Beyond the Black Box: *Using WoE to Transparently Integrate Data*

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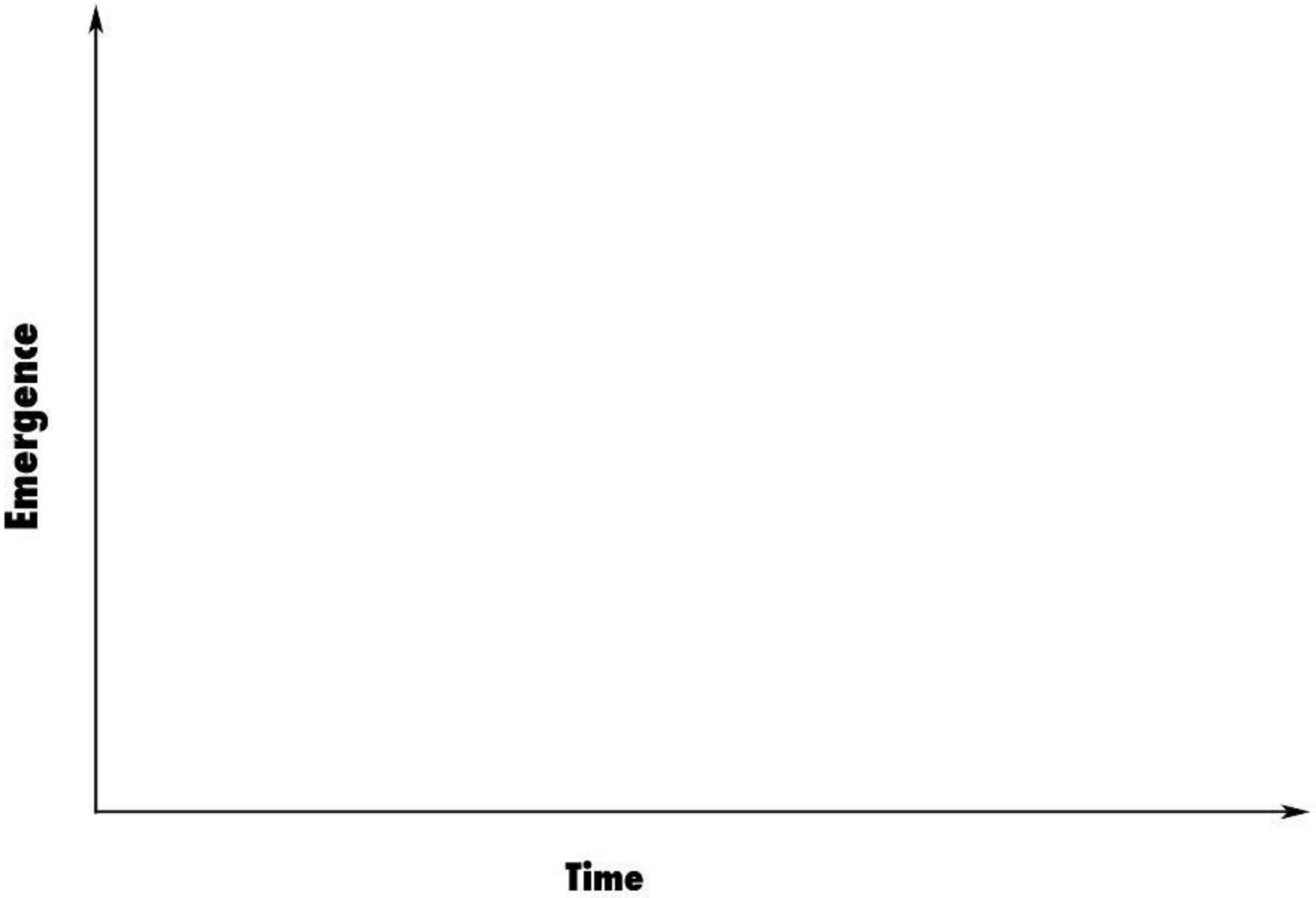
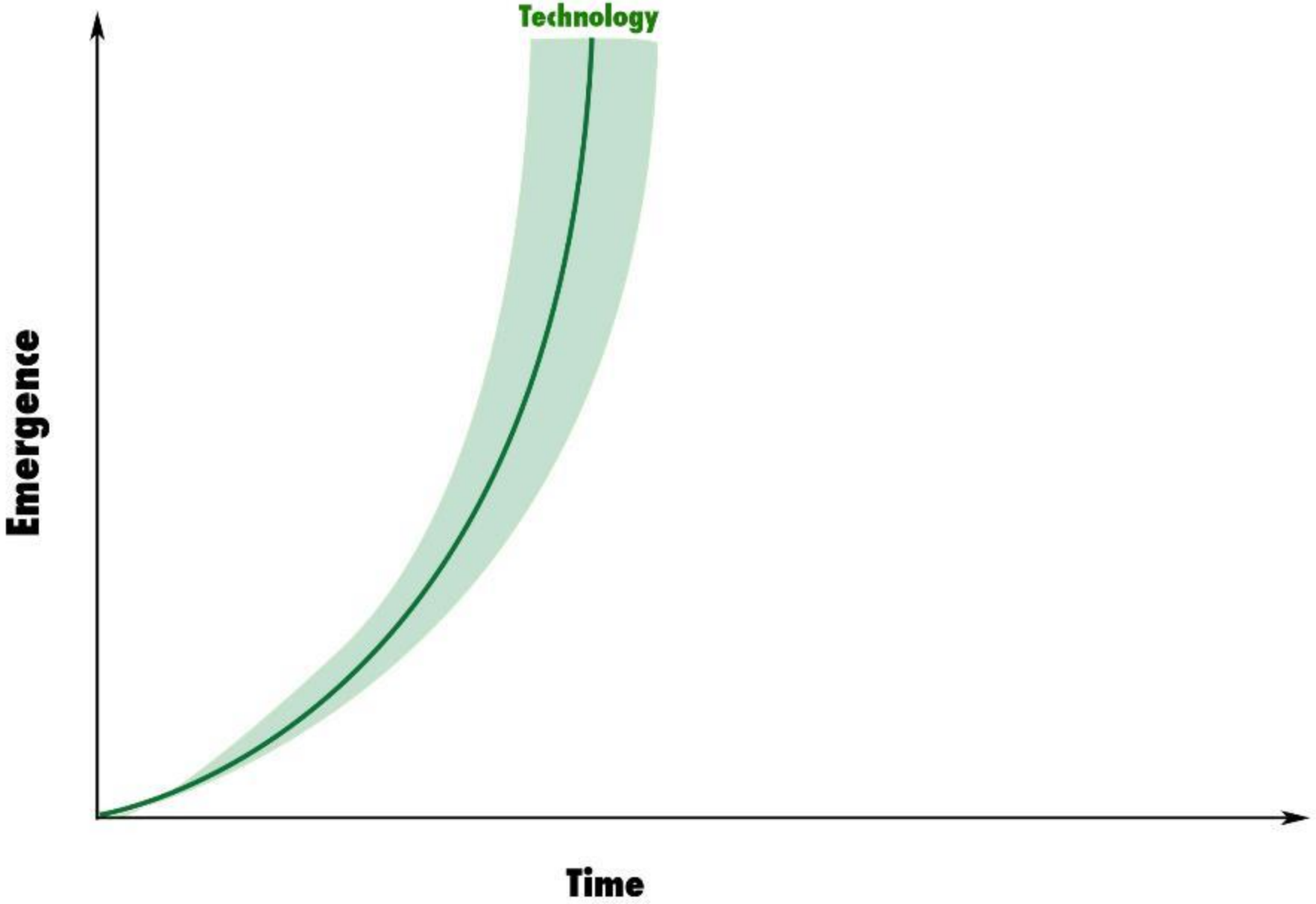
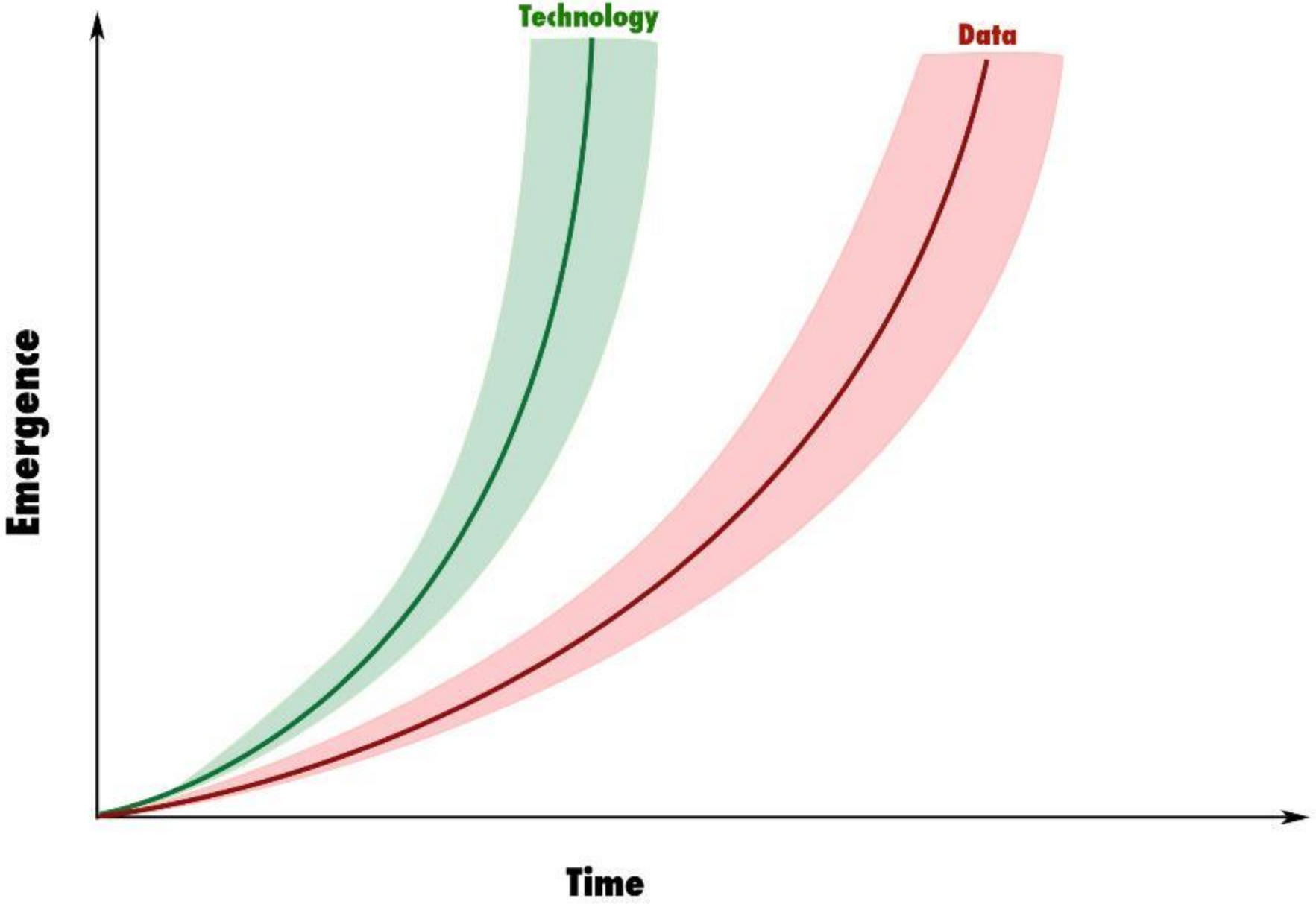
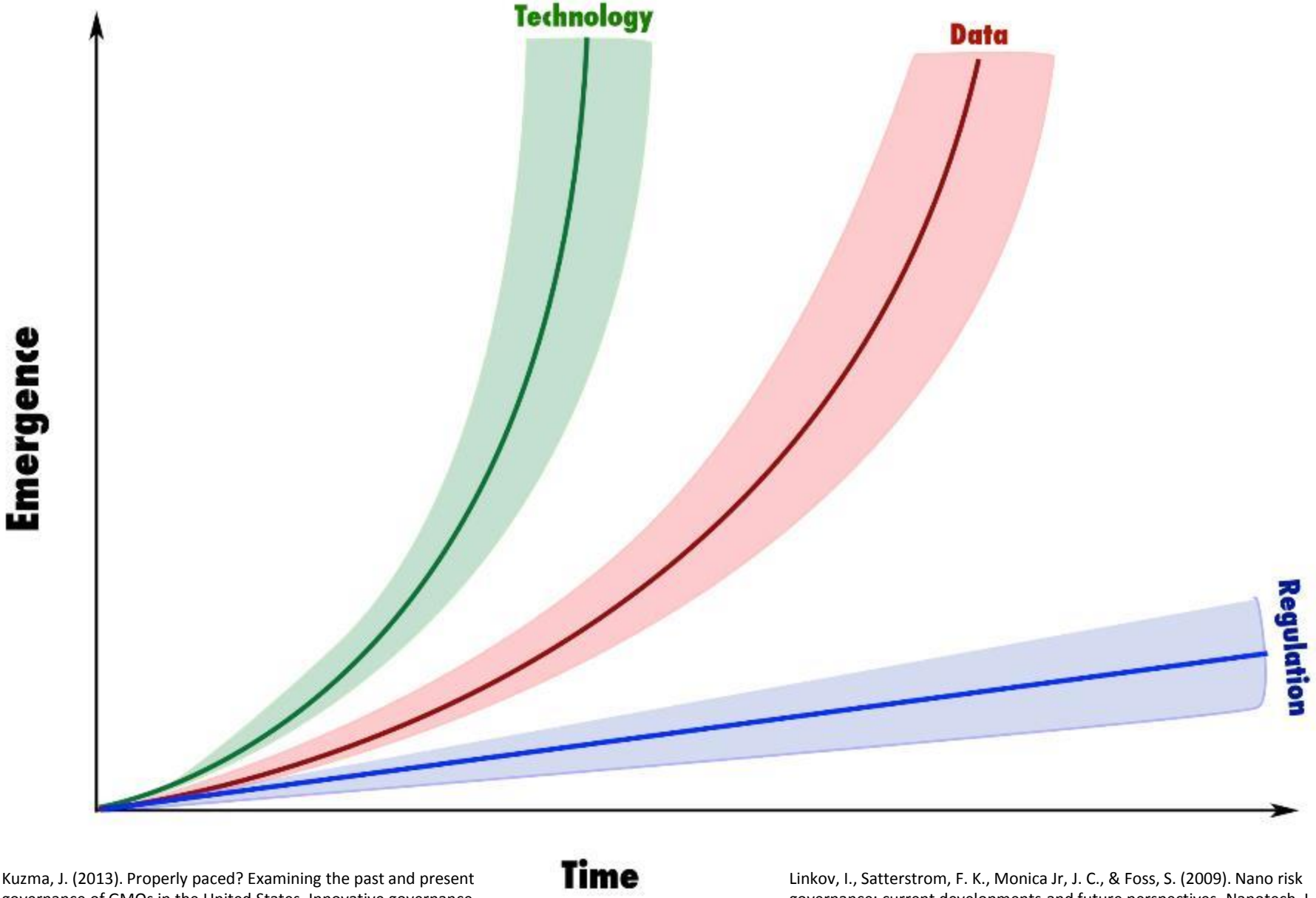
EFSA Challenges of Emerging Technology Innovation

- Pace of invention and innovation is growing
  - Likewise, getting further refined and specified
  - Revolutionary potential to benefit health – pressures to innovate
- For public health, also breaching existing scientific knowledge
  - Nanotechnology, synthetic biology/systems engineering, many others
- Existing governance structures ill equipped to deal with new technologies
  - Often captured under general chemical regulation or other conventional materials
  - Behave differently than conventional technologies, defy existing knowledge of hazard and exposure assessment


Emergence
Time

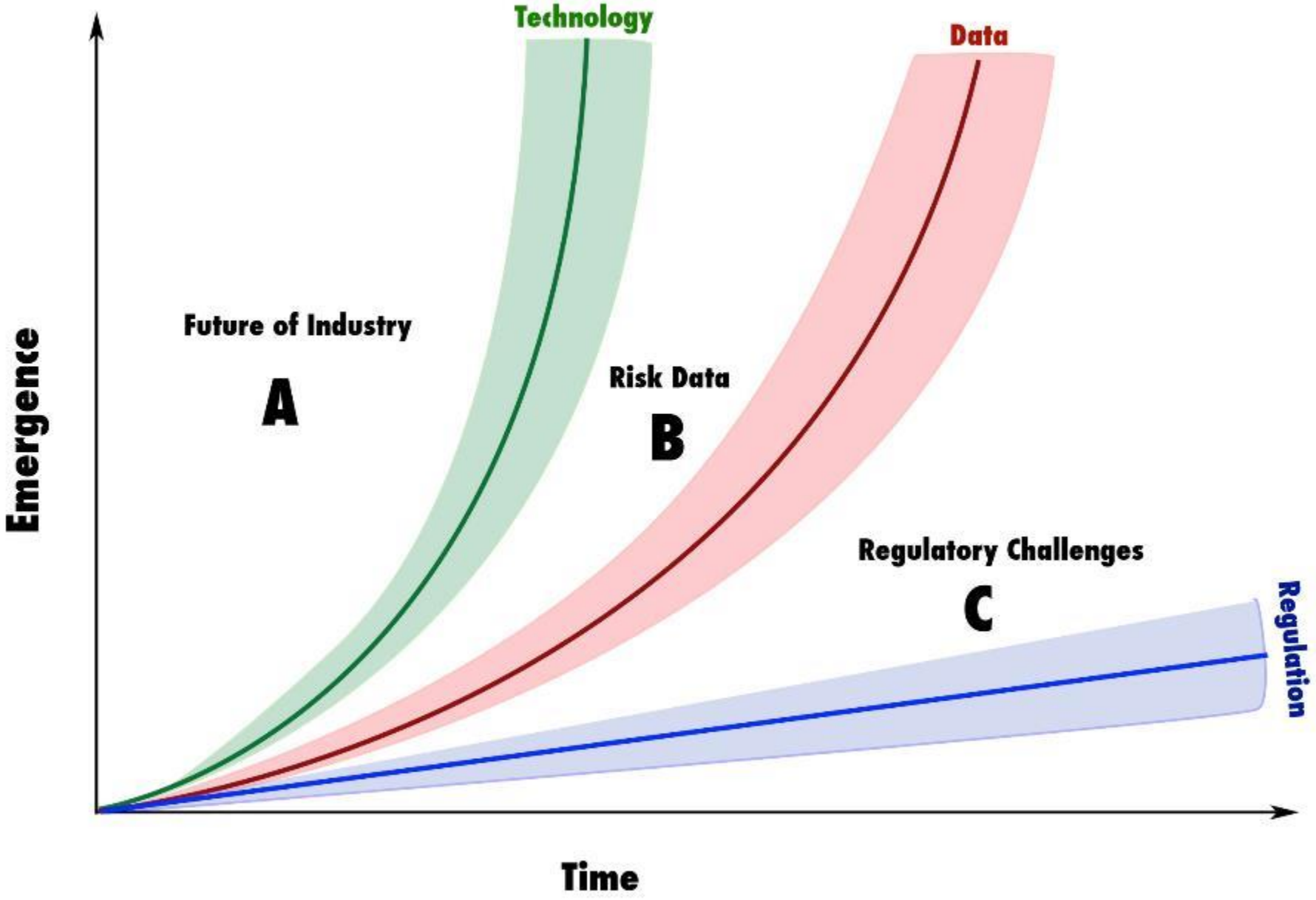

Technology
Emergence
Time


Technology
Data
Emergence
Time

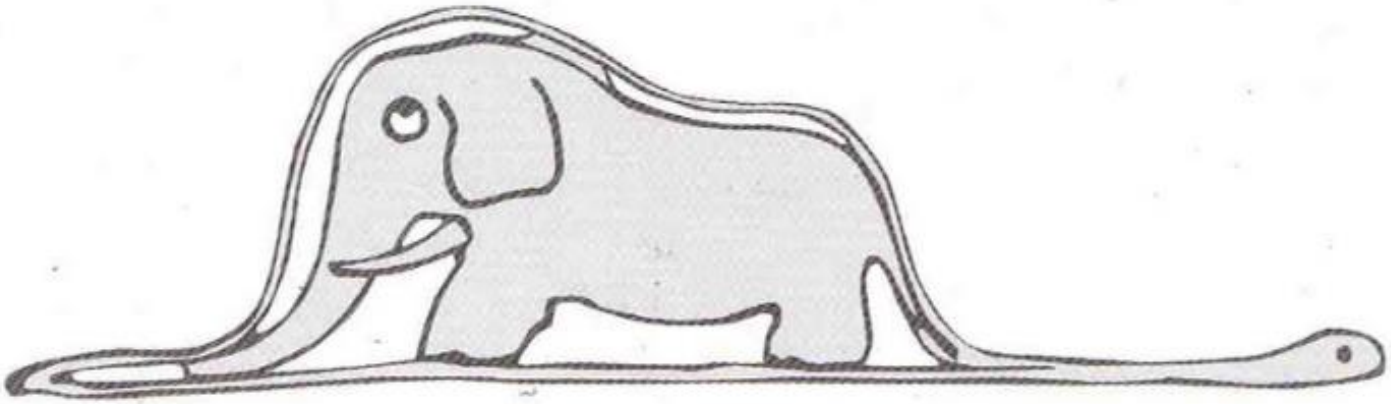


Kuzma, J. (2013). Properly paced? Examining the past and present governance of GMOs in the United States. Innovative governance models for emerging technologies, Edward Elgar, Cheltenham, UK, 176-197.

Linkov, I., Satterstrom, F. K., Monica Jr, J. C., & Foss, S. (2009). Nano risk governance: current developments and future perspectives. Nanotech. L. & Bus., 6, 203.

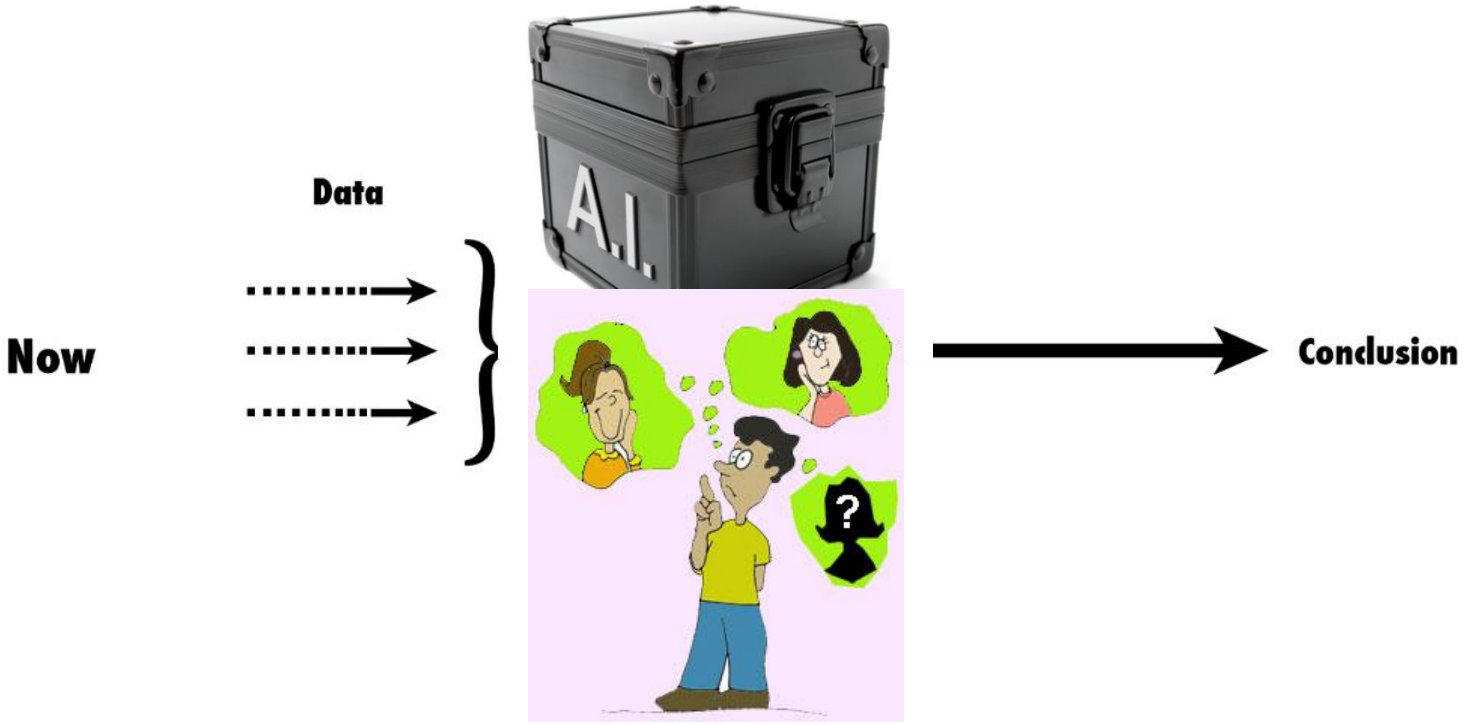

Technology
Data
Future of Industry
A
Risk Data
B
Regulatory Challenges
C
Regulation
Emergence
Time

EFSA - What Do You See?



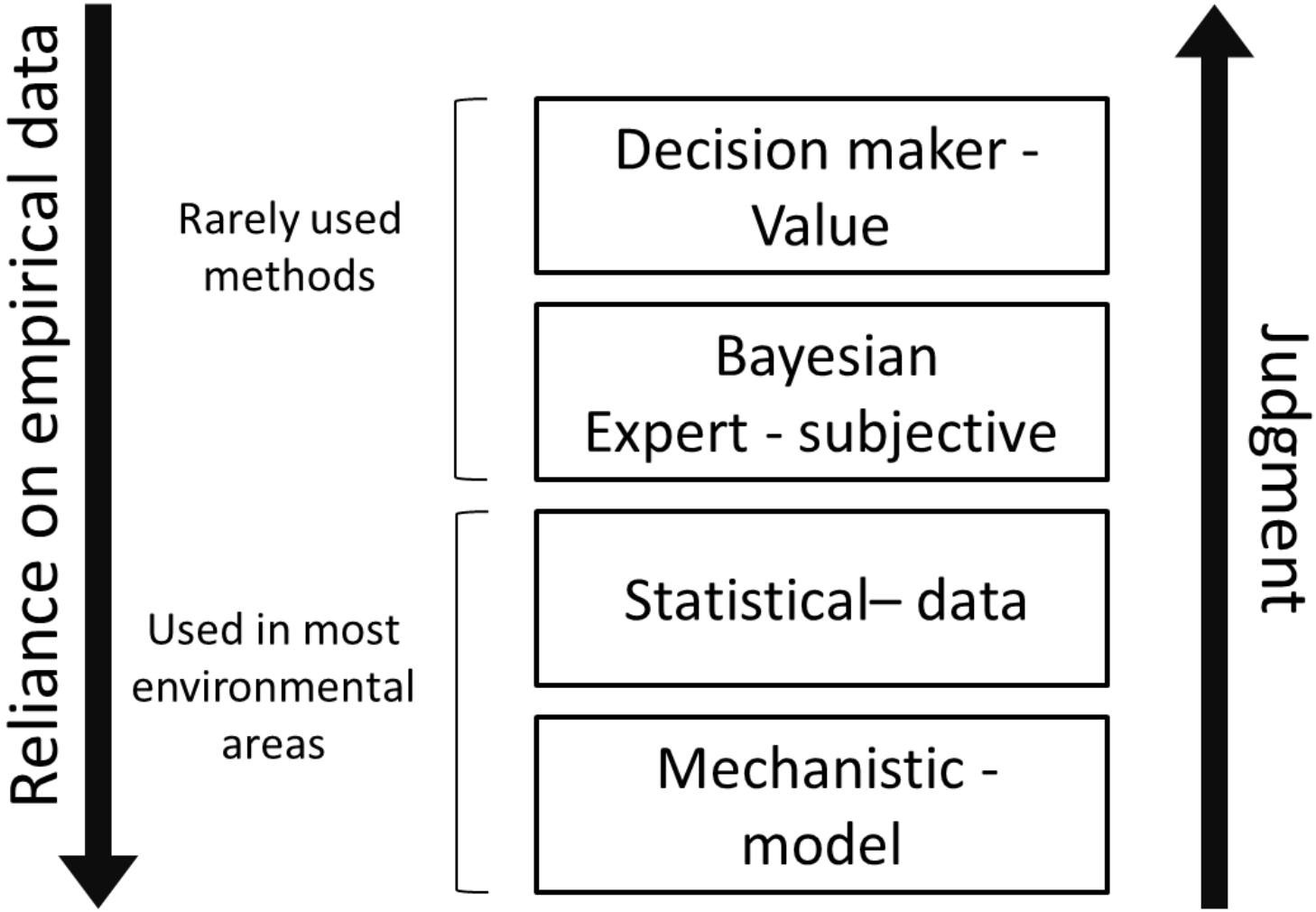
J'ai alors dessiné
l'intérieur du serpent boa, afin que les grandes personnes
puissent comprendre. Elles ont toujours besoin d'explications

Hypothesis free?



Ways to Integrate Evidence

Ways to Model



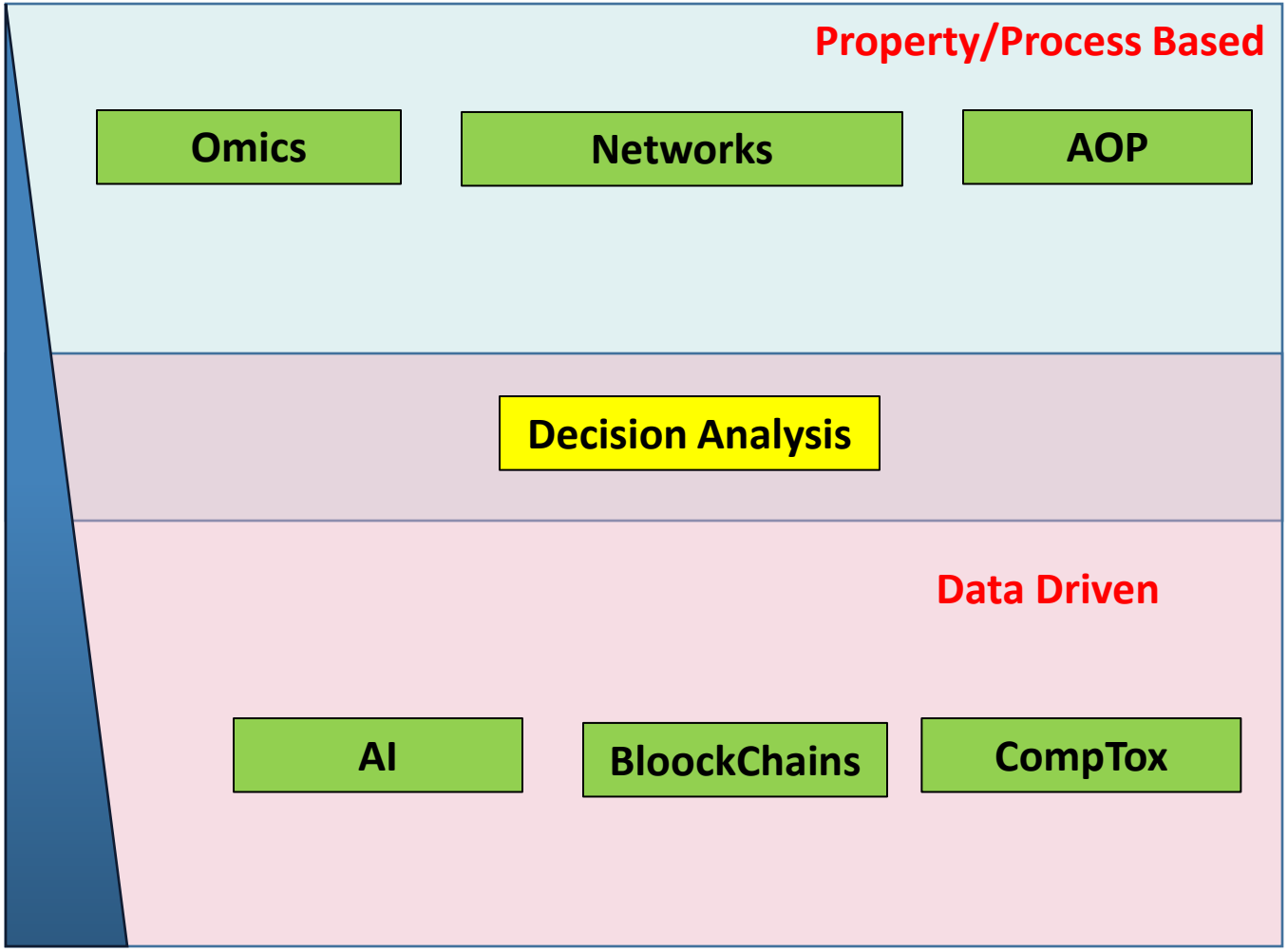
From Keisler and Linkov, 2014

Approaches to Data Integration in Food Safety

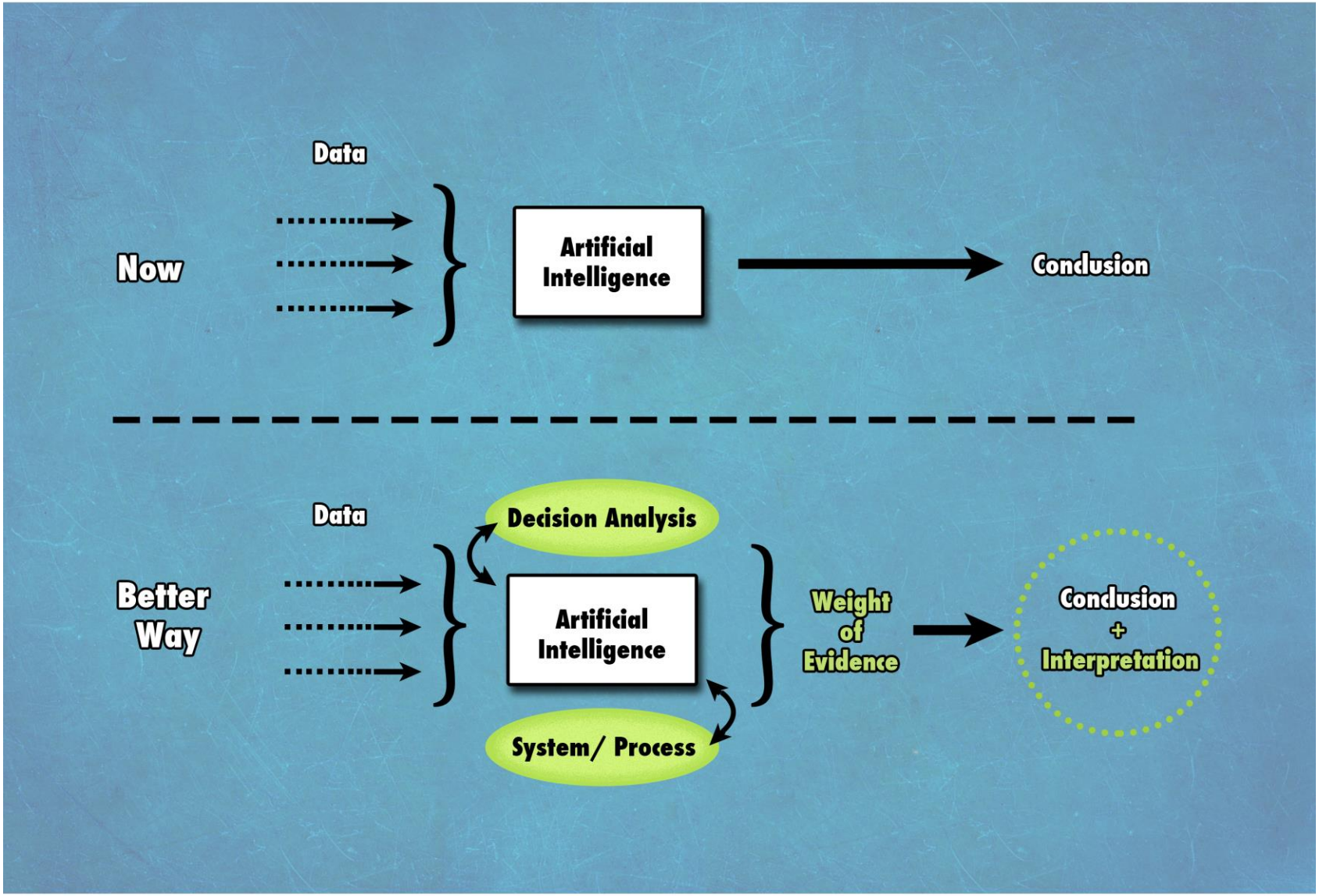
Simplified process models, Less Data Intensive

Expert- or data-driven weights

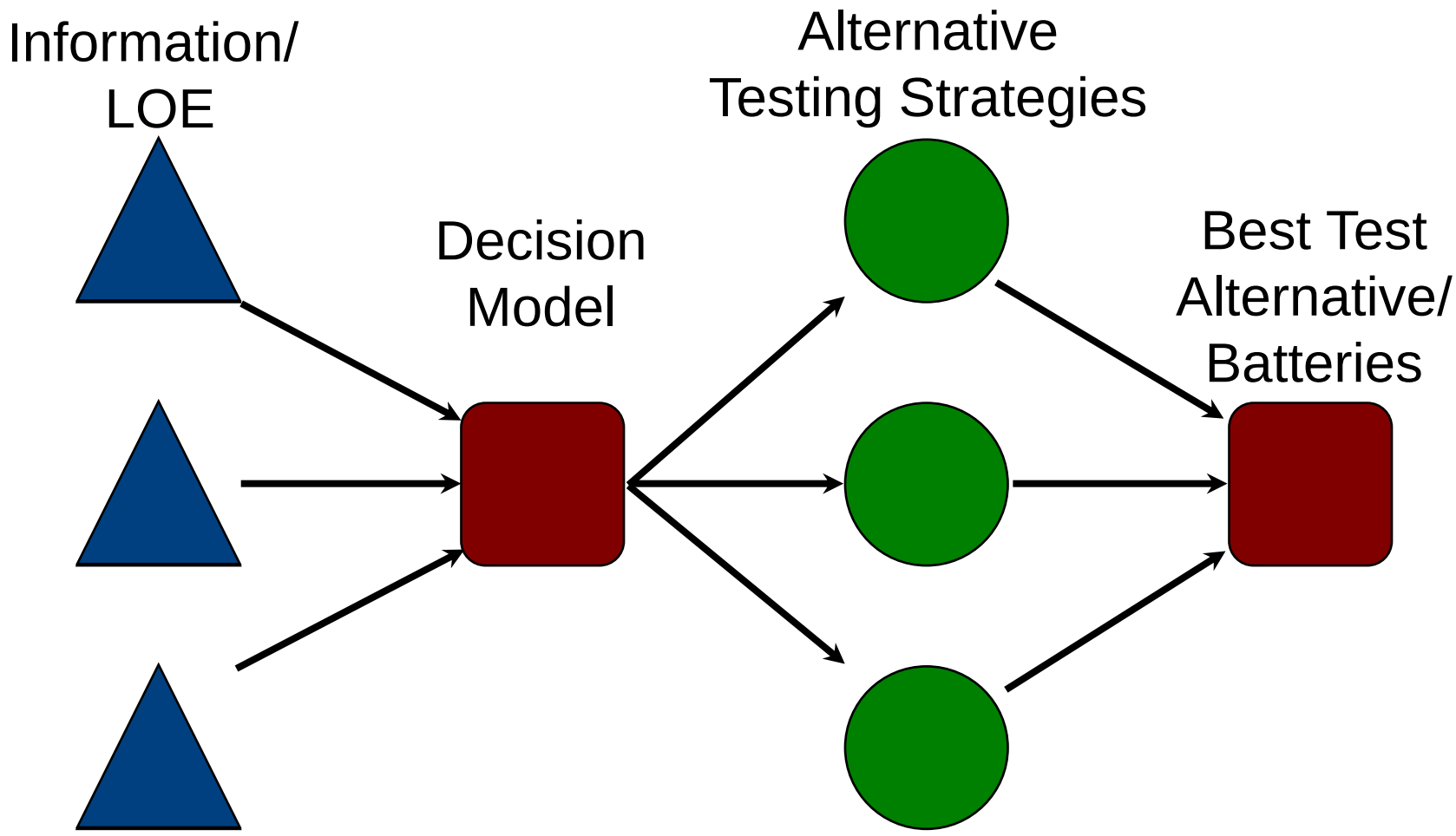
Complex Data Intensive



Proposed Approach



Case 1: Alternative Testing Strategy

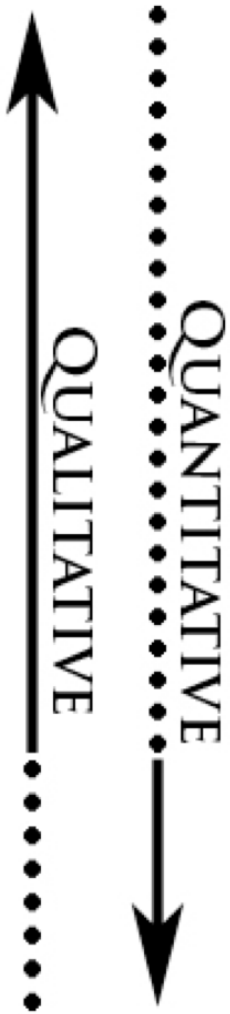


What are the purposes for WOE in ATS context?

- Determine if there is enough evidence to support a determination or action (threshold)
- Compare alternative to see what is better supported (carcinogen MOA)
- Identify gaps in understanding
- Highlight scientific consensus to bolster use of an approach/tool

Selected WOE methodology needs to reflect the reason for the analysis.

WOE: From Qualitative to Quantitative



Past

Present

Future

After Linkov et al., 2009

Implementation in Current Guidelines

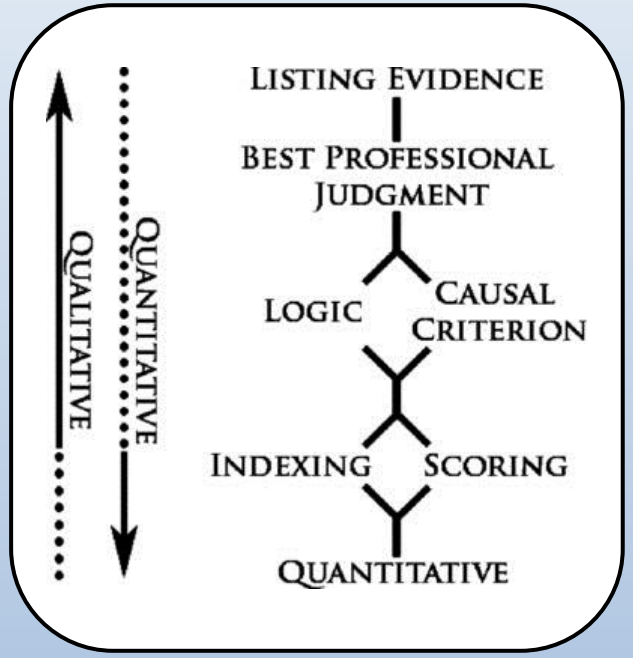
Papers

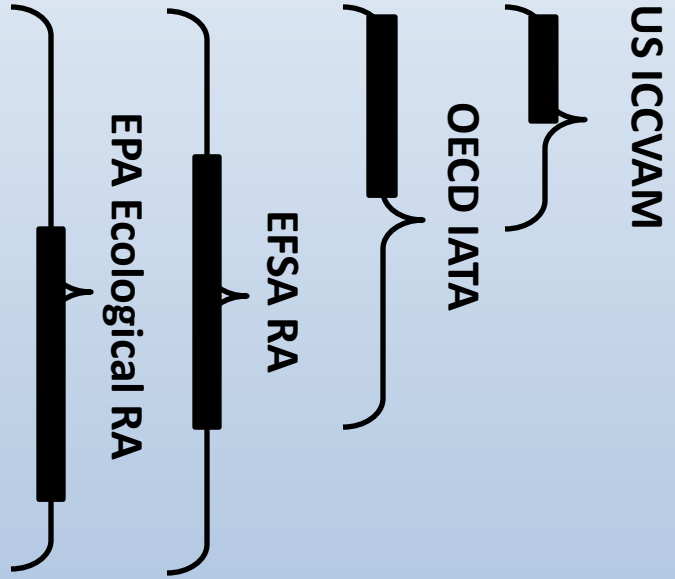
Approaches

Wu et al. →

Becker et al. →

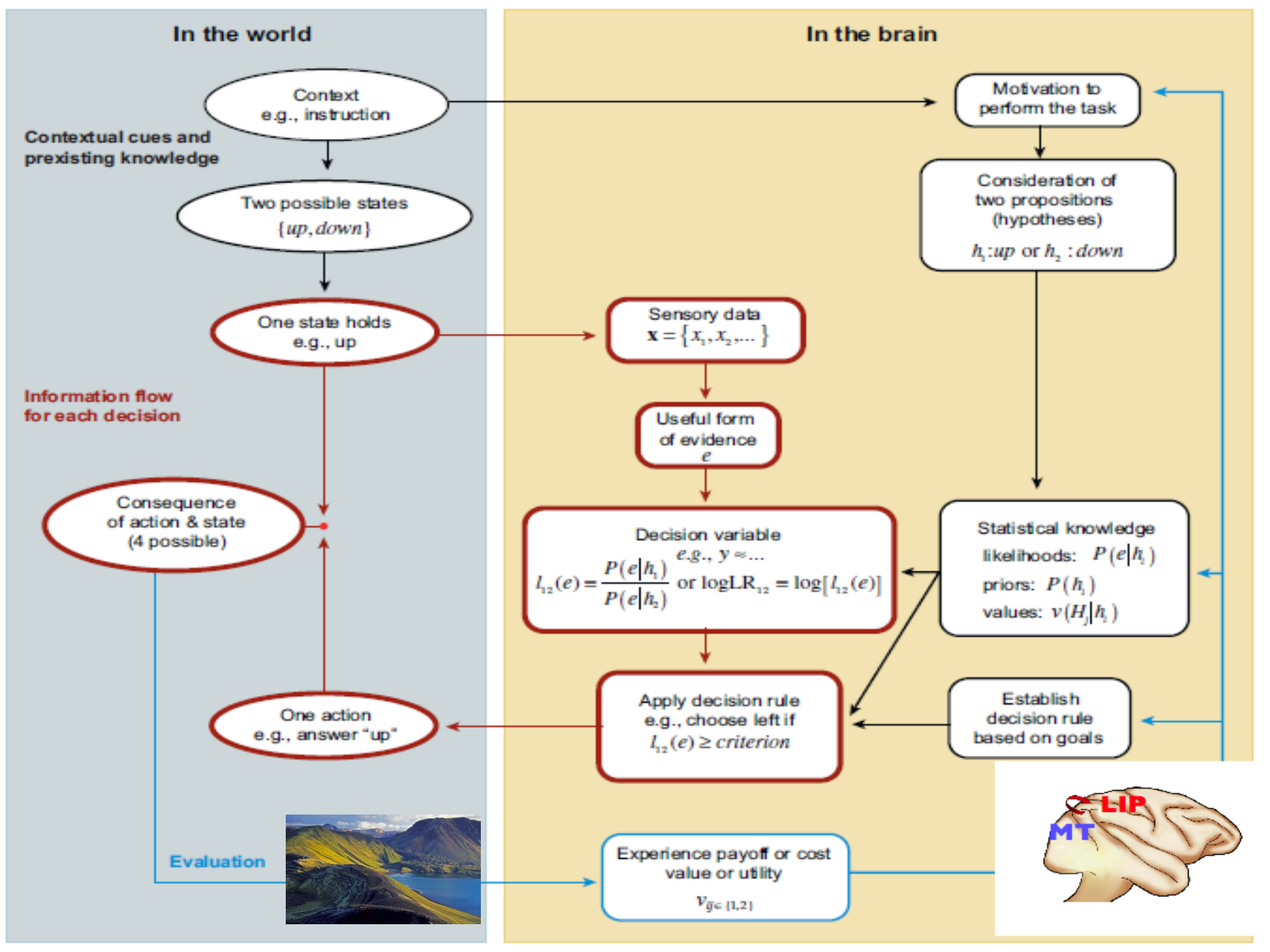
Jaworska →

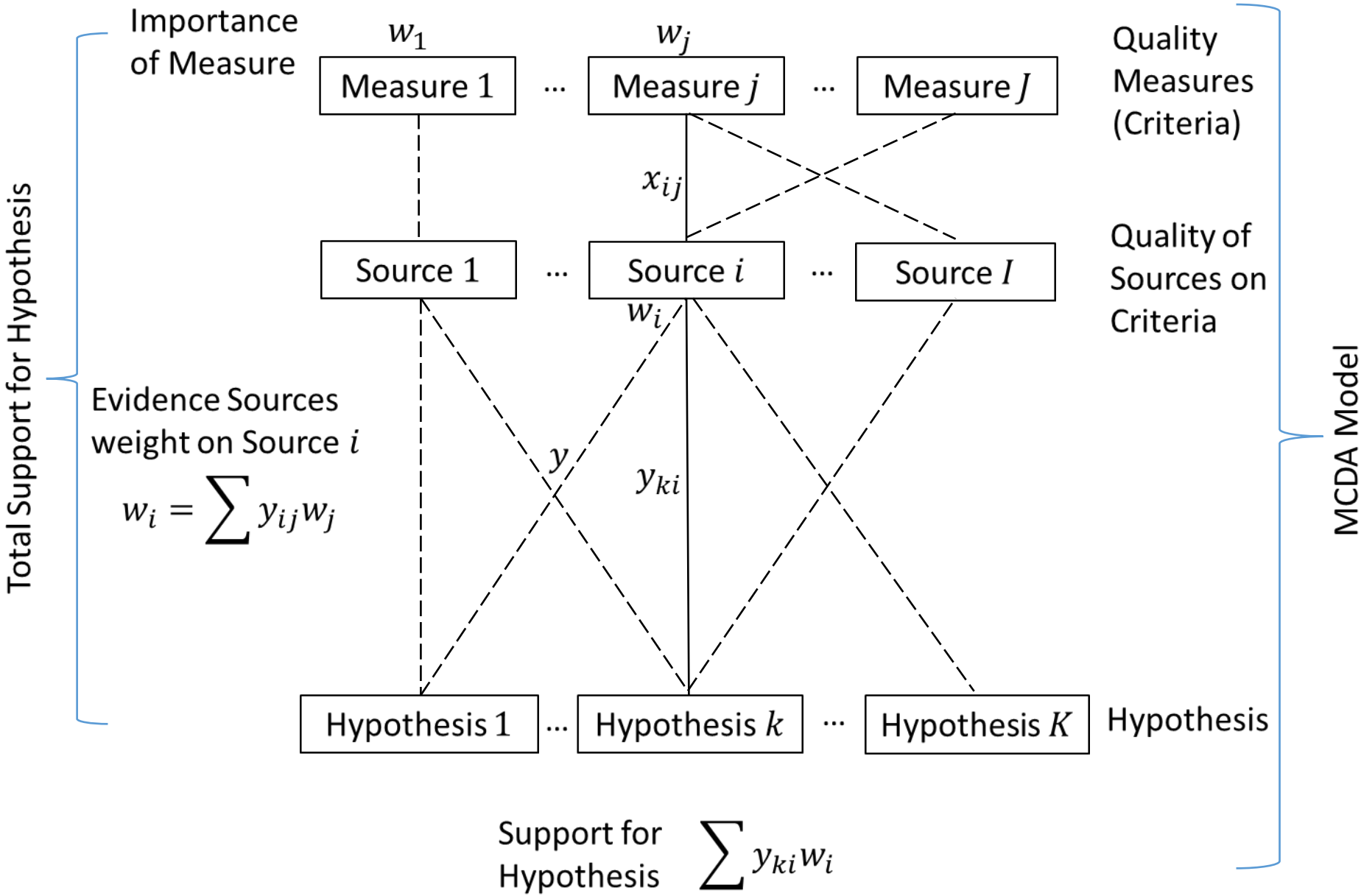




Multi-Criteria Decision Analysis

- Multi-Criteria Decision Analysis (MCDA) methods:
  - Evolved as a response to the observed inability of people to effectively analyze multiple streams of dissimilar information
  - Many different MCDA approaches based on different theoretical foundations (or combinations)
- MCDA methods provide a means of integrating various inputs with stakeholder/technical expert values
- MCDA methods provide a means of communicating model/monitoring outputs for regulation, planning and stakeholder understanding
- Risk-based MCDA offers an approach for organizing and integrating varied types of information to perform rankings and to better inform decisions


In the world
In the brain
Context
e.g., instruction
Contextual cues and prexisting knowledge
Two possible states
{up, down}
One state holds
e.g., up
Information flow for each decision
Consequence of action & state (4 possible)
One action
e.g., answer "up"
Evaluation
Motivation to perform the task
Consideration of two propositions (hypotheses)
h1: up or h2 : down
Sensory data
x = {x1, x2, ... }
Useful form of evidence
e
Decision variable
e.g., y ≈ ...
l12(e) = P(e|h1) / P(e|h2) or logLR12 = log[l12(e)]
Statistical knowledge
likelihoods: P(e|hi)
priors: P(hi)
values: v(Hj|hi)
Apply decision rule
e.g., choose left if
l12(e) ≥ criterion
Establish decision rule based on goals
Experience payoff or cost value or utility
vj∈{1,2}
LIP
MT


Importance of Measure
w_1
w_j
Measure 1
Measure j
Measure J
Quality Measures (Criteria)
x_{ij}
Source 1
Source i
Source I
Quality of Sources on Criteria
w_i
Total Support for Hypothesis
Evidence Sources weight on Source i
$w_i = \sum y_{ij} w_j$
y
y_{ki}
MCDA Model
Hypothesis 1
Hypothesis k
Hypothesis K
Hypothesis
Support for Hypothesis
$\sum y_{ki} w_i$

Considerations when Evaluating Alternative Testing Methods:

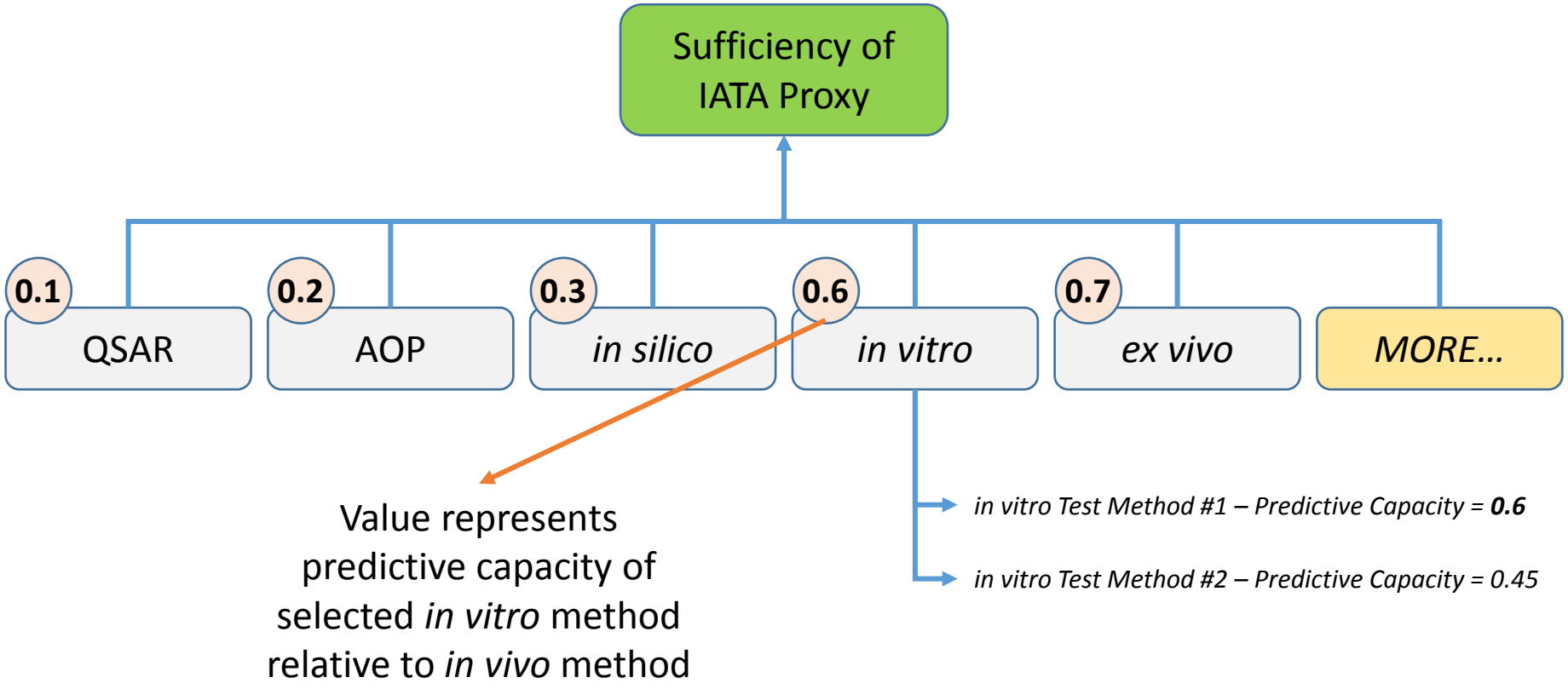
- Does the method follow an existing OECD Test Guideline?
- Does the method adhere to Good Laboratory Practice (GLP)?
- Does the method adhere to OECD guidance specific to that test method?
  - ex. guidance for describing Non-Guideline Test Methods (e.g. TG#211 for *in vitro*); for AOPs (e.g. TG#184); for QSARs; for grouping and read-across strategies
- Is the method or specific tool OECD-sponsored (e.g. AOP KB)?
- Does the method meet the MAD criteria for IATA (to be defined…)?

Output could be list of "OECD Mutually Accepted" IATA methods and tools

* Each Alternative Testing Method will map to its own unique subset of the broader Acceptability Criteria

	Relevance	Reliability	Reproducibility	Quality Assurance	Standardization	Predictive Capacity	Maturity?	Validation Against a Reference?	MORE…
Alternative Method #1* (e.g. OECD QSAR Toolbox)	✓	✓	✓	✓	✓	✓	✓	✓	
Alternative Method #2									

What Batteries of IATA Methods Serve as Sufficient Proxies for *in vivo* toxicological endpoints?



Case 2: Nano Prioritization Tool

- Numerous stakeholders across the globe are concerned with safety of nano-enabled consumer products (a **30-fold increase** from 2005 to 2015)
- Even the largest stakeholders do not have the resources to perform a formal risk assessment for every nano-enabled consumer product

Cosmetic products

(improved cleansing and absorption)

Food packaging

(reduce moisture & bacteria)

Children's toys and blankets

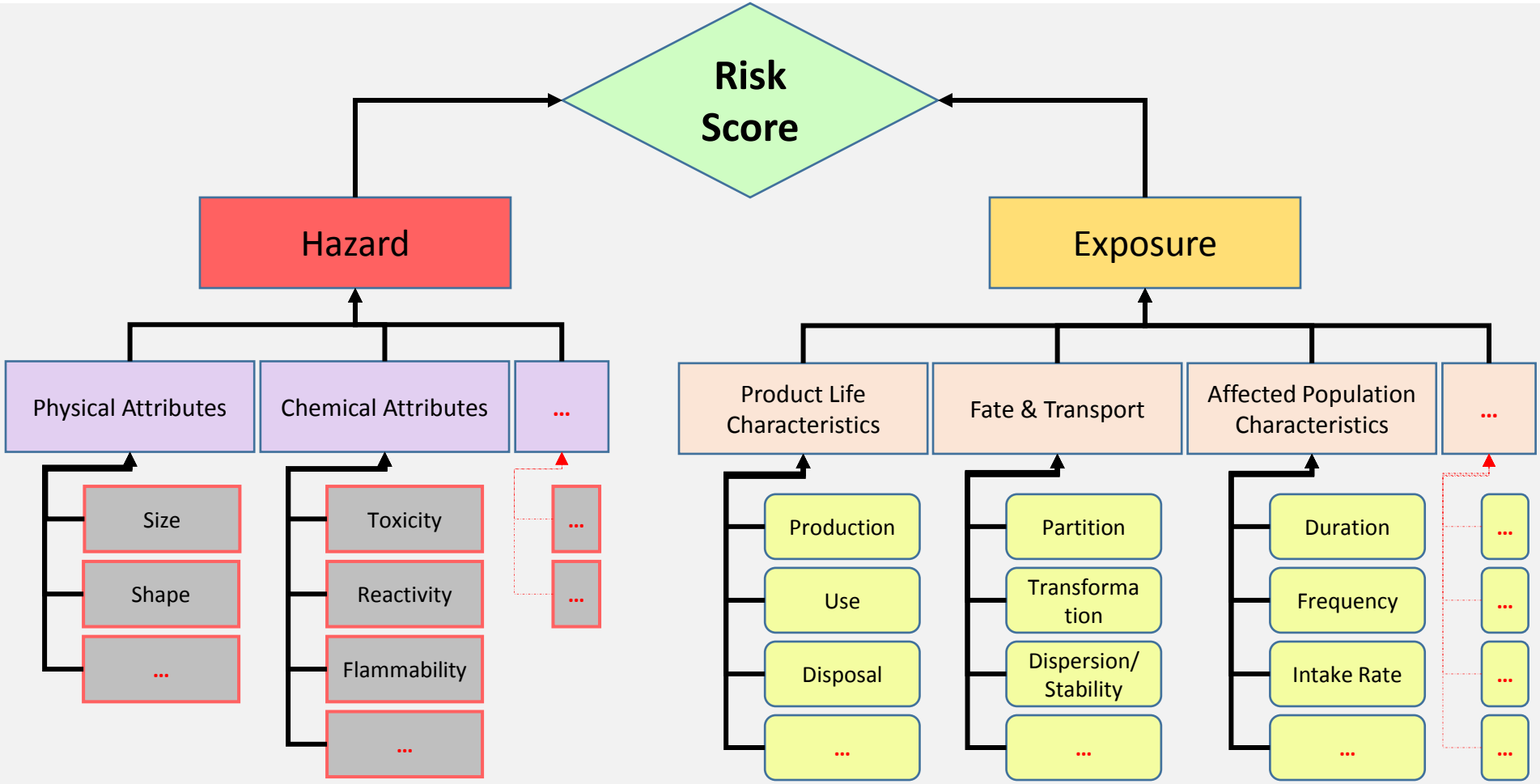
(antimicrobial protection)

Polymer composite materials

(lighter and more durable)

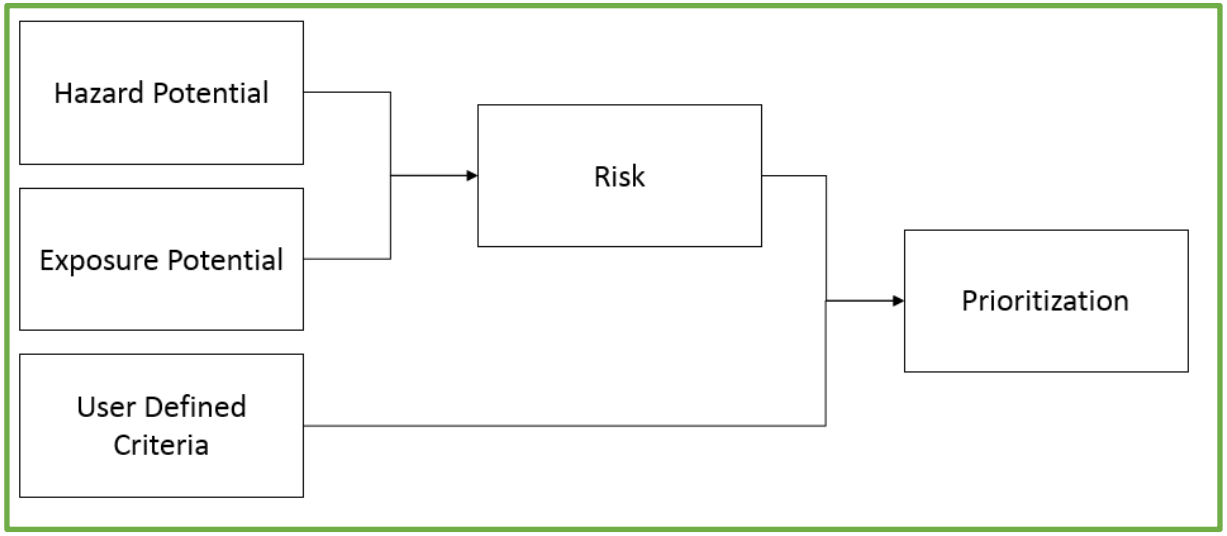
- Stakeholders need the ability to screen and prioritize a diverse array of nano-enabled consumer products in order to prioritize research into risks, triage reported safety concerns, and **allocate limited resources more efficiently**

Best of Risk Assessment: Integrating Metrics through Decision Analysis



How the NPF Works

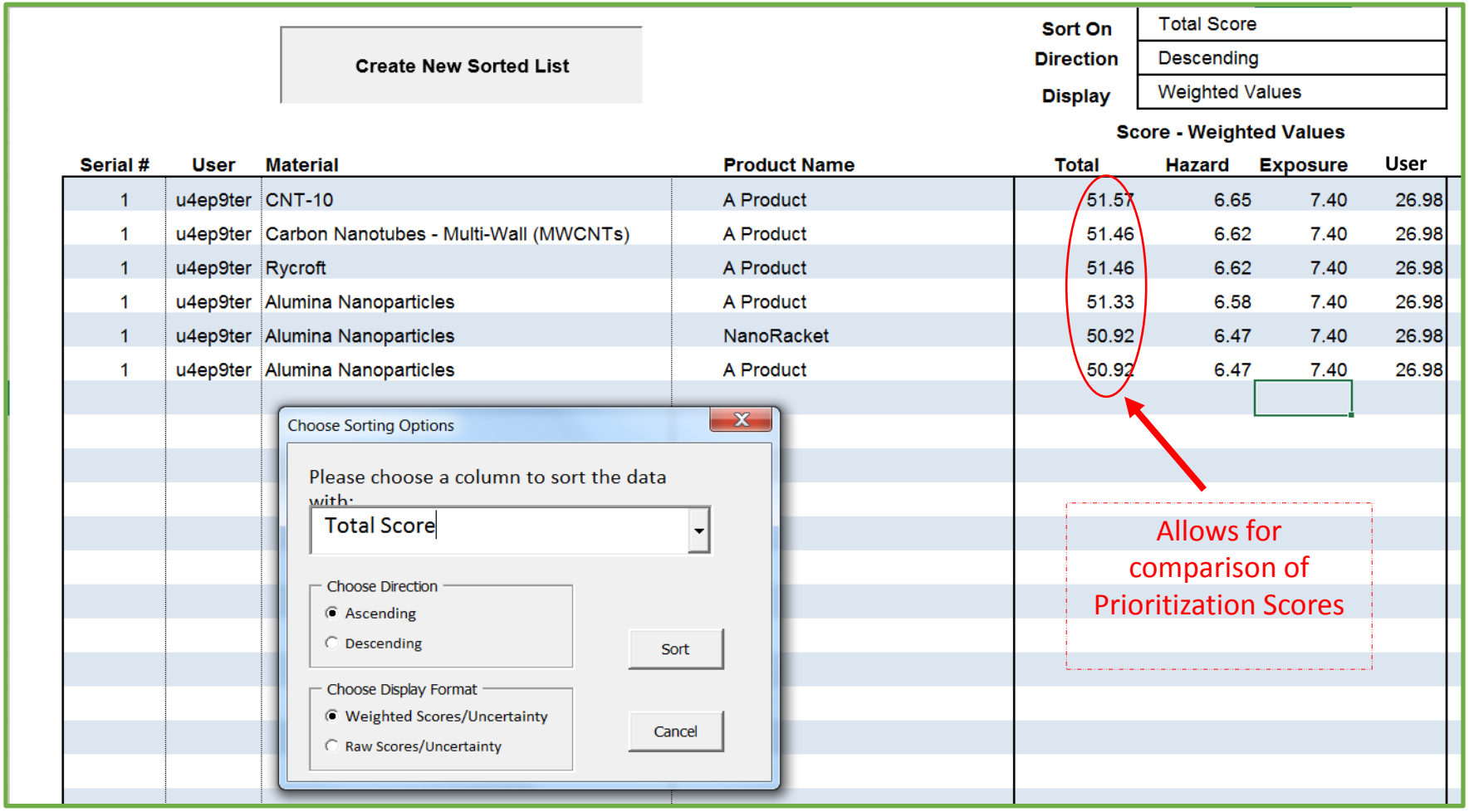
- Three modules:
  - Hazard
  - Exposure
  - User Defined Criteria
- User answers questions within each module



- Answers are scored and integrated into an overall **prioritization score** using **Multi-Criteria Decision Analysis (MCDA)** methods
  - The prioritization score is *relative* – must be compared to other scores in the product catalog

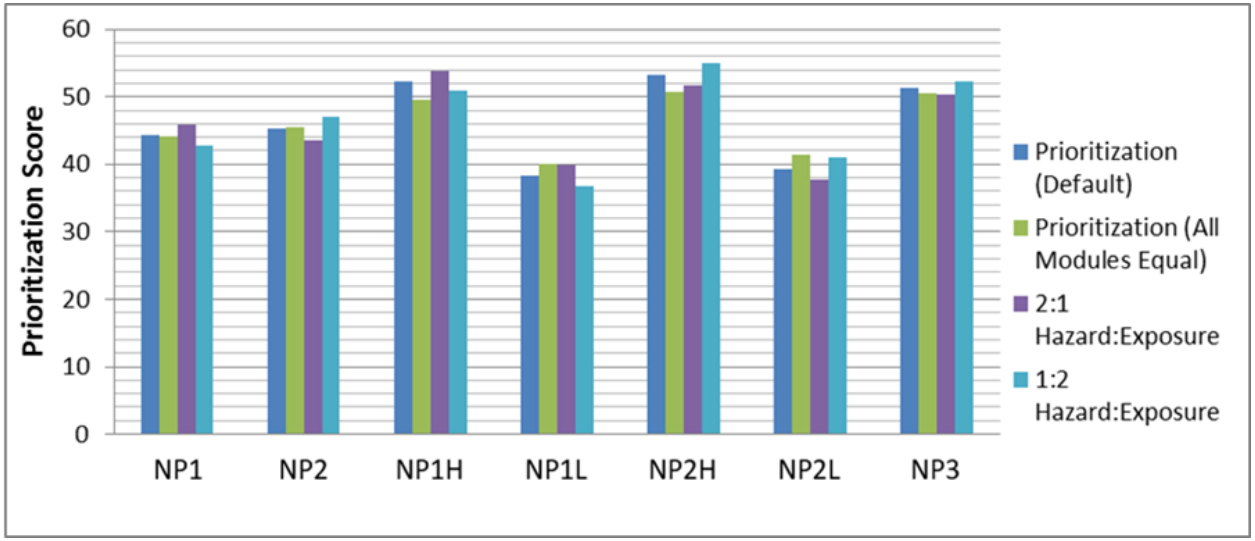
Pilot Tool Product Catalog

- The Product Catalog allows the user to analyze outputs from the Pilot Tool for all products that have been evaluated:



Calibration / Hypothetical Case Study

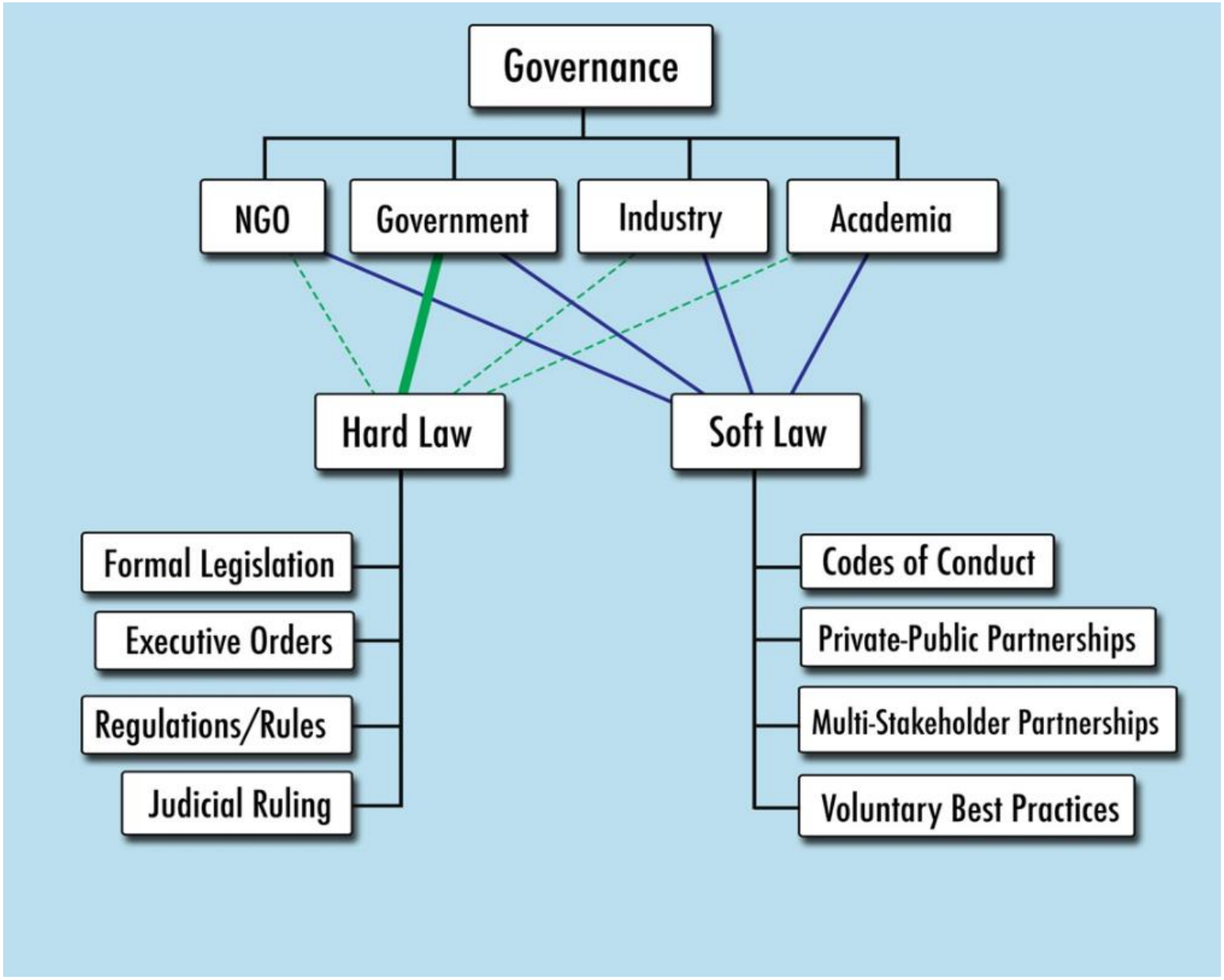
- Seven hypothetical nano-enabled products
- Sensitivity analysis used to recommend default weight schemes



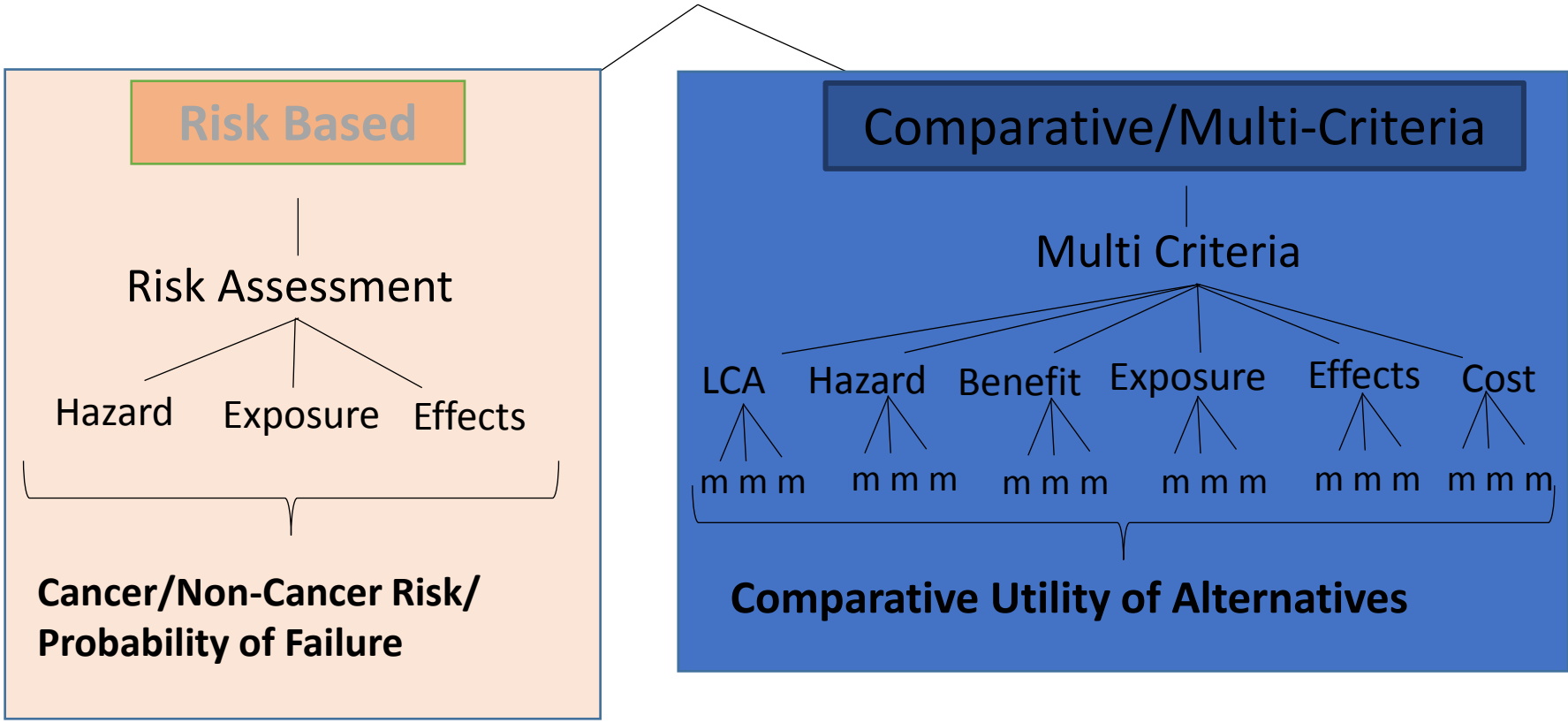
NP1	High hazard score, low exposure score
NP2	Low hazard score, high exposure score
NP1H	NP1 with high User Defined Criteria score
NP1L	NP1 with low User Defined Criteria score
NP2H	NP2 with high User Defined Criteria score
NP2L	NP2 with low User Defined Criteria score
NP3	Mostly unknown inputs across modules

Data-Driven Risk Governance

- **Definition of risk governance** (IRGC)
  - *Governance* refers to the actions, processes, traditions and institutions by which authority is exercised and decisions are taken and implemented.
  - *Risk governance* (RG) applies the principles of good governance to the identification, assessment, management and communication of risks
  - Requires the coordination of multiple stakeholders – cannot simply be a top-down approach to governance
  - ***Traditional RA & RM are important subsections of RG***


Governance
NGO
Government
Industry
Academia
Hard Law
Soft Law
Formal Legislation
Executive Orders
Regulations/Rules
Judicial Ruling
Codes of Conduct
Private-Public Partnerships
Multi-Stakeholder Partnerships
Voluntary Best Practices

Comparative Risk Governance in Practice



ENVIRONMENTAL Science & Technology

Viewpoint

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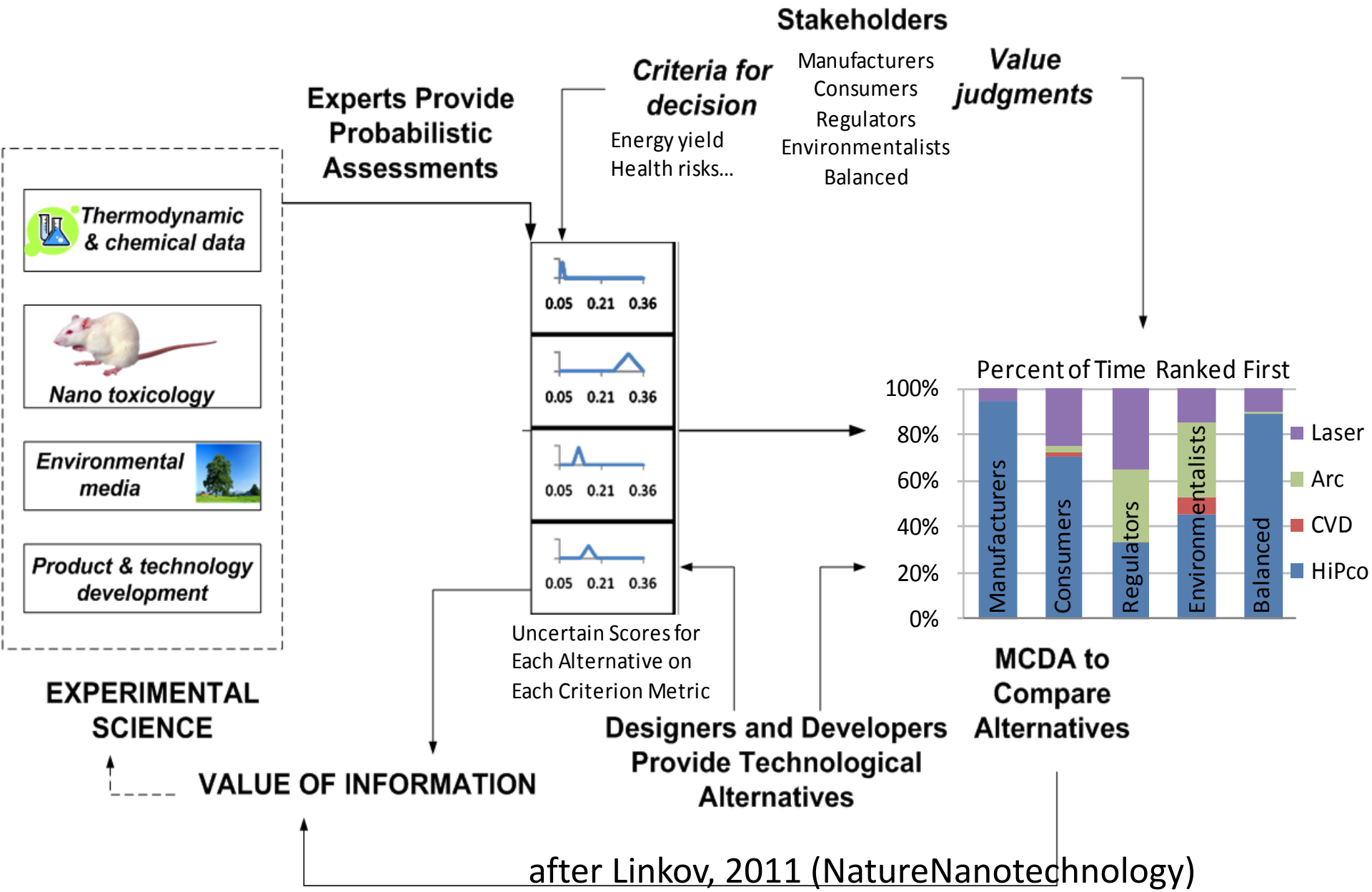
Risk-Based and Prevention-Based Governance for Emerging Materials

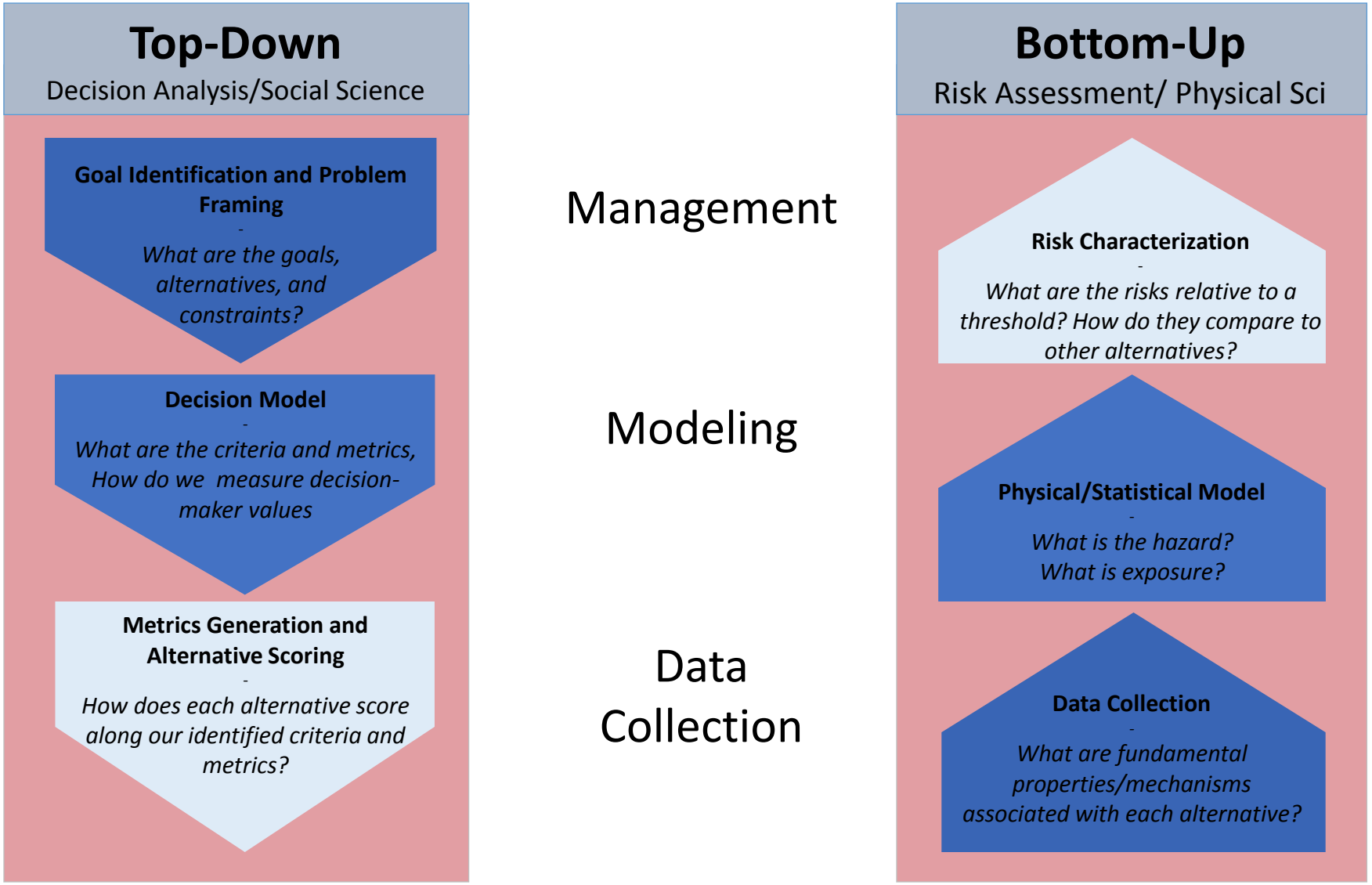
Timothy Malloy,[†] Benjamin D. Trump,[‡,§] and Igor Linkov*[,§]

Approach: Physical and Social Science Integration



after Linkov, 2011 (NatureNanotechnology)

Data-Driven Risk-Governance Integration



Linkov et al., 2014

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Security and Resilience for Emerging Synthetic Biology and Biotechnology Threats

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