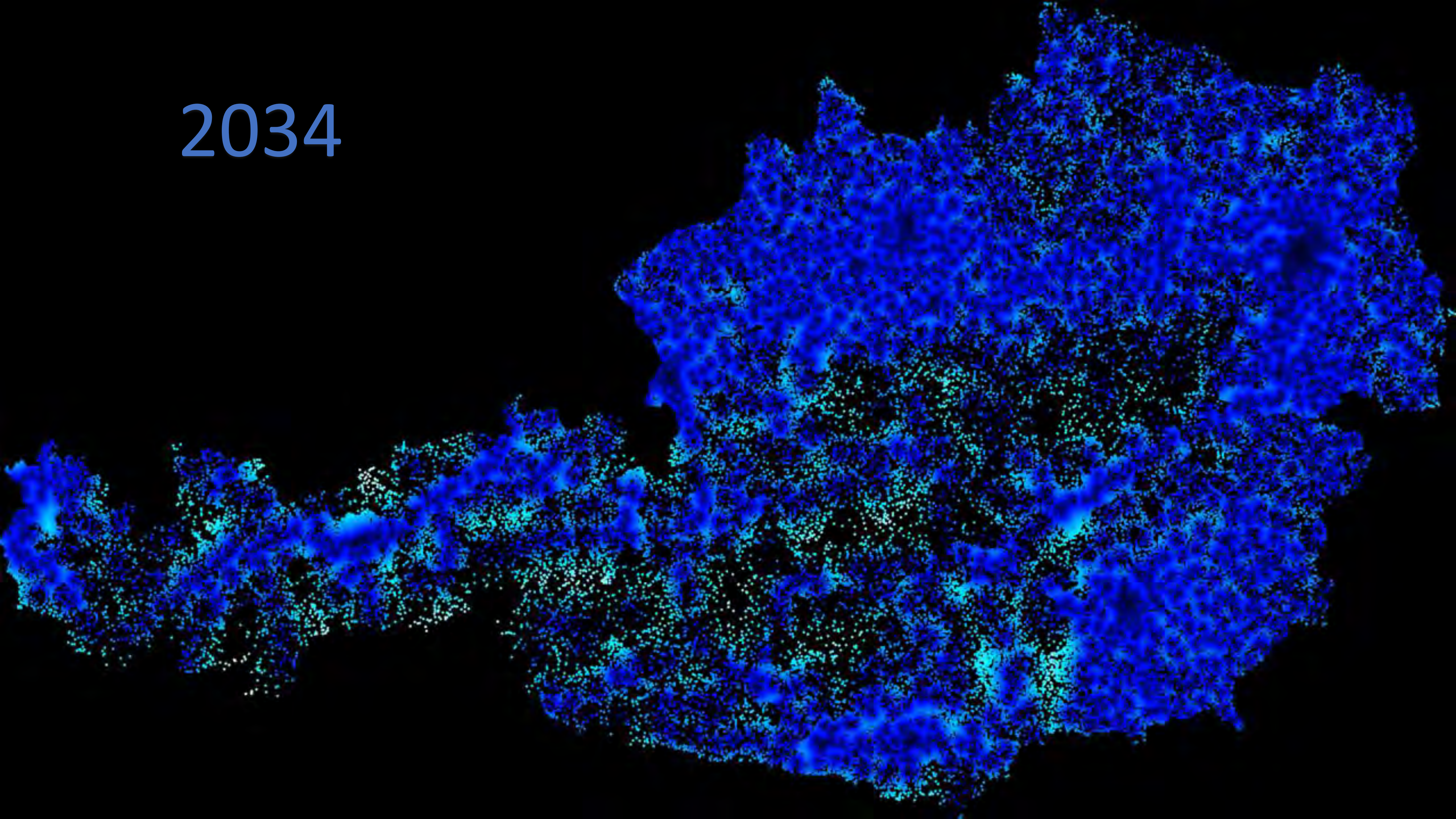


G. Schneckenreither, N. Popper, „Dynamic Multiplex Social Network Models on Multiple Time Scales for Simulating Patterns in Contact Formation and Epidemic Spread“ submitted Winter Simulation Conference 2017

2016



2034



Concept 4

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10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data
3. Modular & Efficient Solutions
4. Reproducible Processes

Reproducible Processes

- No “General Model” possible, because of…
- …different time scales or characteristics.
- Based on Provenance and Modularity
- Managing Tools for Data & Models

METHOD: Validation & Data Citation

Best Practice CEPHOS

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10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data
3. Modular & Efficient Solutions
4. Reproducible Processes

Comparative Effectiveness Research on Psychiatric Hospitalisation

Description: Comparative Effectiveness Research on Psychiatric Hospitalisation by Record Linkage of Large Administrative Data Sets

CEPHOS-LINK is a comparative European register-based study, performed by record linkage technique. It will develop a methods toolkit for conducting record linkage studies in the mental health care field and produce recommendations, guidelines and a set of decision support tools for decision makers in the field of mental health system.

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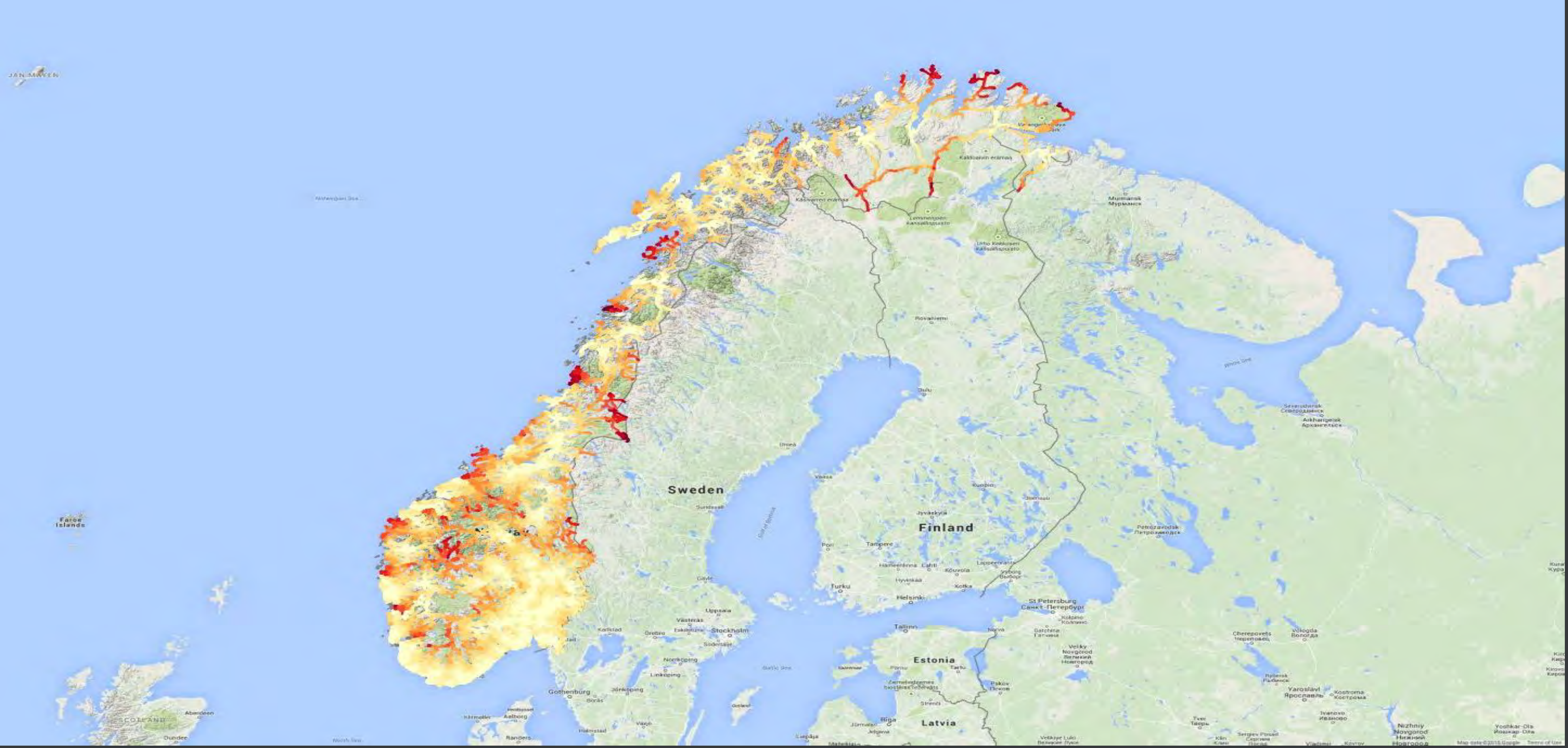

C. Urach, G. Zauner et al "Statistical methods and modelling techniques for analysing hospital readmission of discharged psychiatric patients: a systematic literature review"; BMC Psychiatry (2016)

Best Practice CEPHOS

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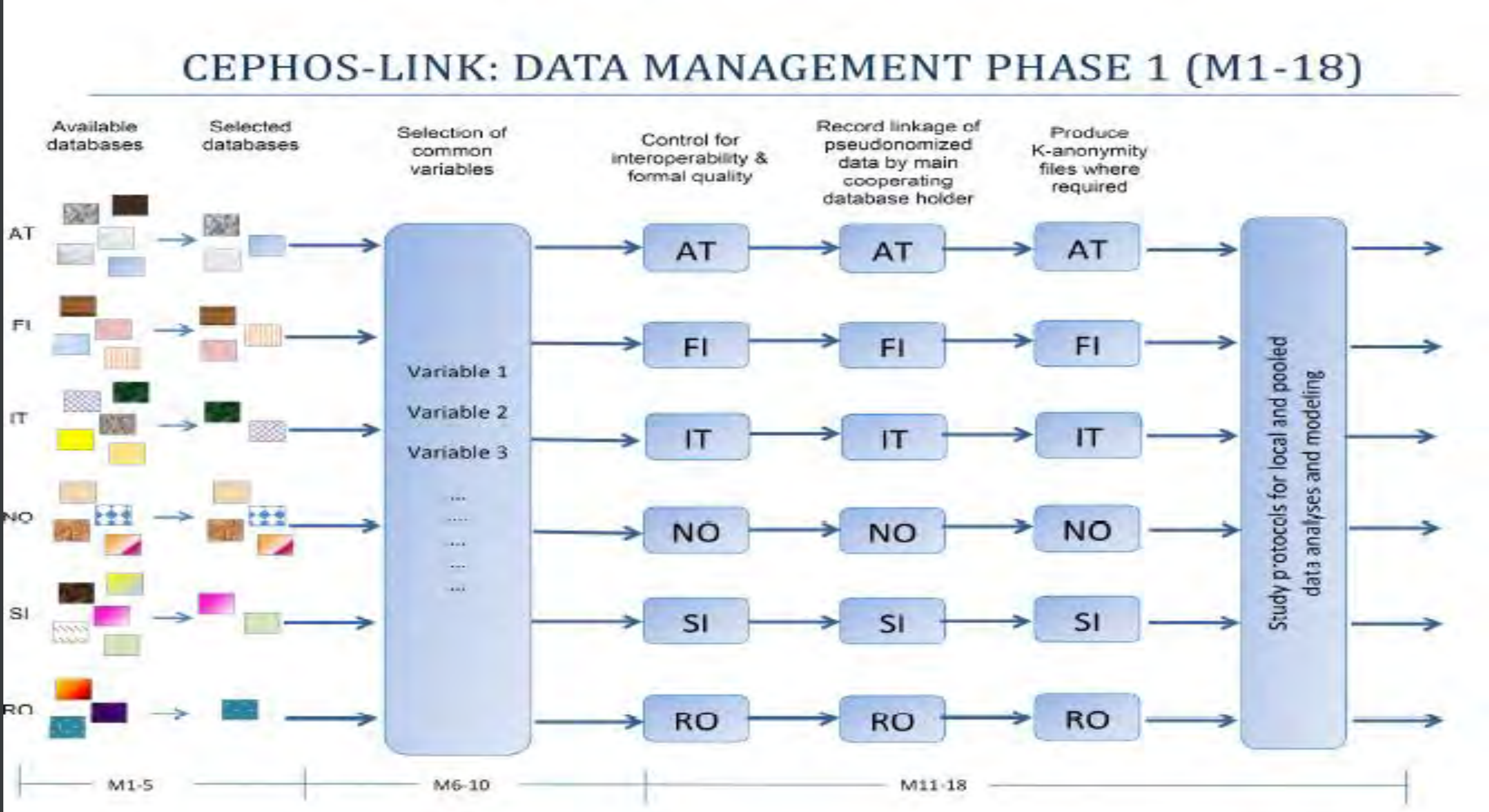

Best Practice CEPHOS

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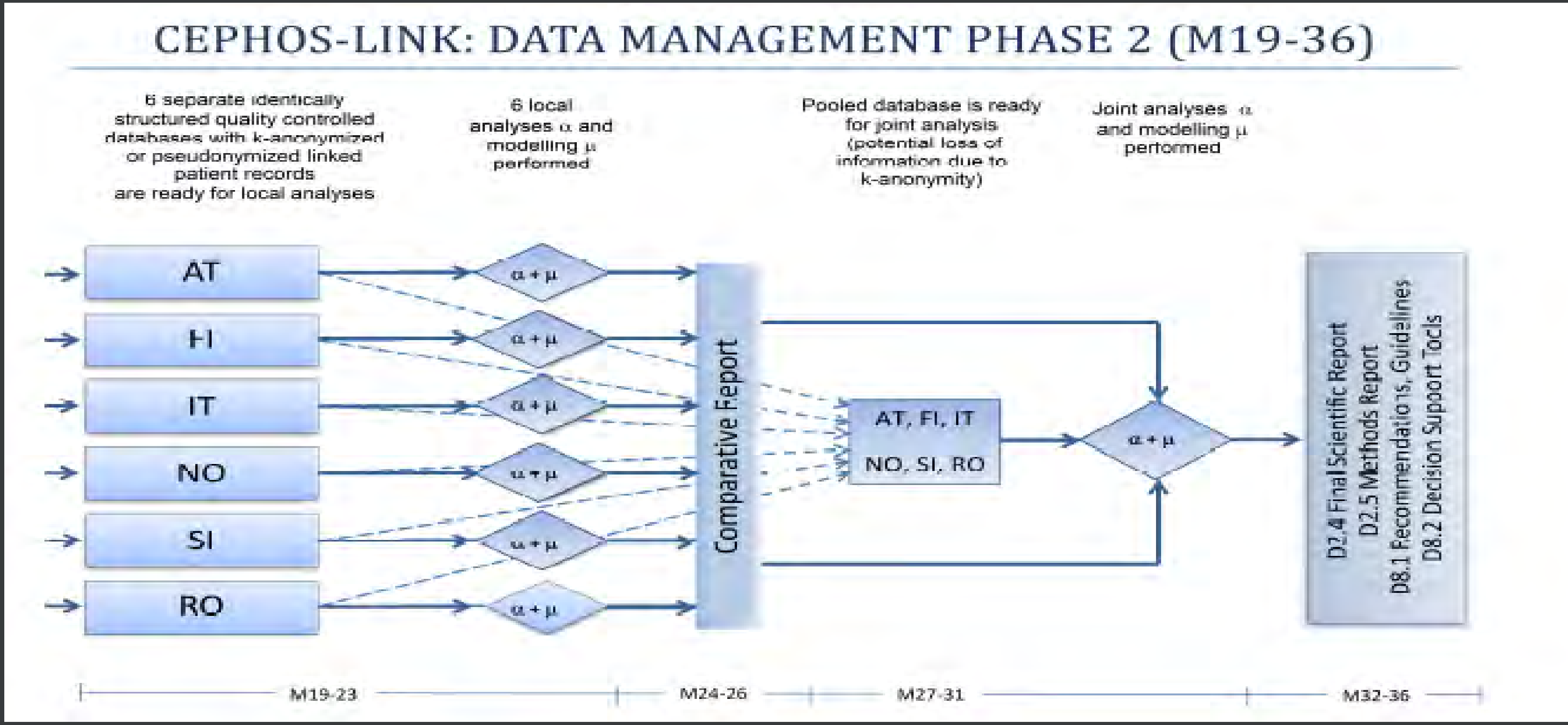


Concept 5

10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data
3. Modular & Efficient Solutions
4. Reproducible Processes
5. Different Methods for Different Questions (Complexity)

Different Models for Different Questions

- Stable model, already checked
- Better Data doesn’t improve
- Model changes don’t improve
- Need to Integrate Complexity/Dynamics
- Different (comparable) methods needed

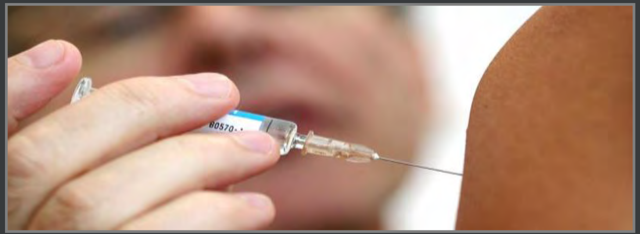
METHOD: Methods for Choosing Models

Example Comparison Vaccination

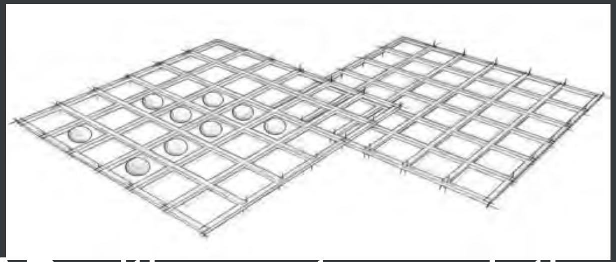
10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data
3. Modular & Efficient Solutions
4. Reproducible Processes
5. Different Methods for Different Questions (Complexity)

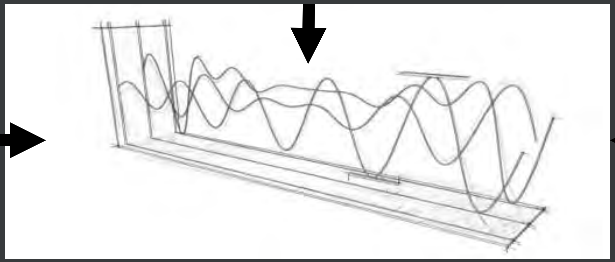
Modelling of infectiuous diseases: Pneumococcal modelling systems



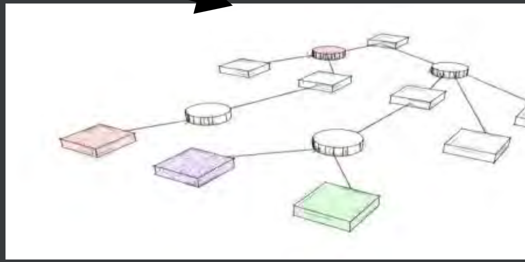
Real world



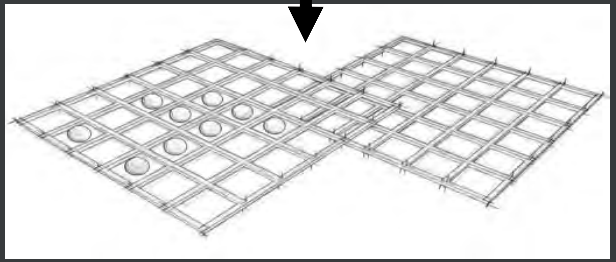
AB with const. population



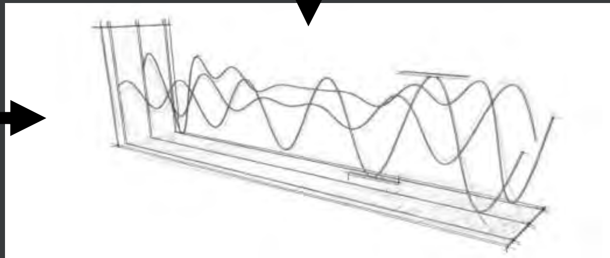
ODE with const. population



Markov Model
- Decicion tree
- Statistics



AB with populationdynamics



ODE with populationdynamics

Example Comparison Vaccination

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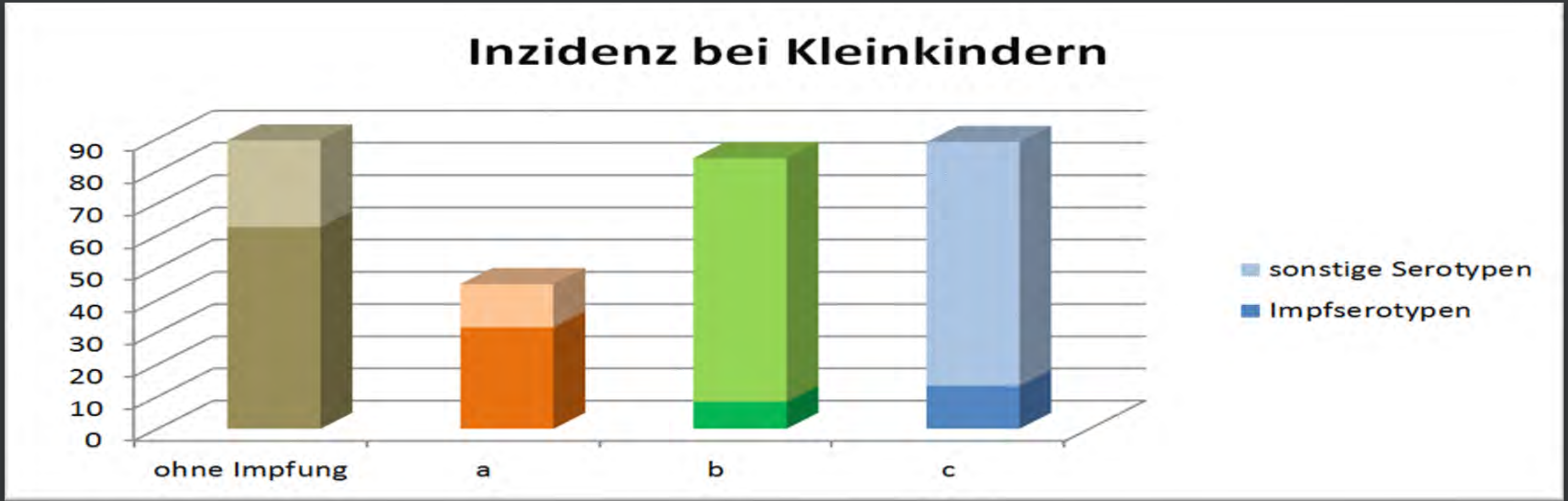
10 Concepts to Integrate

1. Methods to Assess and Improve Quality of Data
2. Potential to Integrate Missing Data
3. Modular & Efficient Solutions
4. Reproducible Processes
5. Different Methods for Different Questions (Complexity)



a) Gebräuchliche Prognosemodelle (Markov-Modelle, auf Österreich umgerechnet): E.D.G. McIntosh, P. Conway, J. Willingham, R. Hollingsworth, and A. Lloyd. The cost-burden of paediatric pneumococcal disease in the UK and the potential cost-effectiveness of prevention using 7-valent pneumococcal conjugate vaccine. Vaccine, 2003 Jun 2,21(19-20):2564-72

b) Dynamisches Pneumokokkenmodell, 2009 – Simulationsergebnisse: u.a.: C. Urach, "Modellierung und Simulation von Impfstrategien gegen Pneumokokkenerkrankungen: Markov- und Differentialgleichungsmodelle im Vergleich" (Diploma Thesis, Inst. f. Analysis und Scientific Computing, Vienna University of Technology, 2009).

c) Erhebung aus den USA, 2010 (auf Österreich umgerechnet): Hsu KK et al. Changing serotypes causing childhood invasive pneumococcal disease: Massachusetts, 2001–2007. Pediatr Infect Dis J 2010 Apr; 29:289

Example Combination Balanced Manufacturing

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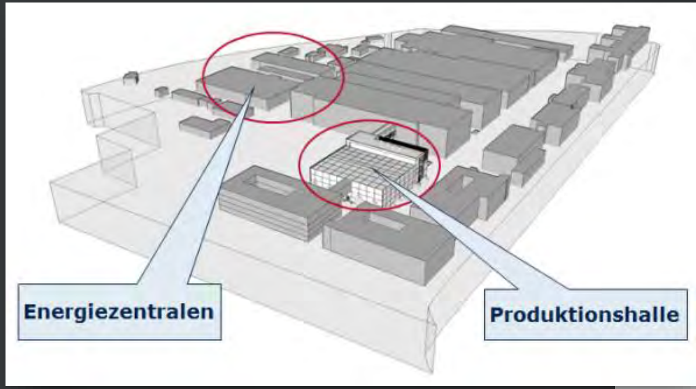
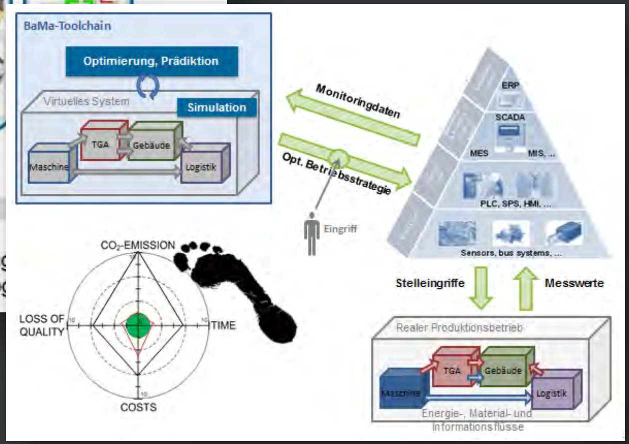
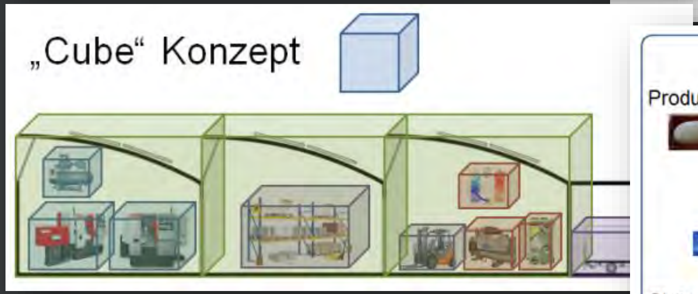
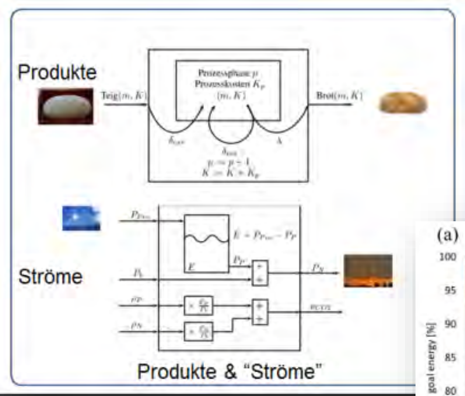








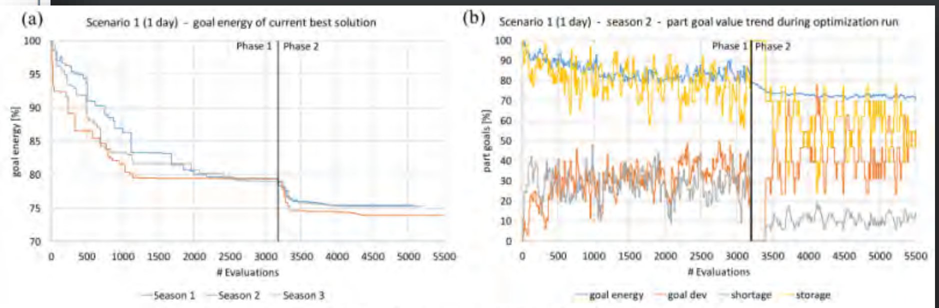
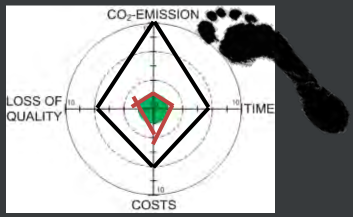


Fig. 2. (a) energy goal trend of current best solution; (b) part goal trends of mean values per generation



Hybrid simulation-based optimization of discrete parts manufacturing to increase energy efficiency and productivity; Thomas Sobottka, Felix Kamhuber, Matthias Rössler, Wilfried Sihn; 15th Global Conference on Sustainable Manufacturing

Example Combination Balanced Manufacturing

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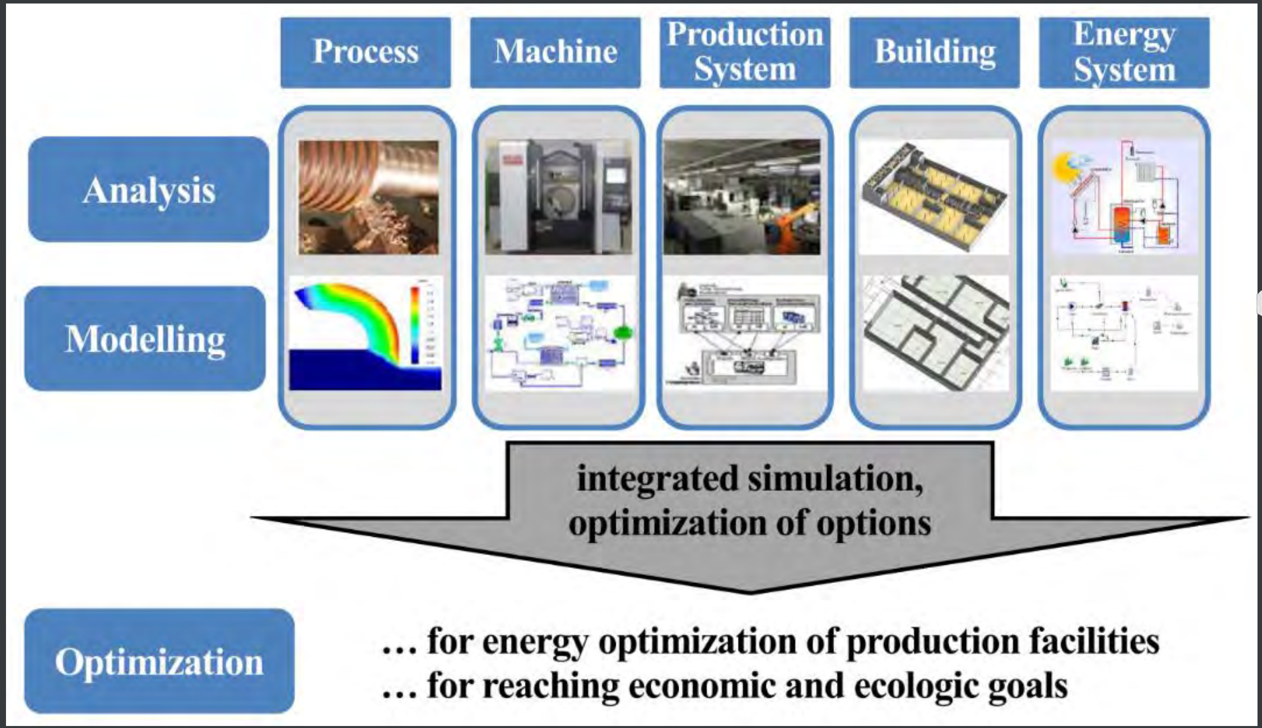

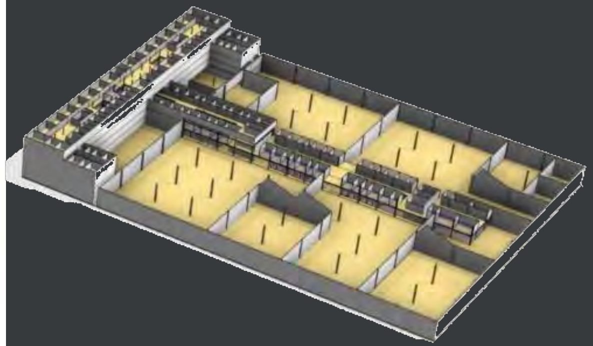

- **Coupled simulation** of the overall system enables holistic view of the energy distribution throughout the system.
- Find **optimization** approaches by simulating and comparing different scenarios.

Concept 6

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10 Concepts to Integrate

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6. Comparability of Results

Comparability of Models and Results

- Qualitative Comparison
- Quantitative Comparison including Parameter Transformation
- Showing Limitations of Modelling Approaches and Implementation

METHOD: Comparative Modelling

Example: Calibration

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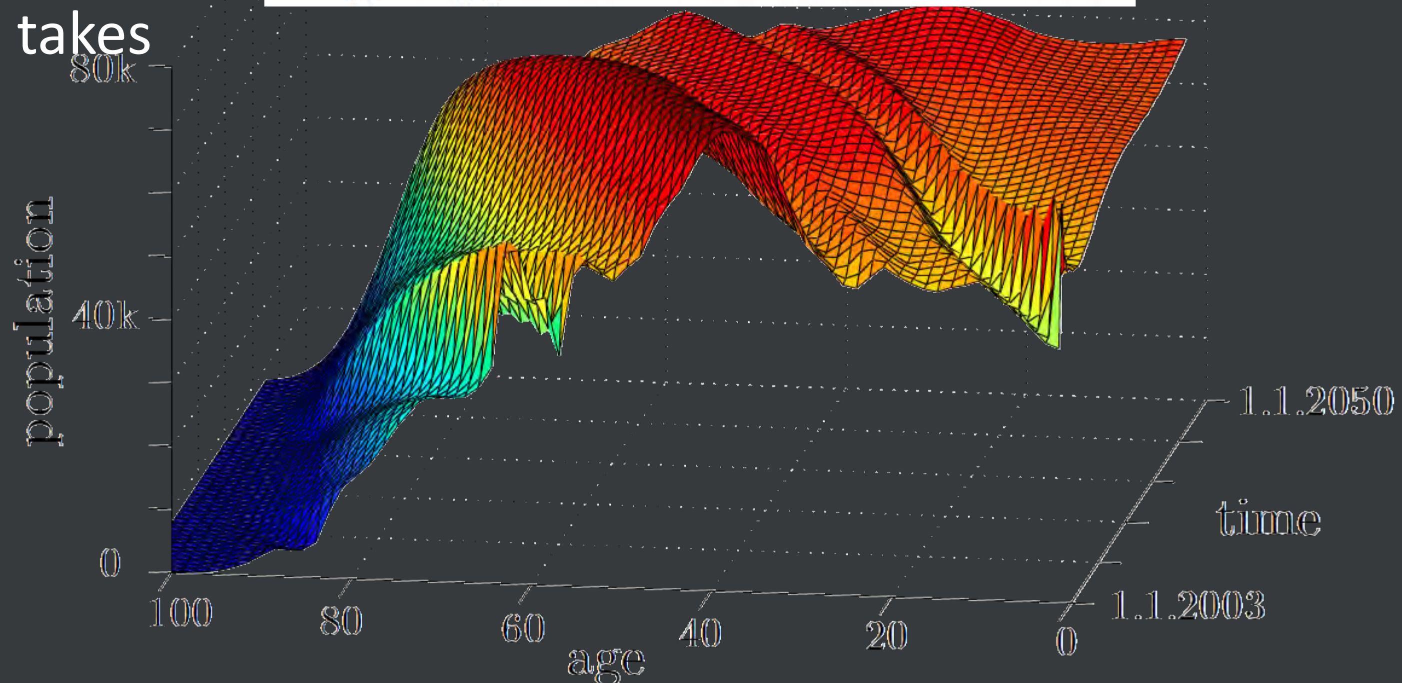
Calibration algorithms require thousands of simulation runs

Problematic

Each simulation run contains random elements and takes some time

Formal model analysis

$$\frac{\partial M}{\partial t} - \frac{\partial M}{\partial a} = \alpha_1 + \gamma_1 \mathbb{1}_{[0,dt)}(a)\Psi(a,t) - M\delta_1$$
$$\frac{\partial F}{\partial t} - \frac{\partial F}{\partial a} = \alpha_1 + \gamma_2 \mathbb{1}_{[0,dt)}(a)\Psi(a,t) - F\delta_2$$



M. Bicher, N. Popper, „Mean-Field Approximation of a Microscopic Population Model for Austria " published Eurosim 2016

Cross Model Validation

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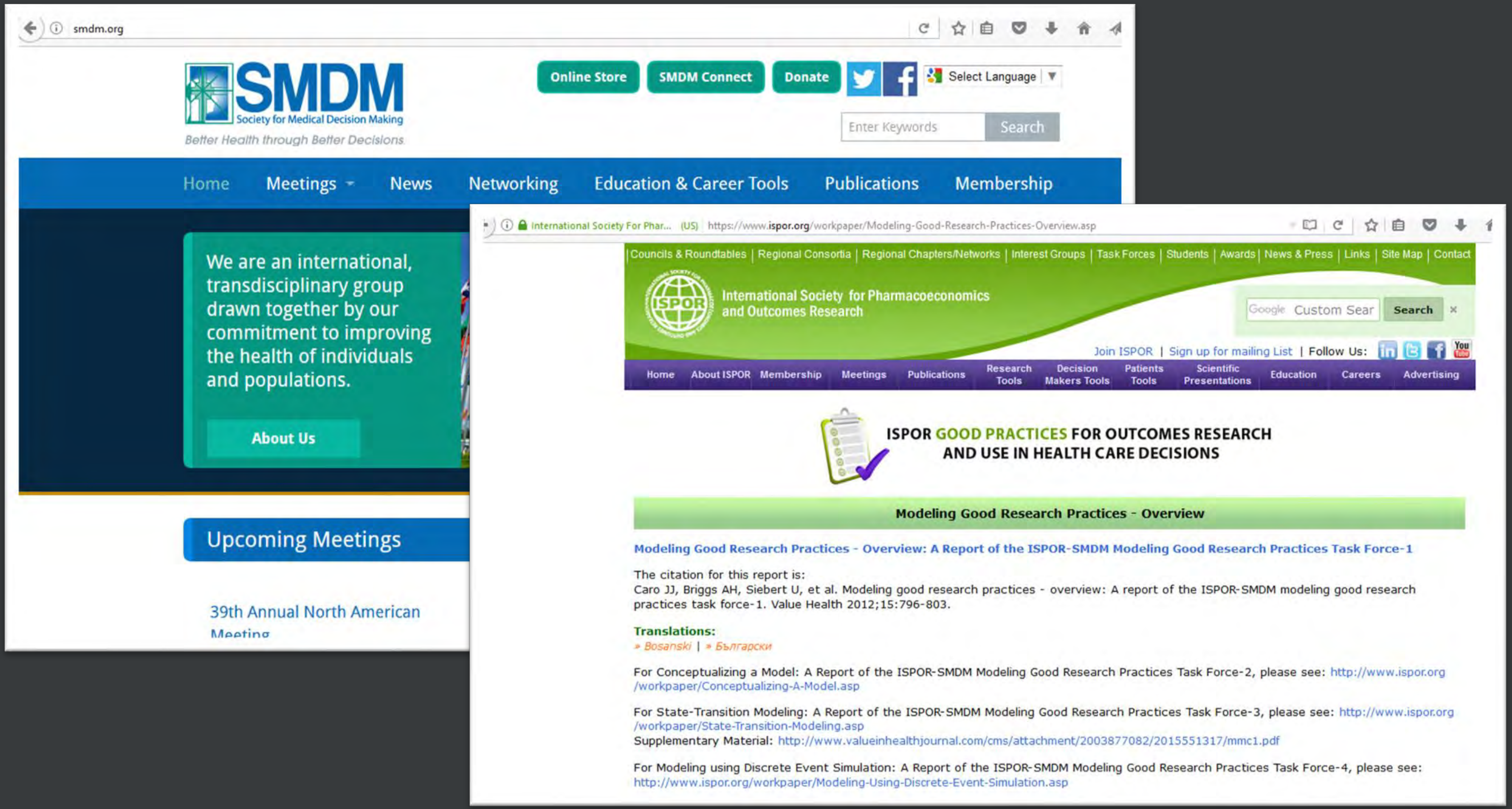

Exact Comparable Definitions of Models. E.g. Formal Definition of a Cellular Automaton

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Cell

Definition

The set of all cells will be denoted M. Consequently a cell is an unique (A set contains by definition unique elements.) element $m \in M$.

There is no limitation in the number of cells. However if only one cell is observed, we call the cellular automaton a trivial cellular automaton.

Special Case

We may call a cellular automaton with a finite number of cells **finite** or otherwise **infinite**.

Lattice

Definition

If M is a set of cells, we call M **indexed** or **regularly arranged** if there exists a bijective mapping $\mathcal{I} : M \to I : m \mapsto \mathcal{I}(m) = i$ between M and an index set I. We call $\mathcal{I}$ an **index mapping** and also use $\mathcal{I}$ for mapping tuples of cells onto tuples of indices $\mathcal{I} : M^k \to I^k : (m_1, \dots, m_k) \mapsto (\mathcal{I}(m_1), \dots, \mathcal{I}(m_k)) =: (i_1, \dots, i_k)$ where $k \in \mathbb{N} \setminus \{0\}$.

$(m_{\mathcal{I}(m)})_{m \in M}$ is the natural indexing for a set of indexed cells.

Definition

Since by now all cells are "arranged" or indexed using an index set $I \subseteq \mathbb{Z}^d$, we call d the **dimension** of the cellular automaton.

Definition

A subset I of $\mathbb{Z}^d$ is called **connected** if for each two elements $a, b \in I$ there exists a series of elements $(z_\alpha)_{\alpha \in \mathbb{N}} \subset I$ for which $\|z_\alpha - z_{\alpha+1}\| = 1\ \forall \alpha \in \mathbb{N}$ and for which $a, b \in (z_\alpha)_{\alpha \in \mathbb{N}}$.

Definition

We call a connected subset $I \subseteq \mathbb{Z}^d$, $d \in \mathbb{N} \setminus \{0\}$ an **index set**.

Special Case

Despite requiring a connected index set, this definition does not exclude exotic or even absurd index sets (i.e. lattices). (TODO)

G. Schneckenreither, Thesis: "Developing Mathematical Formalisms for Cellular Automata in Modelling and Simulation"; 2014

G. Schneckenreither, N. Popper, F. Breitenecker: "Methods for Cellular Automata and Evolution Systems in Modelling and Simulation"; IFAC PapersOnLine, 48 (2015), 1; S. 1 - 944.

Neighbours

Let $k \in \mathbb{N} \setminus \{0\}$.

Definition

A tuple $J := (j_1, \dots, j_k) \in (\mathbb{Z}^d)^k$ where $j_\alpha \neq j_\beta$ is called a **relative index tuple** and for $i \in \mathbb{Z}^d$ the addition respectively subtraction $J \pm i := (j_1 \pm i, \dots, j_k \pm i)$ is well-defined.

Definition

Given a relative index tuple J we define the **index translation** $\mathcal{T}_J$ of an index i by $\mathcal{T}_J : I \to (\mathbb{Z}^d)^k : i \mapsto i + J$ and call the result an **absolute index tuple**.

Note that $i + J$ is not necessarily a subset of I.

Theorem

I is a vector space? (TODO)

Definition

For a cell m_i from an indexed set of cells with index set I and a relative index tuple J we use the resulting absolute index tuple $\mathcal{T}_J(i) = (i_1, \dots, i_k) \in (\mathbb{Z}^d)^k$, to define the **neighbourhood** of m_i as $N_{m_i, J} := (n_1, \dots, n_k) \in (M \cup \{\emptyset\})^k$ where

$$n_\alpha := \begin{cases} m_{i_\alpha} = \mathcal{I}^{-1}(i_\alpha) & i_\alpha \in I \\ \emptyset & i_\alpha \notin I \end{cases} \qquad \alpha \in \{1, \dots, k\}.$$

Furthermore we call k the **neighbourhood dimension**.

The *non-existant cell* $\emptyset$ is required in order to maintain the original tuple structure of the neighbourhood and to be able to indicate that indices which are outside the index set do not refer to a cell.

Special Case

- A cell lies in its own neighbourhood (**reflexive**) if and only if $0 \in \mathbb{Z}^d$ is part of the relative index tuple.
- An index tuple respectively neighbourhood is neither necessarily **symmetric**, **bidirectional** nor **local**.

Theorem

*It is not unusual that neighbourhoods are of **local** character, which means that the neighbourhood relation is defined by the distance between cells. In this case, the index translation can be replaced by the appropriate function $\mathcal{T}_{\text{metric}}$. It is however always possible to find an equivalent relative index tuple J and use $\mathcal{T}_J$.*

Definition

For an indexed set of cells $(M, I, \mathcal{I}, \mathcal{I}^{-1})$ and an index translation $\mathcal{T}$ the **neighbourhood mapping** is defined by $\mathcal{N} := \mathcal{I}^{-1} \circ \mathcal{T} \circ \mathcal{I} : M \to I \to \mathbb{Z}^k \to (M \cup \{\emptyset\})^k : m_i \mapsto i \mapsto (i_1, \dots, i_k) \mapsto (n_1, \dots, n_k)$.

Border

Two types of "special cells" can be destinguised:

Definition

A **border-cell** is a cell, which is located at the boundary of the lattice.

Definition

If the absolute index tuple of a cell m_i does not lie completely within the index set ($\mathcal{T}_J(i) \not\subseteq I$), we talk of (a cell with) a **degraded neighbourhood**.

Optional boundary conditions must be applied to cells with a degraded neighbourhood!

In order to manipulate the geometry of the lattice (periodic boundary conditions for example) we modify the index translation:

Definition

Given a relative index tuple J, the **generalised index translation** is defined by $\mathcal{T}_J : I \to I^k : i \mapsto (i_1, \dots, i_k)$ where

$$i_\alpha := \begin{cases} i + j_\alpha & i + j_\alpha \in I \\ \tau(i + j_\alpha) & i + j_\alpha \notin I \end{cases} \qquad \alpha \in \{1, \dots, k\}$$

and $\tau : \mathbb{Z}^d \setminus I \to I$.

Special Case

What kind of preconditions to or charactersitics of τ generate which type geometry? (TODO)

- a toroid geometry for a two-dimensional cellular automaton (coll. "periodic boundary condition"[a]) can be achieved by using the modulus function...
- the same is true for a cylindrical geometry...
- what about a spherical surface?

[a] actually in this situation ther is no boundary!

State

Let $k \in \mathbb{N} \setminus \{0\}$ be the neighbourhood dimension.

Definition

There exists a **(temporary) state mapping** from the set of all cells M to the **set of all possible states** $\mathbb{S}$, which assigns a state to each cell $\mathcal{S} : M \to \mathbb{S} : m \mapsto \mathcal{S}(m) = s$. We also use $\mathcal{S}$ as $\mathcal{S} : (M \cup \{\emptyset\})^k \to (\mathbb{S} \cup \{\emptyset\})^k : (m_1, \dots, m_k) \mapsto (s_1, \dots, s_k)$ where

$$s_\alpha := \begin{cases} \mathcal{S}(m_\alpha) & m_\alpha \in M \\ \emptyset & m_\alpha \notin M \iff m_\alpha = \emptyset \end{cases} \qquad \alpha \in \{1, \dots, k\}$$

The *non-existent state* $\emptyset$ is required to maintaine the tuple structure and to indicate a degraded neighbourhood.

Special Case

- The set of all possible states $\mathbb{S}$ may contain a **finite** or **infinite** number of states.
- A "state-space" (coll.) can be a vector space, a ring or any other algebraic structure.
- By introducing a partitioning on the set of all possible states, different cell types can be distinguished.

A non-trivial cellular automata features more than one different element in $\mathbb{S}$.

Update

Let $k \in \mathbb{N} \setminus \{0\}$.

Definition

An **update rule** (also **update rules**) is a mapping $\mathcal{F} : (\mathbb{S} \cup \{\emptyset\})^k \to \mathbb{S} : (s_1, \dots, s_k) \mapsto s$

To calculate a new state for a cell:

$\mathcal{F} \circ \mathcal{S} \circ \mathcal{N}$:

$M \to (M \cup \{\emptyset\})^k \to (\mathbb{S} \cup \{\emptyset\})^k \to \mathbb{S}$:

$m \mapsto (m_1, \dots, m_k) \mapsto (s_1, \dots, s_k) \mapsto s$

actually, in detail:

$\mathcal{F} \circ \mathcal{S} \circ \mathcal{I}^{-1} \circ \mathcal{T} \circ \mathcal{I}$:

$M \to I \to \mathbb{Z}^k \to (M \cup \{\emptyset\})^k \to (\mathbb{S} \cup \{\emptyset\})^k \to \mathbb{S}$:

$m \mapsto i \mapsto (i_1, \dots, i_k) \mapsto (m_1, \dots, m_k) \mapsto (s_1, \dots, s_k) \mapsto s$

Remark

- An update rule (update rule set) can be the explicit definition of a mapping but also a (continuous) function or a combination of functions.
- Since degraded neighbourhoods contain non-existent cells respectively states ($\emptyset$), an update rule must react on a degraded neighbourhood and implement (arbitrary) "**boundary conditions**".

Warning

- An update rule never defines the geometry of the lattice!
- We exclude stochastic update rules from a basic definition since the neccessary introduction of a probability space would be an extension to our formal definition (TODO).

Definition

An update rule must be defined for every possible neighbourhood configuration. Otherwise we deal with **undefined behaviour**.

- An update rule must be **compatible with the index set**: All occuring degradations of neighbourhoods must be taken into account.
- An update rule must be **self-contained** since all possible state-configurations[a] arrise from the update rule.

[a] except for the initial condition, see later

Global State

Definition

The state of all cells is accumulated in the temporary state mapping $\mathcal{S}$ which can be identified with an element of $\mathfrak{S} := \mathbb{S}^M$. We then also call $\mathcal{S}$ the **(temporary) global state**.

Definition

Given a neighbourhood mapping $\mathcal{N}$, a temporary state mapping $\mathcal{S}$ and an update rule $\mathcal{F}$ we define the **local evolution operator** $\tilde{\mathcal{S}} := \mathcal{F} \circ \mathcal{S} \circ \mathcal{N} : M \to (M \cup \{\emptyset\})^k \to (\mathbb{S} \cup \{\emptyset\})^k \to \mathbb{S} : m \mapsto (m_1, \dots, m_k) \mapsto (s_1, \dots, s_k) \mapsto s$.

We can see that a local evolution operator is a state mapping and a global state.

Iteration

Definition

A **(global) evolution operator** is a mapping $\mathcal{E} : \mathfrak{S} \to \mathfrak{S} : \mathcal{S} \mapsto \tilde{\mathcal{S}} := \mathcal{F} \circ \mathcal{S} \circ \mathcal{N}$.

Definition

An **iterative process** can be obtained by defining $\mathcal{S}_{t+1} := \mathcal{E}(\mathcal{S}_t) = \mathcal{F} \circ \mathcal{S}_t \circ \mathcal{N}$ where $n \in \mathbb{N}$.

Definition

For an iteration, an **initial state** or **initial condition** $\mathcal{S}_0$ must be given. It is neccessary that the initial condition is **compatible with the update rules**.

Only the states of the cells and accordingly the state mapping may change during iteration!

Automaton

Definition

A **cellular automaton** comprises ...

(i) an indexed set of cells
(ii) an initial state mapping $\mathcal{S}_0$
(iii) a ralative index tuple J
(iv) a generalised index translation (only if the geometry shall be "manipulated")
(v) an update rule $\mathcal{F}$
(vi) the iterative application of an evolution operator

Exact Comparable Definitions of Models. E.g. Formal Definition of a Cellular Automaton

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10 Concepts to Integrate

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5. Different Methods for Different Questions (Complexity)
6. Comparability of Results

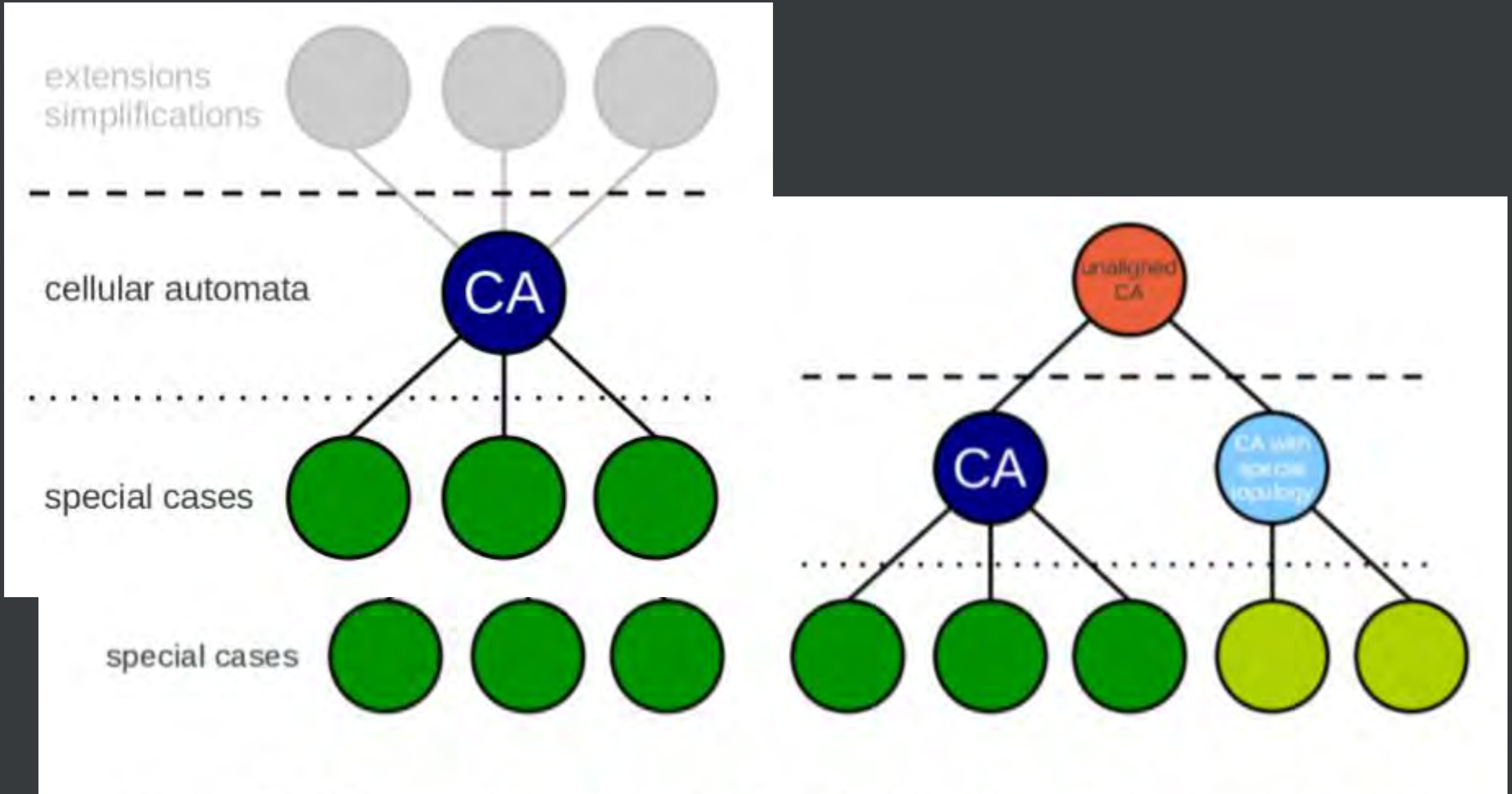

Figure 1: Different hierarchies for the classification of cellular automata.

Concept 7

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6. Comparability of Results
7. Make it Understandable

Complicated Models and Various Results

- Good data & an “improvable” Model
- Right Model & good Results
- Nobody understands.

-> Change Management & Interdisciplinarity

METHOD: Data Representation & Human Computer Interfaces (HCI)

Concept 7

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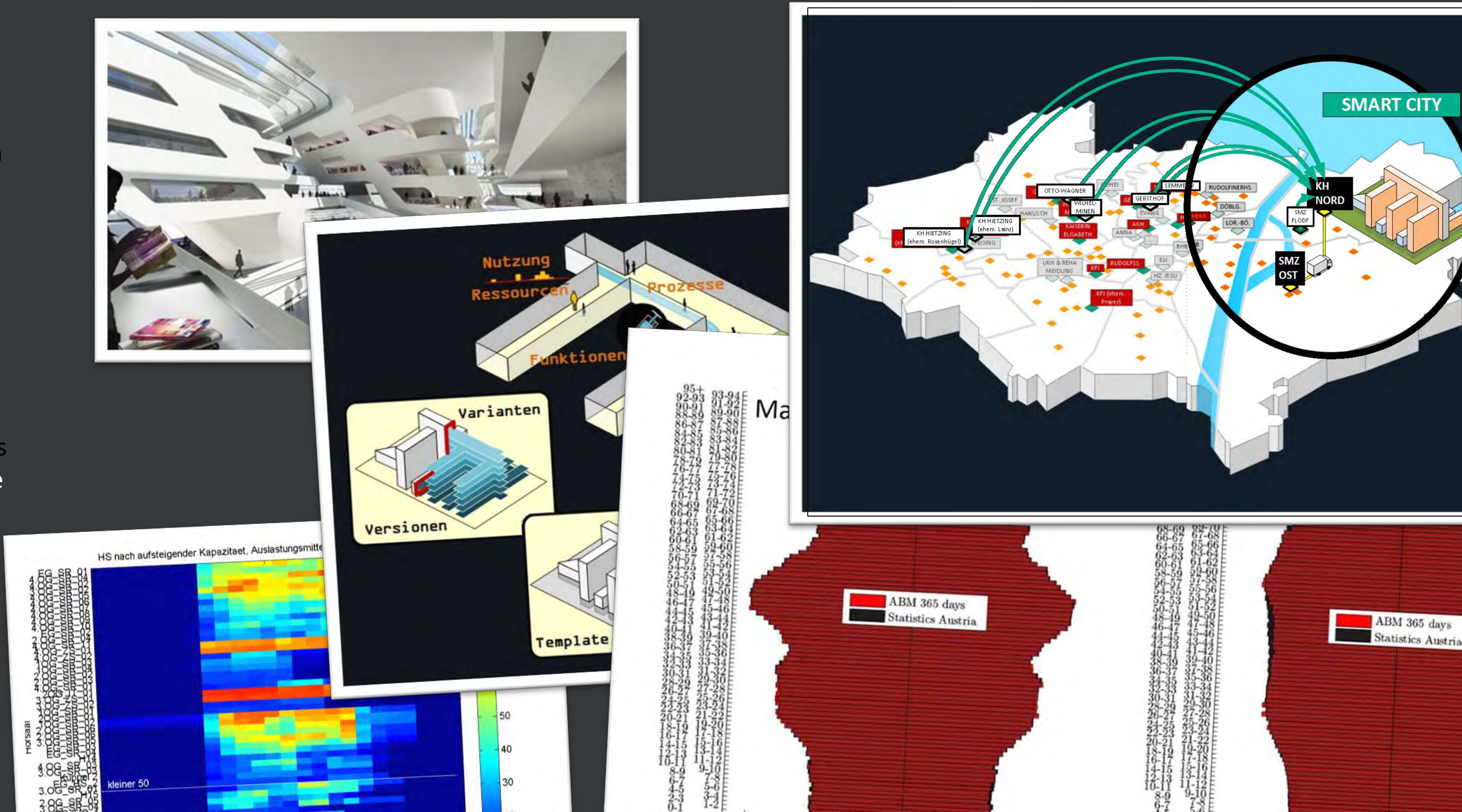

Having Fun with Epidemics and Herd Immunity…

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„On the benefits of explaining herd immunity in vaccine advocacy“, Nature Human Behaviour, 6.3.2017

Concept 8

10 Concepts to Integrate

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6. Comparability of Results
7. Make it Understandable
8. Open and Independent Solutions

Open and Independent Solutions

- Publication limited because of Economic Exploitation & Stakeholder Interests
- Lack of Comparability of Different Models
- Rules and Guidelines needed

METHOD: Open Access & Public Domain

Additional Sources: Example Web Scraping

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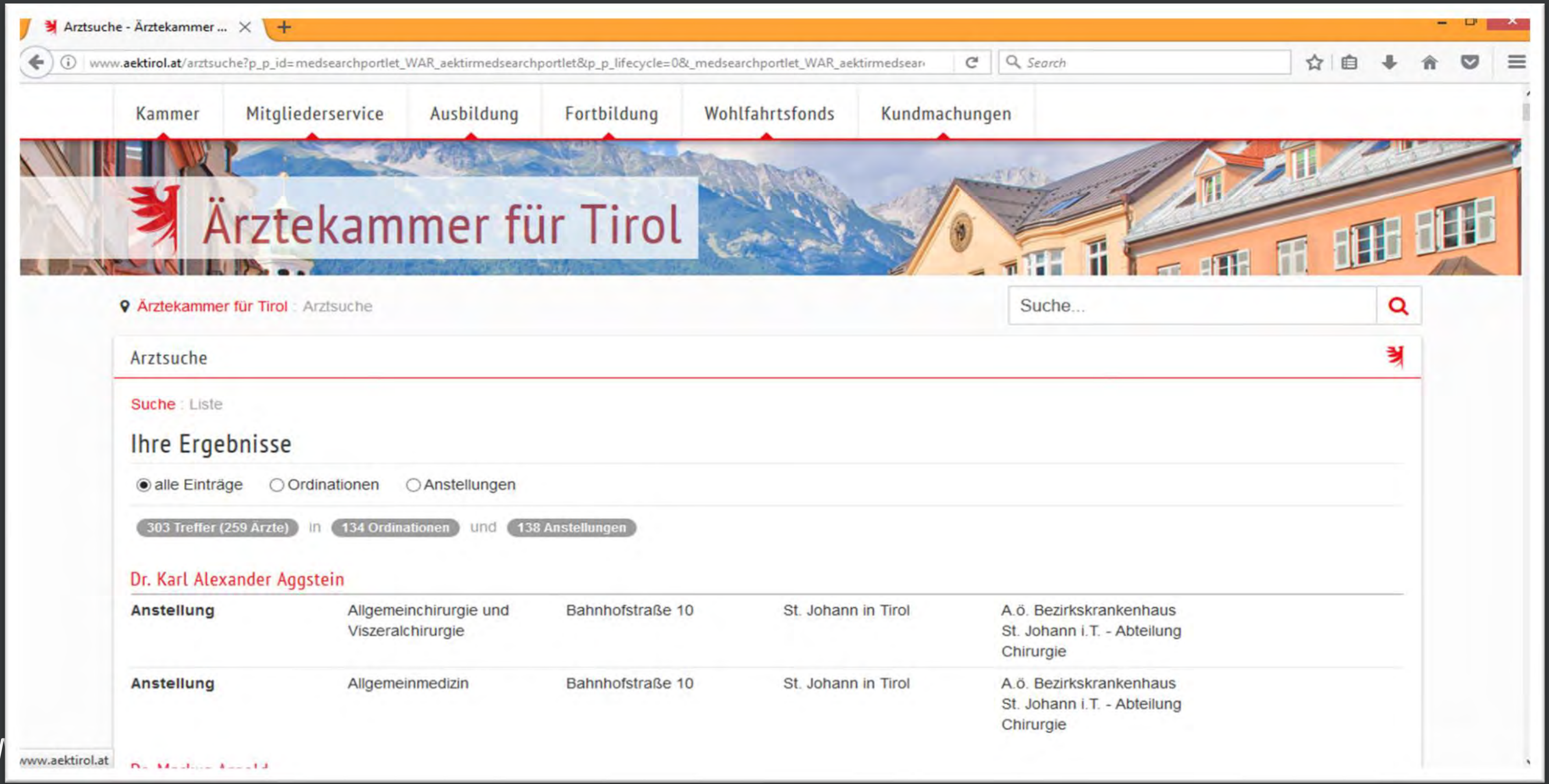
8. Open and Independent Solutions

Integration of Data from Web Pages of Physicians – Actualisation monthly



Health Care: Physicians

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7. Make it Understandable
8. Open and Independent Solutions

- Physicians total: 16.500
- Medical Practices: 20.219
- Medical Practices with GPS Coordinates: 13.607
- Total Hours per Week: 193.899 h
- GPs:
  - Medical Practices: 8.062
  - Contracts with Social Incurances: 3841
  - Total Hours per Week: 89.594 h

Health Care: Physicians

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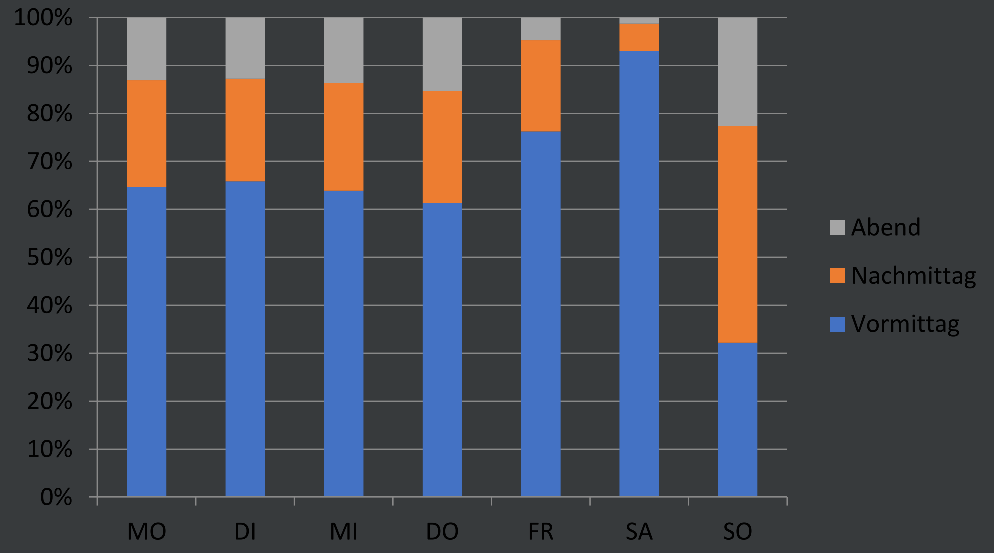
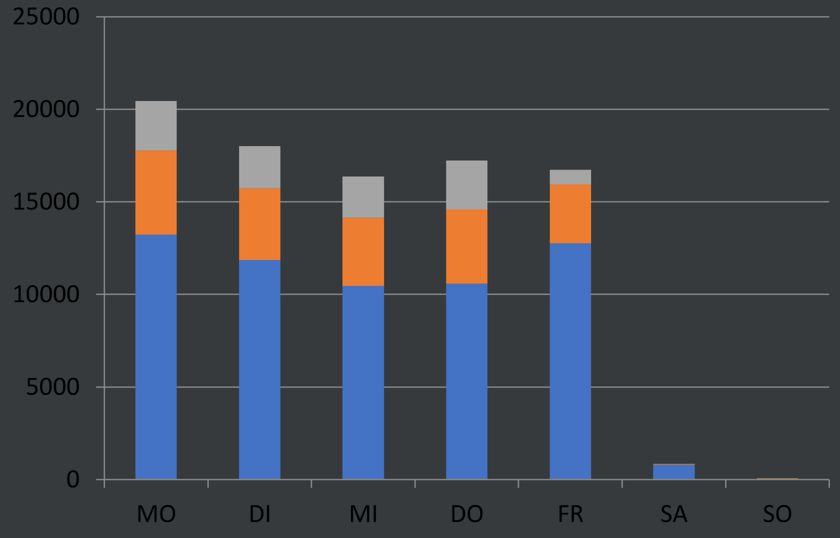
8. Open and Independent Solutions

Example Medical Practices Hours :

relative



absolut



Concept 9

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7. Make it Understandable
8. Open and Independent Solutions
9. Priority for Data Security and Stake Holder Interests

Priority for Data Security and Stakholders

- Additional Requirements e.g. with the new EU General Data Protection Regulation
- Quality can be reduced by missing data
- Transparent Processes are Needed in advance

METHOD: Data Security & Governance

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DEXHELPP Research Server

10 Concepts to Integrate

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7. Make it Understandable
8. Open and Independent Solutions
9. Priority for Data Security and Stake Holder Interests

1. **Data:** Temporary and restricted to well defined Research
2. **Access:** Restricted and Reproducible
3. **Methods:** Usage of all Modelling & Simulation Methods
4. **Export:** Well defined Rules for Export and Usage

Processes according to Guidelines of Research Data Alliance (RDA)

Concept 10

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10 Concepts to Integrate

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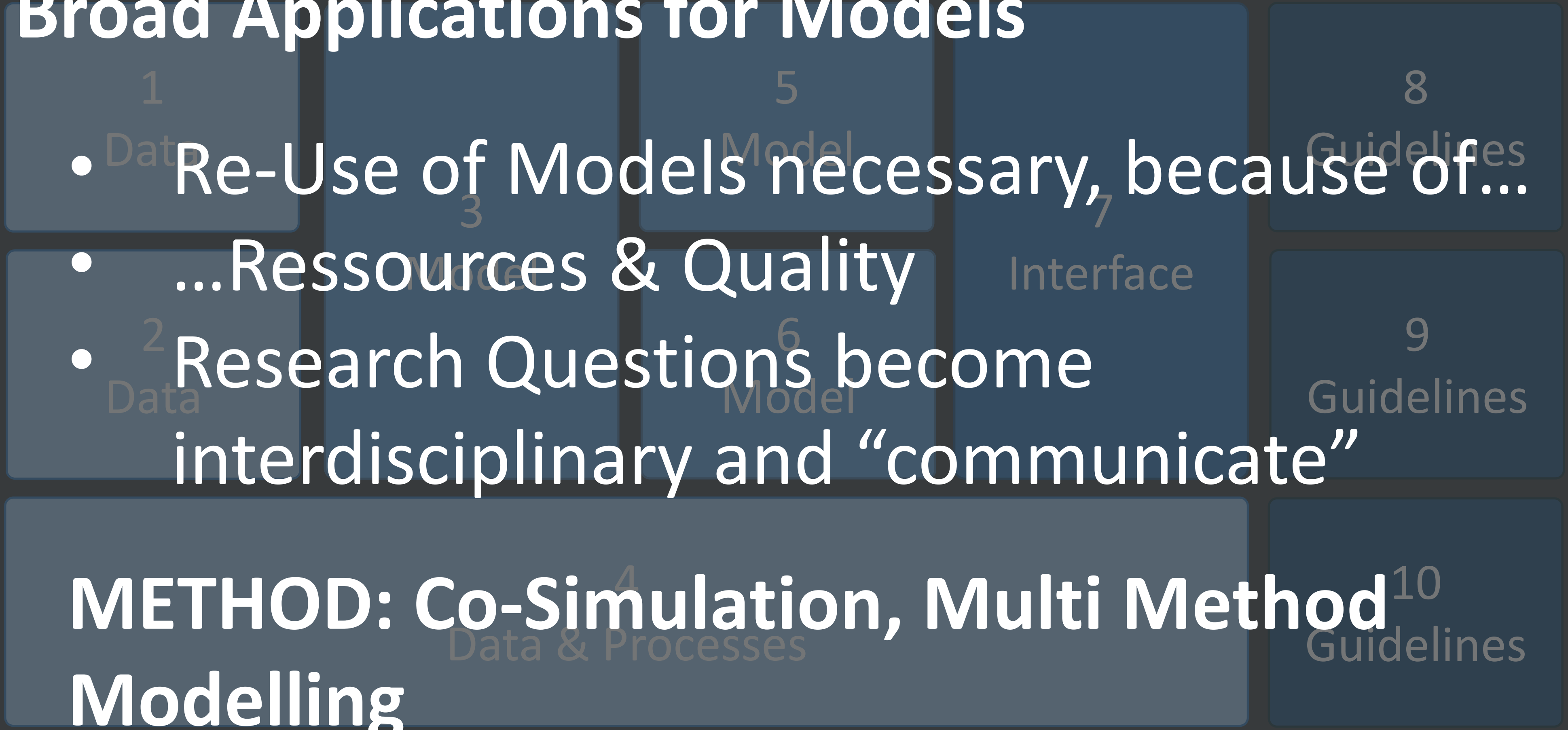
3. Modular & Efficient Solutions
4. Reproducible Processes
5. Different Methods for Different Questions (Complexity)
6. Comparability of Results
7. Make it Understandable
8. Open and Independent Solutions
9. Priority for Data Security and Stake Holder Interests
10. Broad Applications (Health System, Energy, Industry, Energy, Mobility, Infra-structure)

Broad Applications for Models



- Re-Use of Models necessary, because of…
- …Ressources & Quality
- Research Questions become interdisciplinary and “communicate”

METHOD: Co-Simulation, Multi Method Modelling

Multi-Method Airport Modelling

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Exploring Advantages of Multi-Method Modelling and its applications in large socio-technical infrastructure systems

Glock et al, ASIM 2016

Multi-Method Airport Modelling

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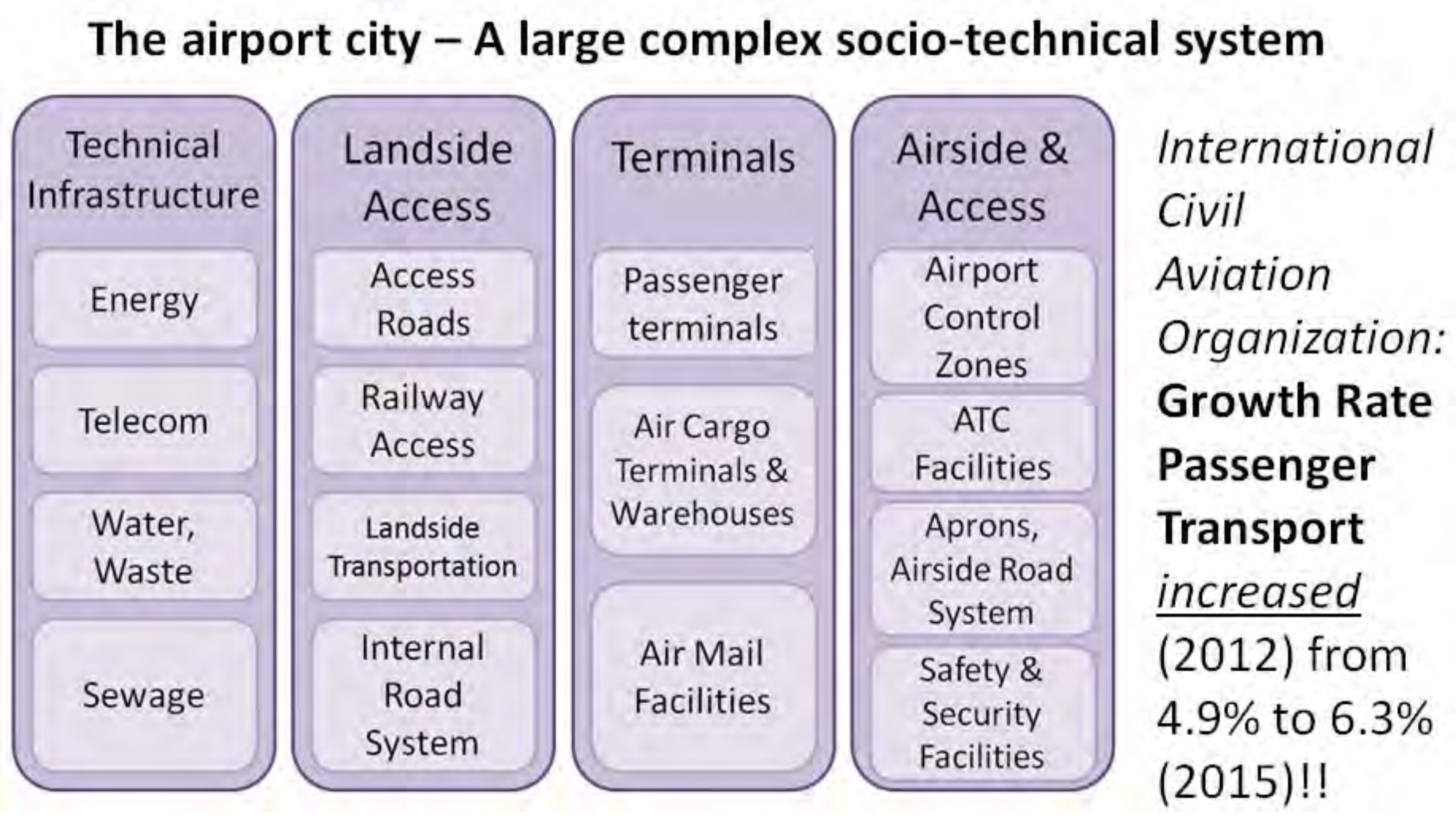

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Multi-Method Airport Modelling

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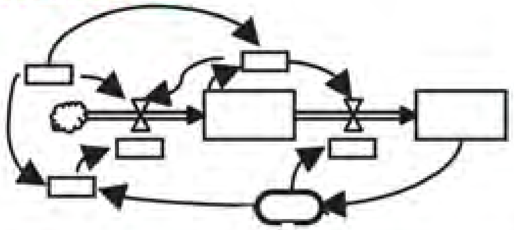
System Dynamics

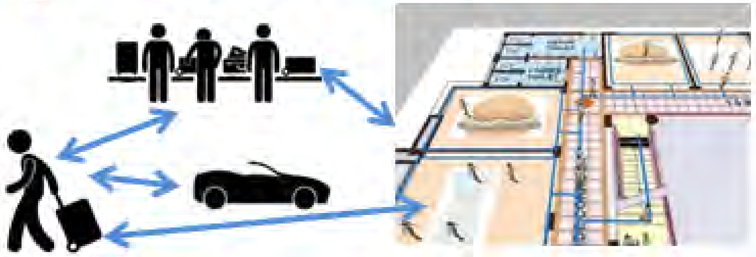


Aggregated states
Time-continuous
Causal Links & Feedback
average computing times

Discrete Events Simulation

Individuals (Entities) & Resources
Changes in discrete time (Events)
Given processes
average computing times

Agent-Based Models



Individuals
Time-continuous
Spatial aspects
Interaction (agents, environment)
High computing times

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Multi-Method Airport Modelling

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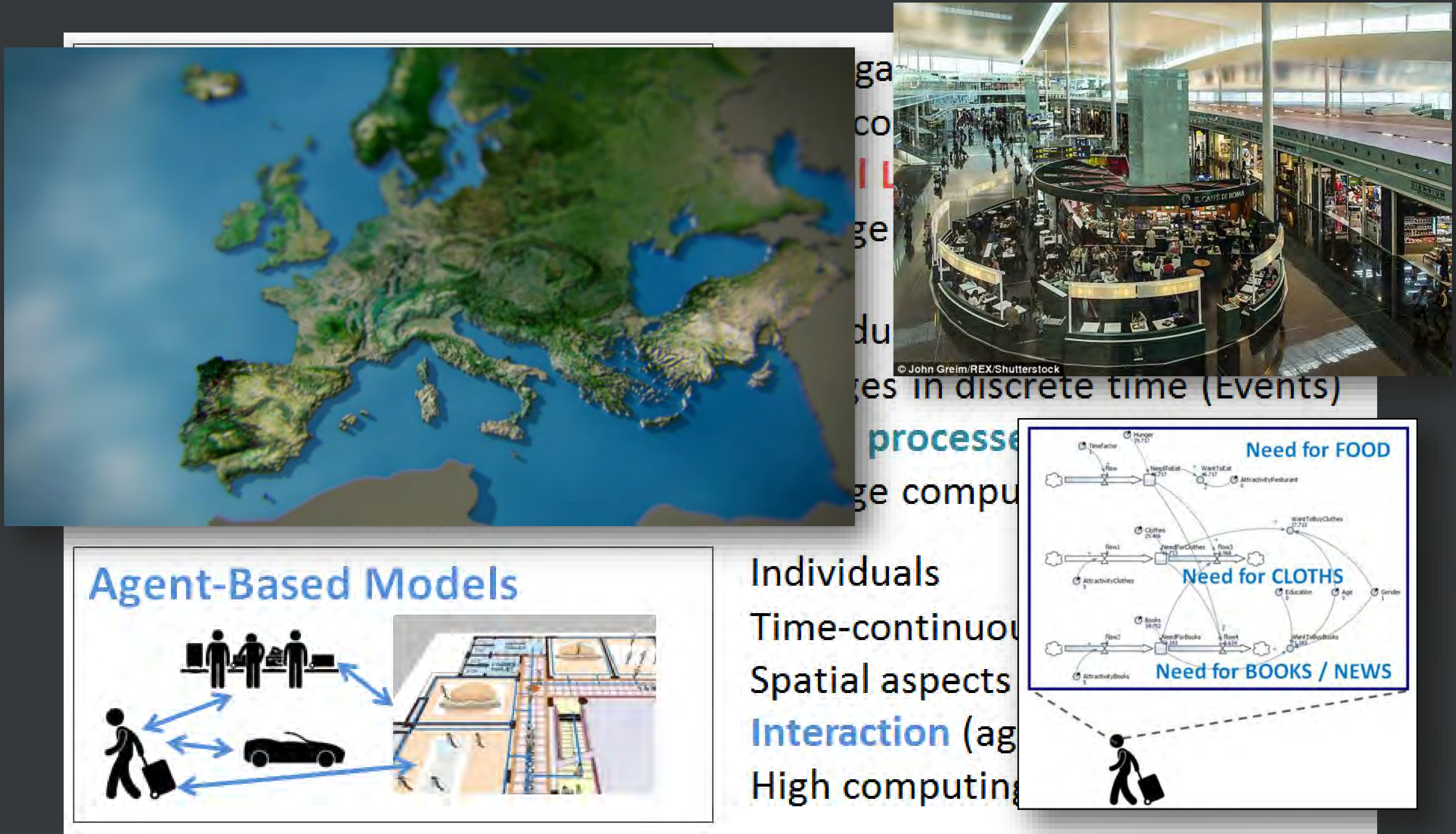

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Methods & Concepts to be Developed and Integrated

- Explorative Visual Computing –Visual Analytics and Statistics
- Data Processes (Integration & Linkage) & Modelling Tools (Parametrization & Calibration)
- Modular Models, Coupling of Models
- Validation & Data Citation
- Methods for Choosing Models
- Comparative Modelling
- Data Representation & Human Computer Interfaces (HCI
- Open Access & Public Domain
- Data Security & Governance
- Co-Simulation, Multi Method Modelling

1 Data
2 Data
3 Model
4 Data & Processes
5 Model
6 Model
7 Interface
8 Guidelines
9 Guidelines
10 Guidelines

Implementation DEXHELPP

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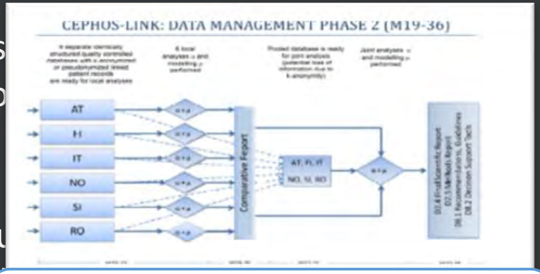

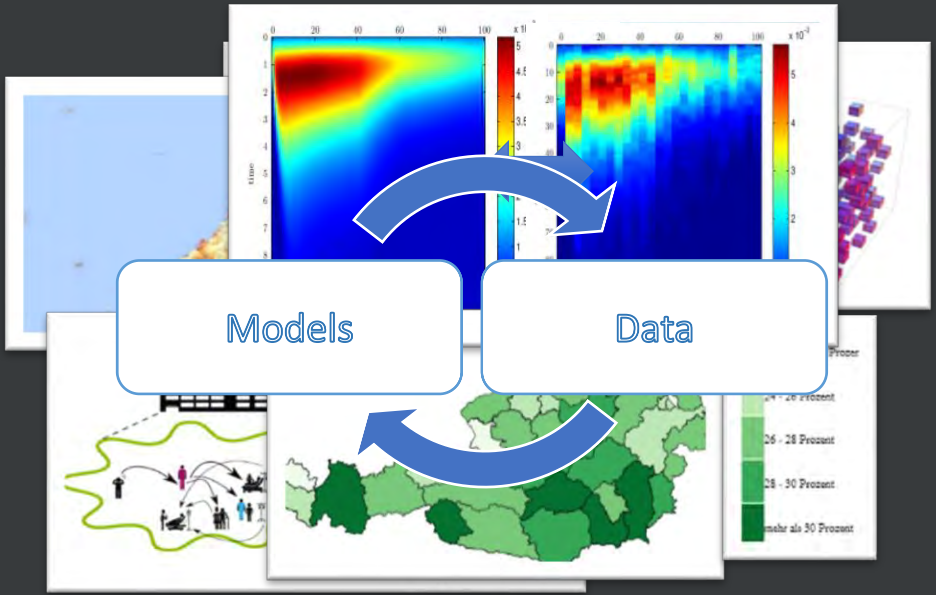

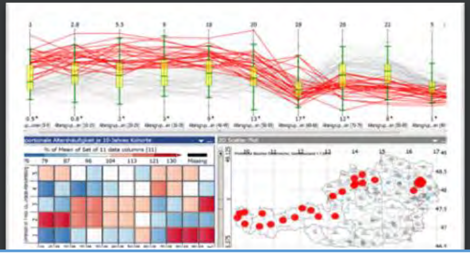

EUROSIM Initiative
DDSS Technical Committee

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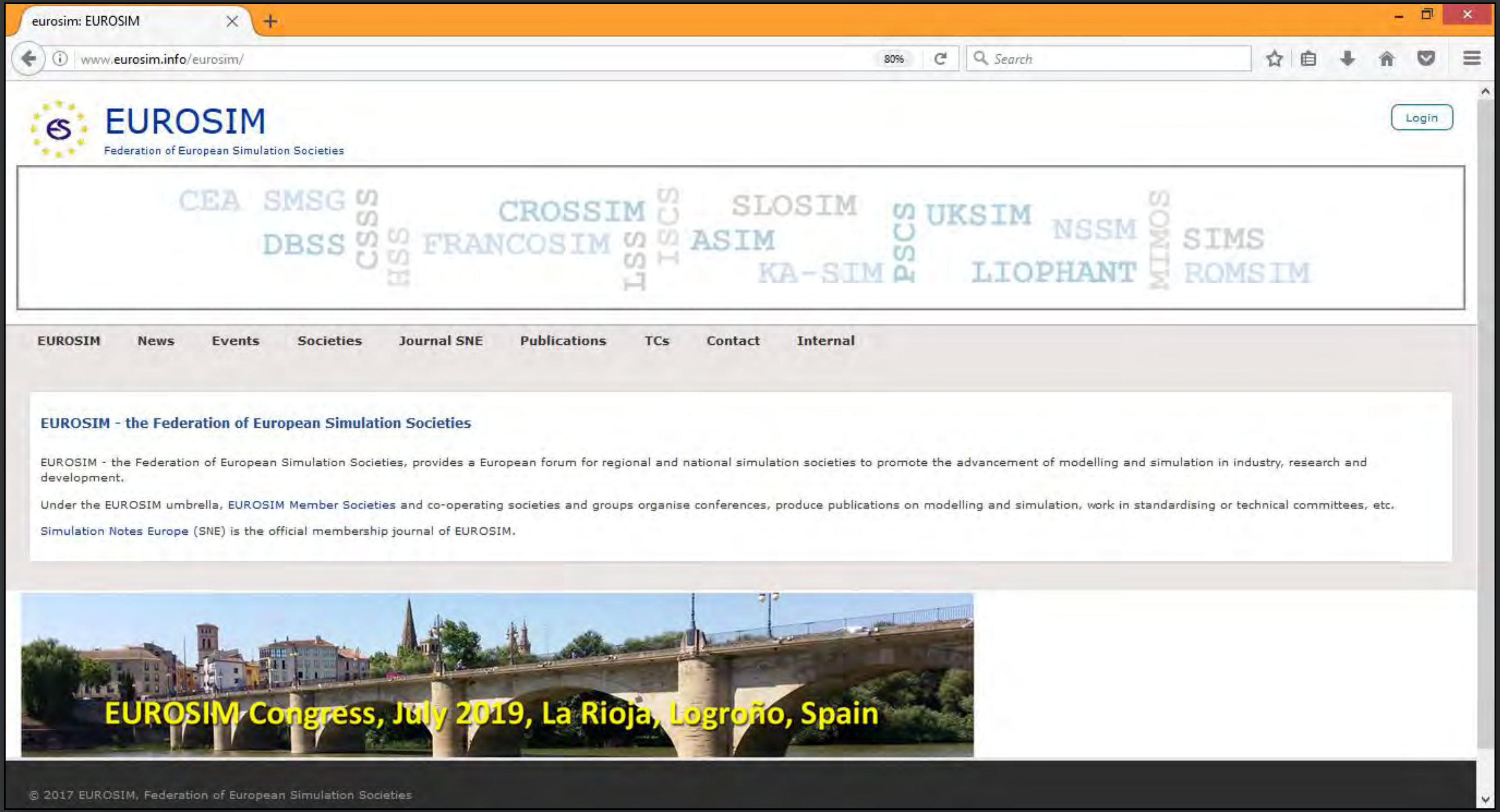

https://www.eurosim.info/tcs/tc-ddss/

Studies, Policies & Recommendations

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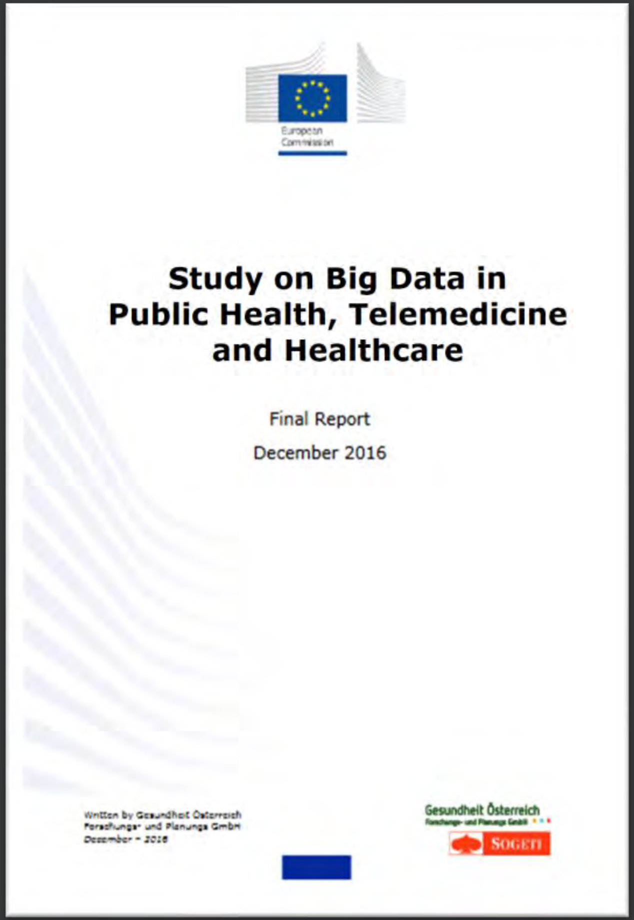
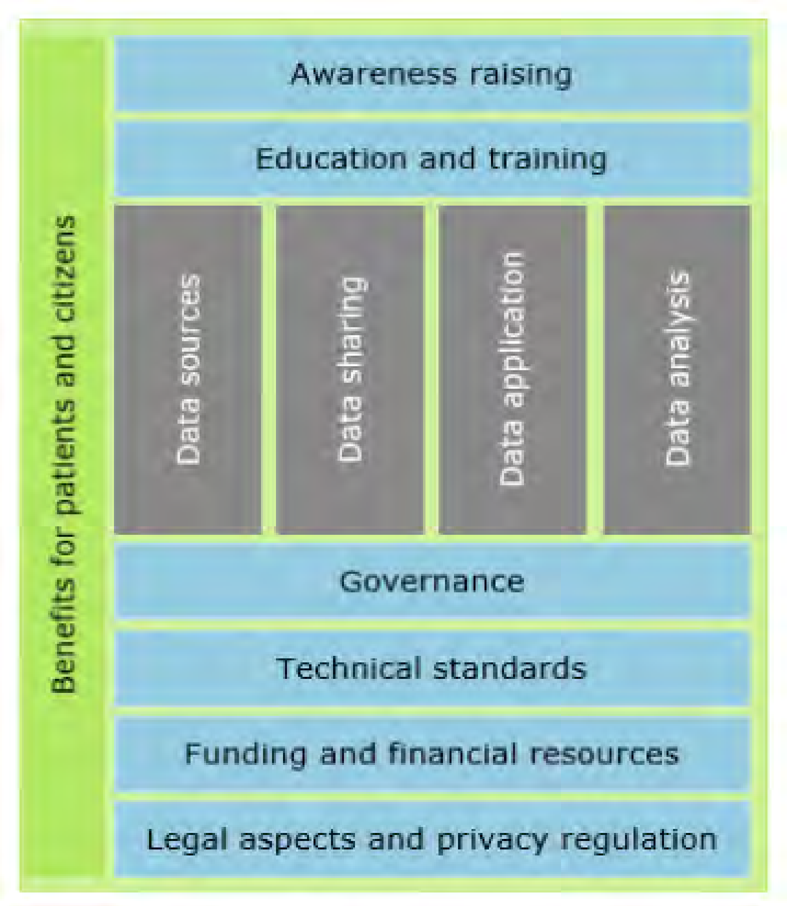


Study on Big Data in Public Health, Telemedicine and Healthcare

Final Report

December 2016



Overview of fields of policy recommendations

https://ec.europa.eu/health/sites/health/files/ehealth/docs/bigdata_report_en.pdf

Studies, Policies & Recommendations

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The following twenty examples of use of Big Data in Health were identified and selected for further analysis:

- Comet K-Project DEXHELPP – AT
- The Shared Care Platform – DK
- E-Estonia – National Identity Scheme – EE
- AEGLE (An analytics framework for integrated and personalized healthcare services in Europe) – UK, IT, GR, SE, BE, NL, PT, FR
- The Business Intelligence database system – GR
- PASSI (Progressi delle Aziende Sanitarie) – IT
- Arno Observatory – IT
- The Swedish Big Data Analytic Network – SE
- Clinical Practice Research Datalink (CPRD) – UK
- Sentinel Stroke National Audit Programme (SSNAP) – UK
- Hospital Episode Statistics (HES) – UK (England)
- The YODA Project (Yale University open data access) – US
- FDA Adverse Event Network Analyser - US
- CEPHOS-LINK – FI, AT, RO, NO, SI, IT
- Twitter (Adverse drug reactions and public health) – International
- Flatiron – US
- UK Biobank – UK
- Semantic Data Platform for Healthcare (SEMCARE) – DE, NL, AT, UK, ES
- Integrated BioBank of Luxembourg (IBBL) – LU
- Spanish Rare Diseases Registries Research Network (SpainRDR) – ES

Studies, Policies & Recommendations

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Recommendations

- Recommendation 1 on Awareness Raising:
  Develop and implement a communication strategy to increase the awareness of the added value of Big Data in Health and encourage a positive public mind set towards Big Data in Health
- Recommendation 2 on Education and Training
  Strengthen human capital with respect to the increasing need for a workforce that can utilize the potential of Big Data in Health
- Recommendation 3 on Data Sources:
  Expand existing and explore new sources of Big Data in Health and secure their quality and safety
- Recommendation 4 on Open Data and Data Sharing:
  Promote open use and sharing of Big Data in Health without compromising patients' rights to privacy and confidentiality
- Recommendation 5 on Applications and Purposes:
  Increase target-oriented application of Big Data analysis in health based on the needs and interests of stakeholders including patients

Studies, Policies & Recommendations

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Recommendations

- Recommendation 6 on Data Analysis:
  Identify the potentials of Big Data analysis, improve analytical methods and facilitate the use of new and innovative analytical methods
- Recommendation 7 on Governance of Data Access and Use:
  Implement governance mechanisms to ensure secure and fair access and use of Big Data for research in health
- Recommendation 8 on Standards:
  Develop standards for Big Data in Health to enhance and simplify its application and improve interoperability
- Recommendation 9 on Funding and Financial Resources:
  Ensure purposeful investment steered by the European Commission to warrant cost-effectiveness and sustainability
- Recommendation 10 on Legal Aspects and Privacy Regulations:
  Clarify and align existing legal and privacy regulation of Big Data in Health

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Outlook

- Putting it all together – a huge challenge, but necessary because of external reasons
- A new “Process for Processes” instead of “Modelling & Simulation” integrating all areas of research (4th Paradigm of Jim Gray)
- Not only for models, but also for the modelling process: not static anymore -> dynamic approaches - also for smaller models
- Huge methodolical Differences between “Data Driven” and “Model Driven” Approaches – e.g. Data Driven Journalism
- No “Generic World Model” possible (e.g. Co-Morbidities), but there are Processes to generate controllable complex and dynamic models

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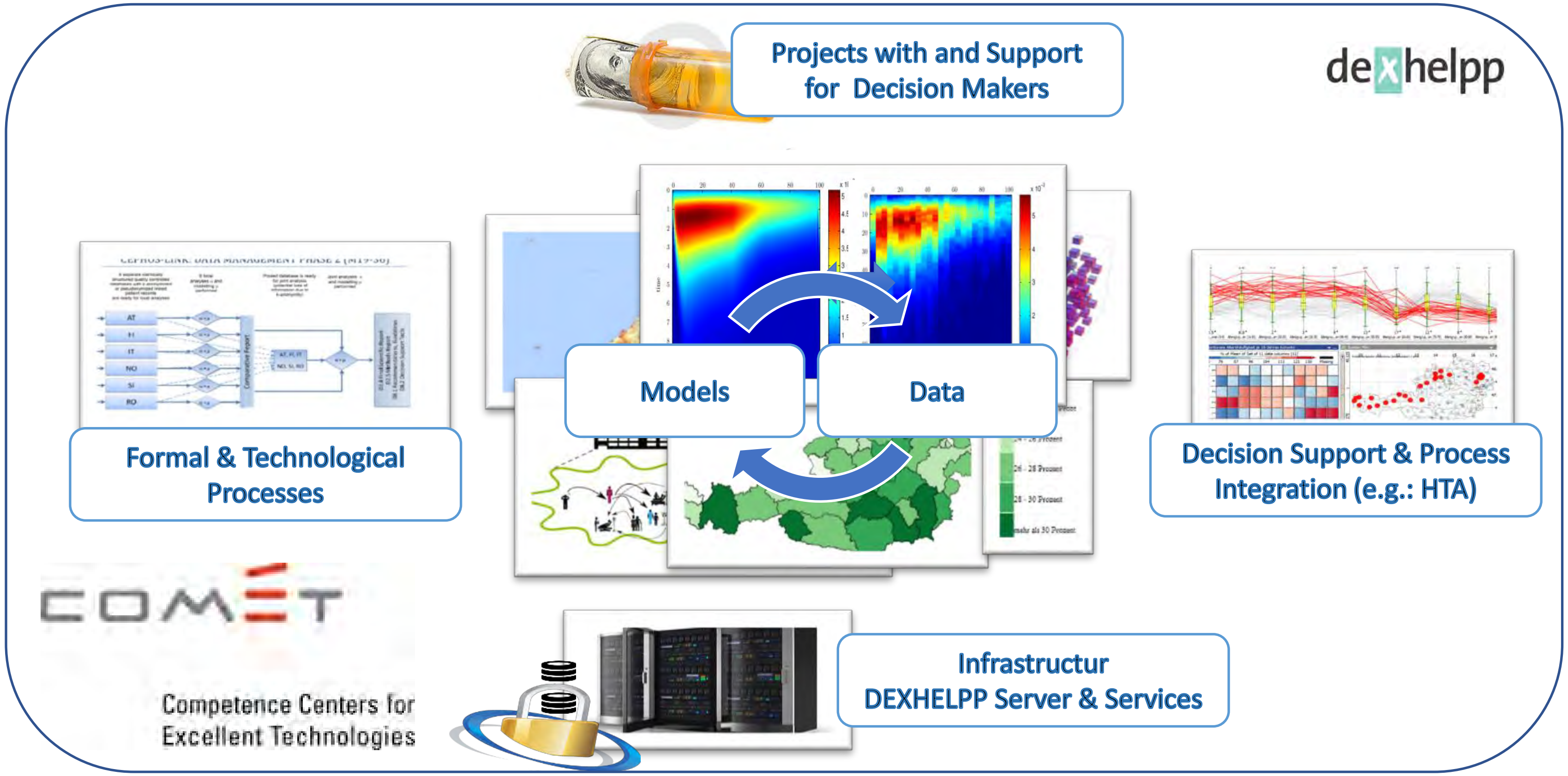

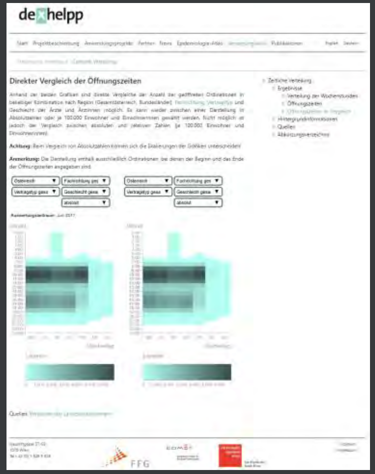

Hauptverband der österreichischen Sozialversicherungsträger

Gesundheit Österreich GmbH

ÖBIG BIQG FGÖ

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vrvis

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IMEHPS improving mental health pathways

SYNTHESIS Forschung

UMIT the health & life sciences university

secure sba-research.org

wirtschafts agentur wien Ein Fonds der Stadt Wien

bmvit Bundesministerium für Verkehr, Innovation und Technologie

bmwfw Bundesministerium für Wissenschaft, Forschung und Wirtschaft

COMET Competence Centers for Excellent Technologies

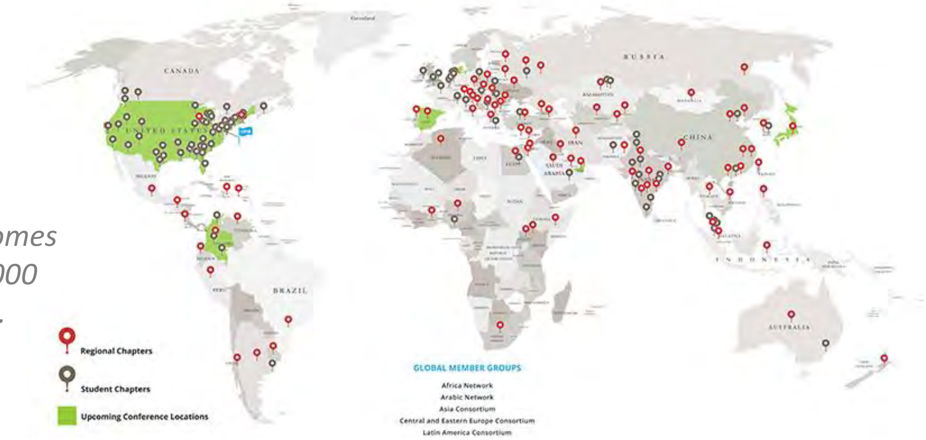
FFG

ISPOR

Improving healthcare decisions

ISPOR - The Professional Society for Health Economics and Outcomes Research is a multistakeholder organization with more than 20,000 individual and chapter members from 110+ countries worldwide.

ISPOR Worldwide Chapters



Upcoming Conferences and Education

ISPOR Warsaw 2019
27-28 MARCH 2019 | WARSAW | POLAND

ISPOR 2019
MAY 18-22, 2019 | NEW ORLEANS, LA | USA

ISPOR Latin America 2019
12-14 SEPTEMBER 2019 | BOGOTÁ | COLOMBIA

ISPOR Europe 2019
2-6 NOVEMBER 2019 | COPENHAGEN | DENMARK

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