US-EU CoR Meeting, Arlington, USA, December 2013

The Use of Systems Biology by the US-EU CoRs

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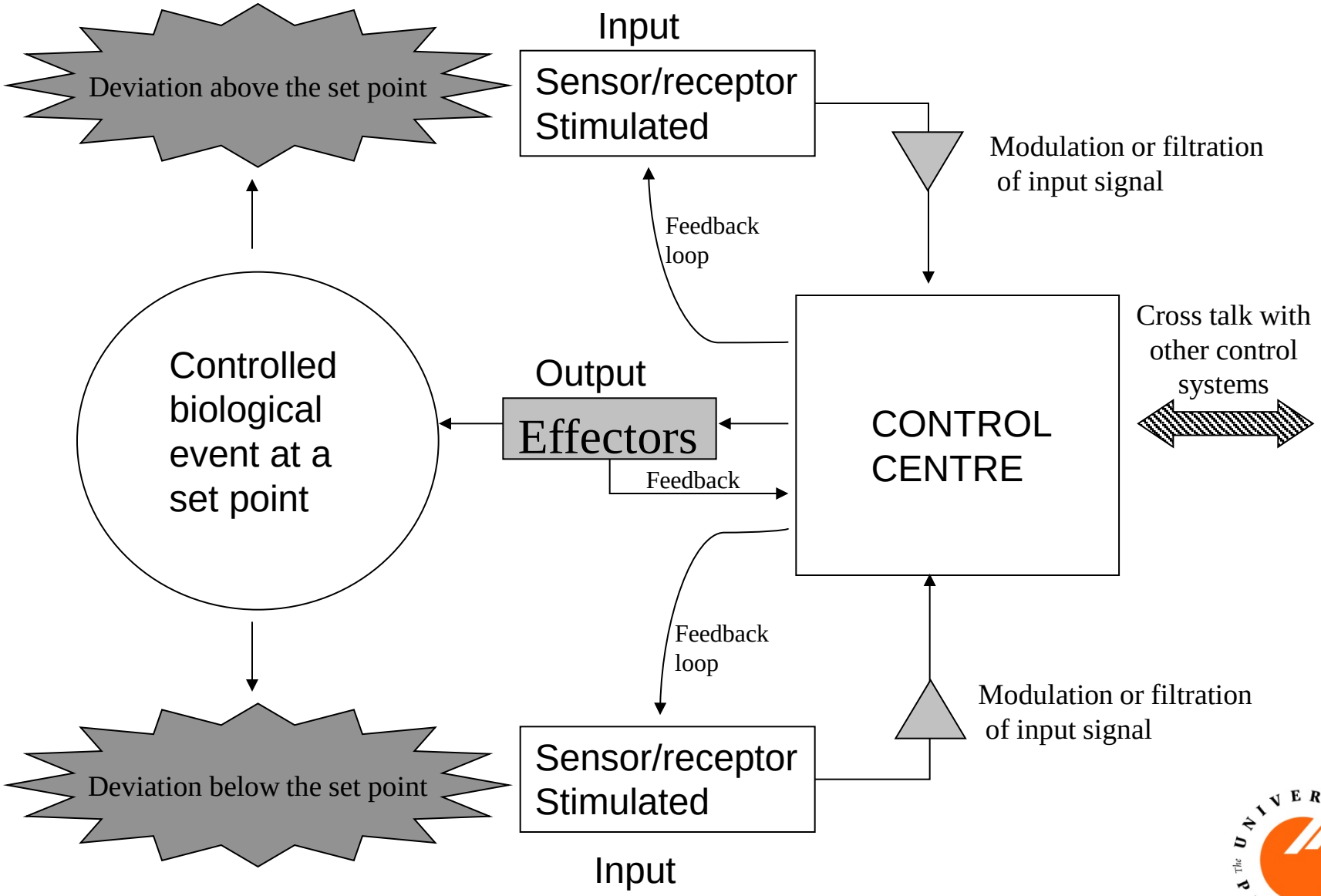
Background

- Systems Biology is a “hot topic” in Europe.
- A number of research projects have incorporated omics and/or systems biology approaches.
- Computational power for prospective hazard assessment.
- Potential for computational methods to merge chemical, physical and biological data sets.

What is Systems Toxicology?

Example Biological Control System

Handy 2008 In: Comparative Toxicogenomics, Hogstrand & Kille (eds)



Systems Toxicology

- ***Systems biology*** aims to quantitatively understand biological control at the cellular level.
- If we can understand how a cell works then we can model the functions of the cell.
- Create an experimental and/or theoretical tool (model) to predict the responses of the cell to stimuli.
- "***Systems Toxicology***" takes these ideas from cell biology and computer science, then applies them to chemicals.
- We expand the concept to higher levels of biological organisation; organ and body system that are relevant to toxicity.
- Or even organisms or ecosystems.

“Bottom Up” Models

- Basic components of the toxicological process and exposure to construct a model of the cell, organ, or organism response.
- Modular approach.
- Input data: genomics data, biochemistry, physiological measurements, abiotic factors such as pH, temperature, hardness, salinity, pollutant concentration etc.
- Output: model predictions of response.

Inputs of data from experiments or data bases

Computational Modelling

Predicted Outputs

Genomics, proteomics, or metabolomics data from organism exposed to pollutants.

Data on the effects of pollutants on components of the organism e.g. measured biochemical and physiological variables.

Kinetics data on absorption, distribution, metabolism & excretion.

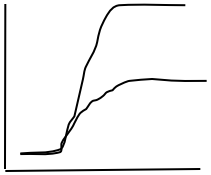
Data on exposure concentration. e.g. variable exposure concentrations or continuous concentrations

Data on exposure time e.g. intermittent exposure, chronic, acute, multiple exposure.

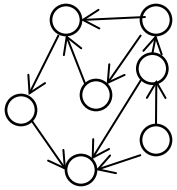
Data on ecosystem variables e.g. environmental geochemistry, hydrology, number and types of species, habitat data.

Modules of input data

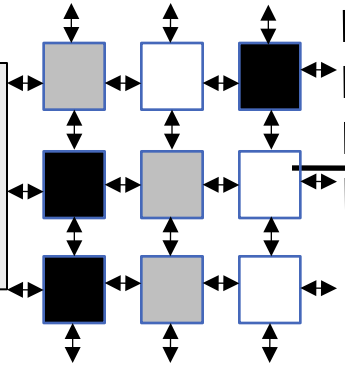
Similarity and differences modelled using differential equations and related methods



Creation of networks using Boolean logic, Petri nets



Cellular automata exploring nearest neighbour and matrix effects.

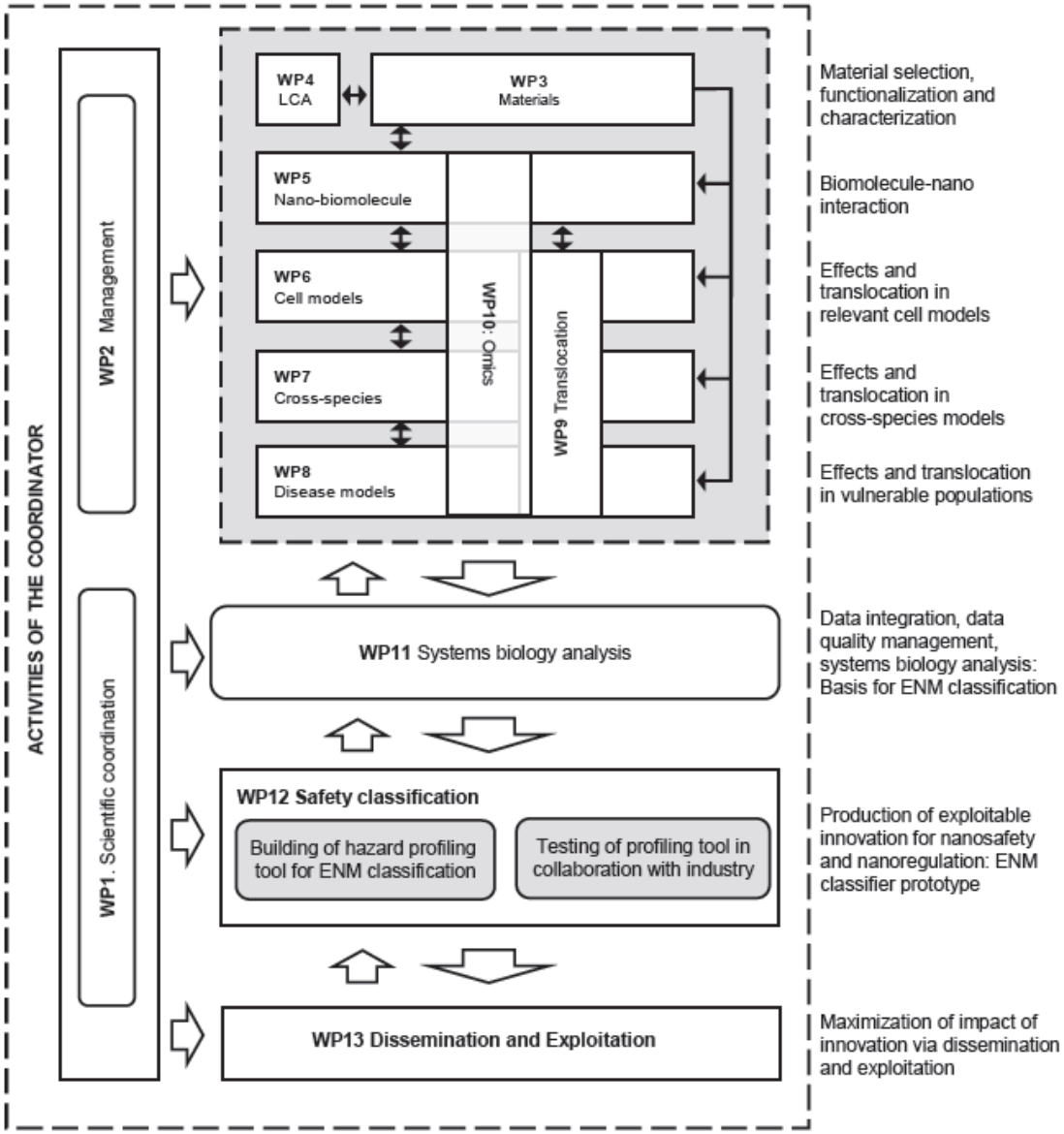


Complex functions of the cell, organ, organisms, or ecosystem response to pollutants

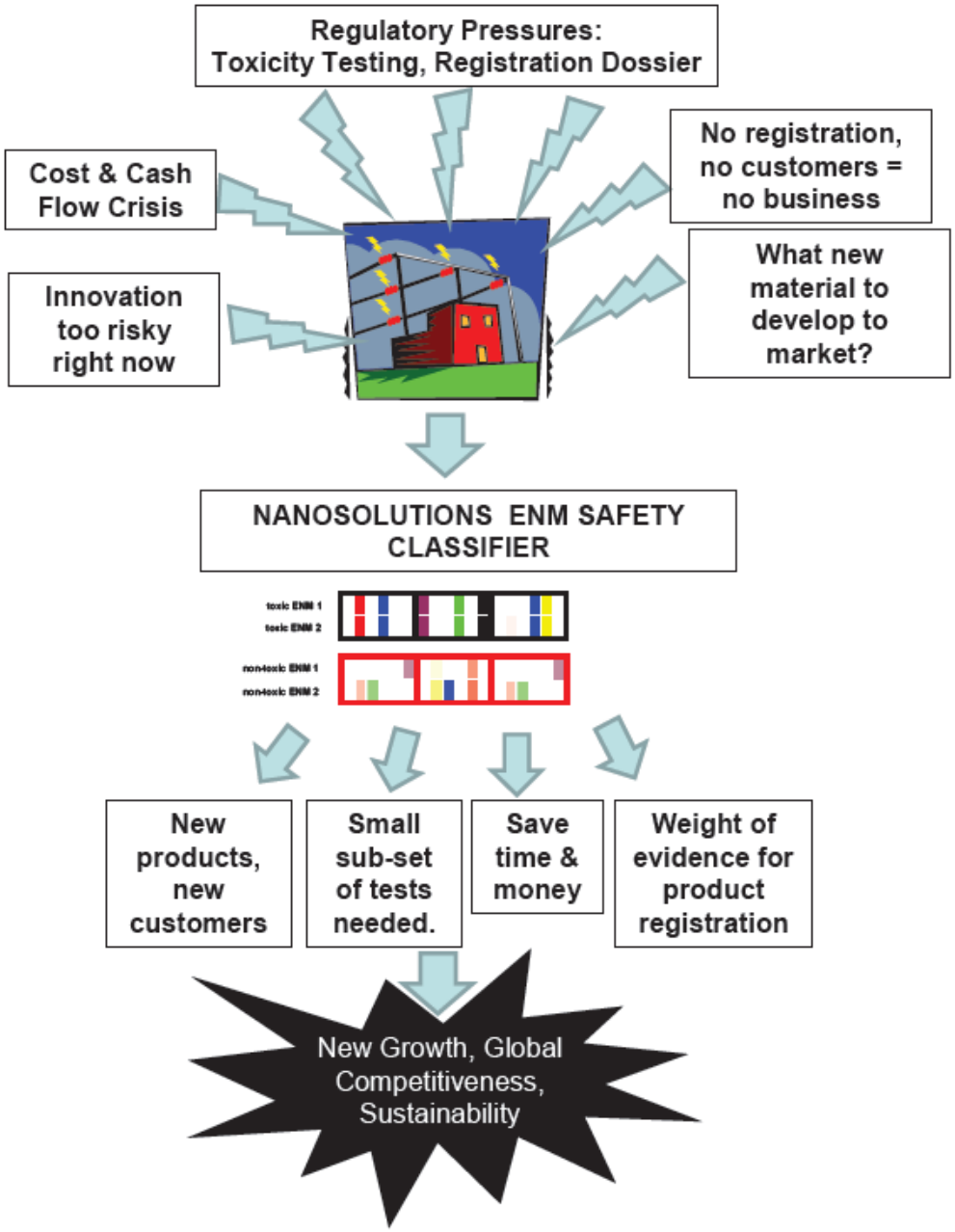
Handy 2008 In: Comparative Toxicogenomics, Hogstrand & Kille (eds)

UNIVERSITY of The PLYMOUTH

Work Flow NANOSOLUTIONS project



SME Case Study Nanosolutions



SEVENTH FRAMEWORK PROGRAMME

nano Solutions

The University of Plymouth

Questions for the CoR

- What systems biology data will be generated by US and EU projects with the CoRs?
- Added value – data that could be made available for computational systems mathematics?
  - Merge physico-chemical behaviour and biological effects data.
  - Model unintuitive or unexpected events.
- Regulatory perspective
  - Gene expression data is only just being accepted from a regulatory view point.
  - Some way off for regulatory acceptance of systems biology…but the road must start somewhere….