



Cumulative Risk Assessment Issues

Dr. Larry T. Cupitt

Associate Director for Health

National Exposure Research Laboratory

US EPA

MIT Summer Symposium August 4, 2004

Why Cumulative Risk?

- Issues with mixtures and multiple modes of action and health effects
- It's the way people are exposed; it's a scientific need; it's the law
 - NRC and others
 - Food Quality Protection Act (1996)
 - Aggregate and cumulative risk
 - Executive Order 12898

Although this work was reviewed by EPA and approved for publication, it may not necessarily reflect official Agency policy.

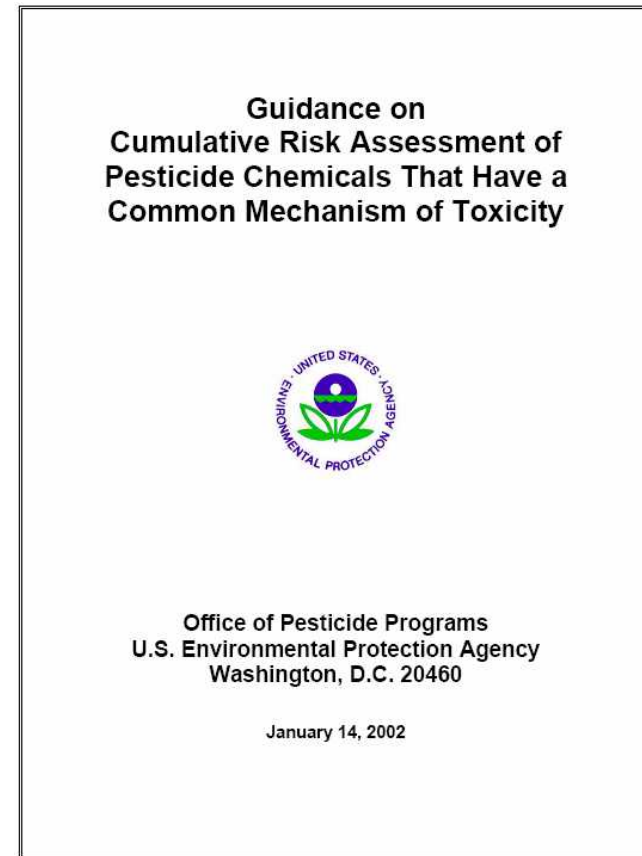


RESEARCH & DEVELOPMENT

Building a scientific foundation for sound environmental decisions

Cumulative Risk: FQPA Approach

- FQPA requires EPA to:
- Consider potential health risks for the individual
- From all pathways of dietary and nondietary exposures (aggregate)
- To more than one pesticide acting through a common mechanism of toxicity.



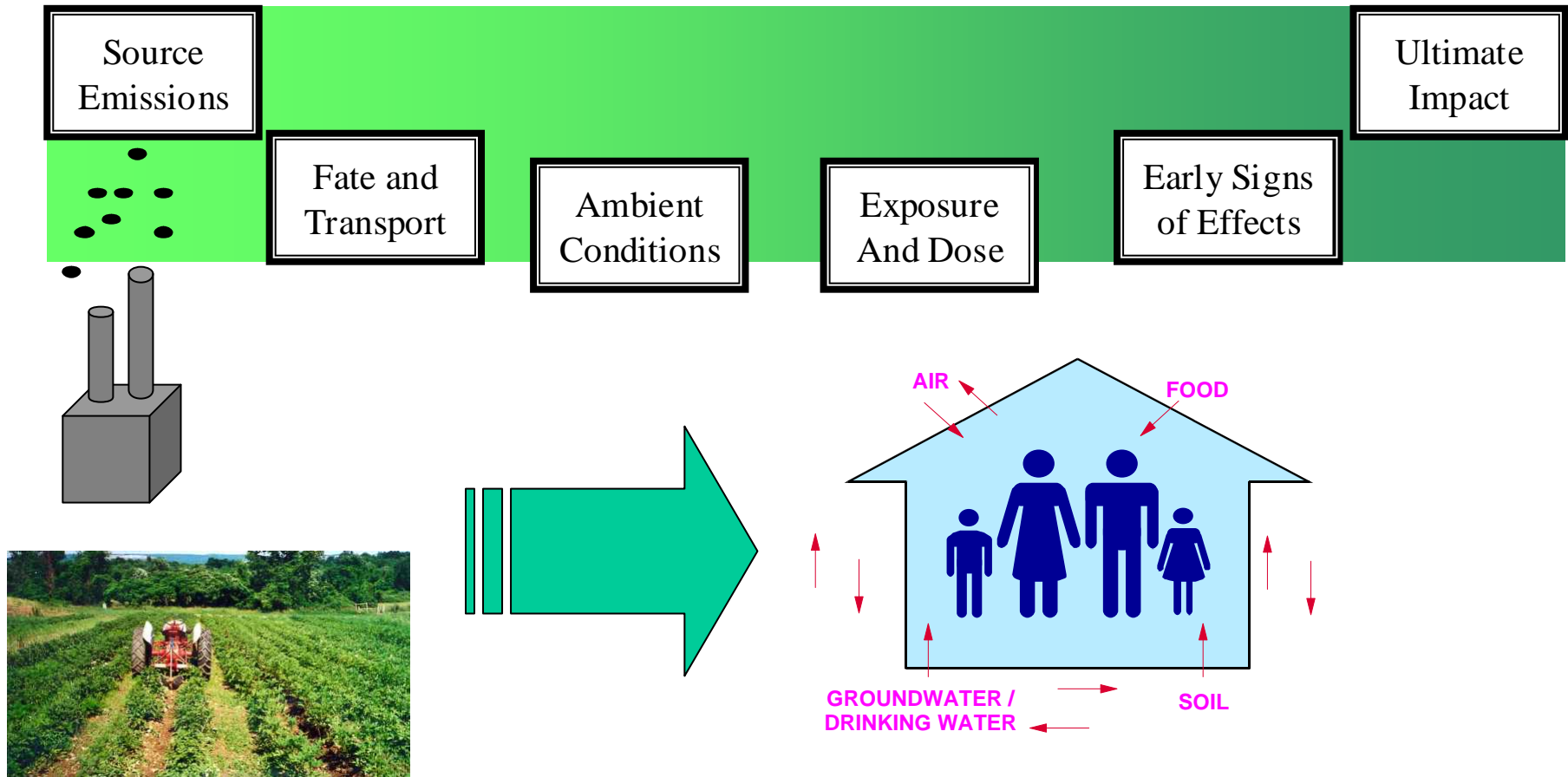
www.epa.gov/oppfead1/trac/science/cumulative_guidance.pdf



RESEARCH & DEVELOPMENT

Building a scientific foundation for sound environmental decisions


FQPA Shifts Focus from Pollutant Source to Population - Individual and All Pathways



RESEARCH & DEVELOPMENT

Building a scientific foundation for sound environmental decisions

Cumulative Risk: FQPA Application

Address  <http://www.epa.gov/oppsrrd1/cumulative/pr-a-op/>  Go Links 

 **U.S. Environmental Protection Agency**

Pesticides: Cumulative Risks

[Recent Additions](#) | [Contact Us](#) | [Print Version](#) Search: 

[EPA Home](#) > [Pesticides](#) > [Cumulative Risks](#) >

[Meetings](#) | [Schedule & Milestones](#) | [Getting Involved](#)

Organophosphate Pesticides: Preliminary OP Cumulative Risk Assessment Table of Contents

[Press Release](#) | [Summary](#) | [Overview](#) | [Questions & Answers](#)

December 3, 2001: EPA released today its preliminary assessment of the cumulative risks of organophosphorus pesticides. EPA considers the results to be preliminary and is seeking both scientific peer review and widespread public comment on its analysis and the many new scientific techniques used to develop the risk assessment. EPA will soon open a comment period in which the public and all interested parties are invited to submit comments on the preliminary assessments. Comments should directly relate to the issues and information in the assessment.

The Agency is examining the results of these analyses. Therefore, it is too soon to draw firm conclusions about risks or consider risk management possibilities. The Agency cautions against premature conclusions based on this preliminary assessment, and against any use of information contained in these documents out of their full context. The risk mitigation measures that have already been taken on individual members of this group of pesticides have led to significant reduction in potential risk. The Agency is reviewing the results of the assessment to determine if any issues may need to be addressed related to food commodities, drinking water and residential uses. However, EPA has confidence in the overall safety of our food supply and emphasized the importance of eating a varied diet rich in fruits and vegetables.

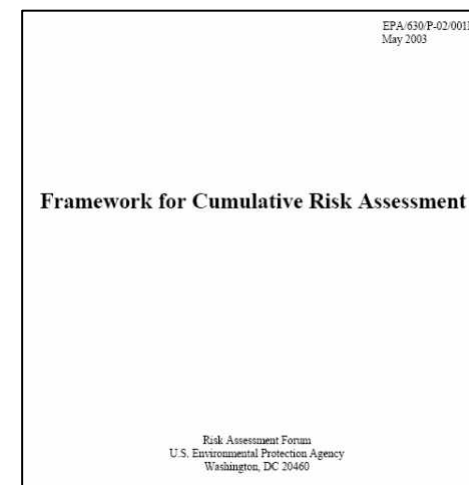


RESEARCH & DEVELOPMENT

Building a scientific foundation for sound environmental decisions

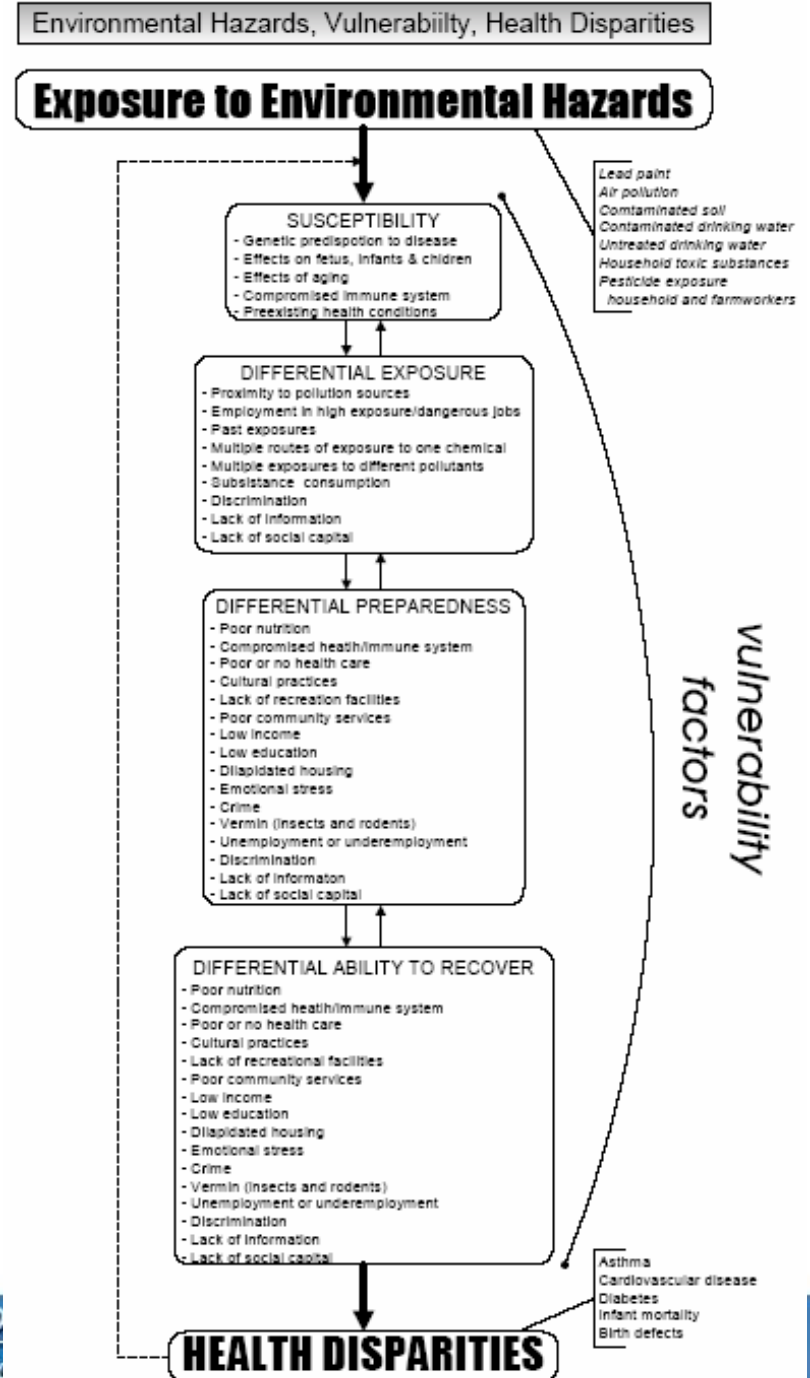
EPA's Risk Assessment Forum Framework for Cumulative Risk Assessment

- Approaches Cumulative Risk as “the combined risks from aggregate exposures to multiple agents or stressors”
 - Multiple agents or stressors
 - Not just chemicals
 - Combined risks
 - Over time

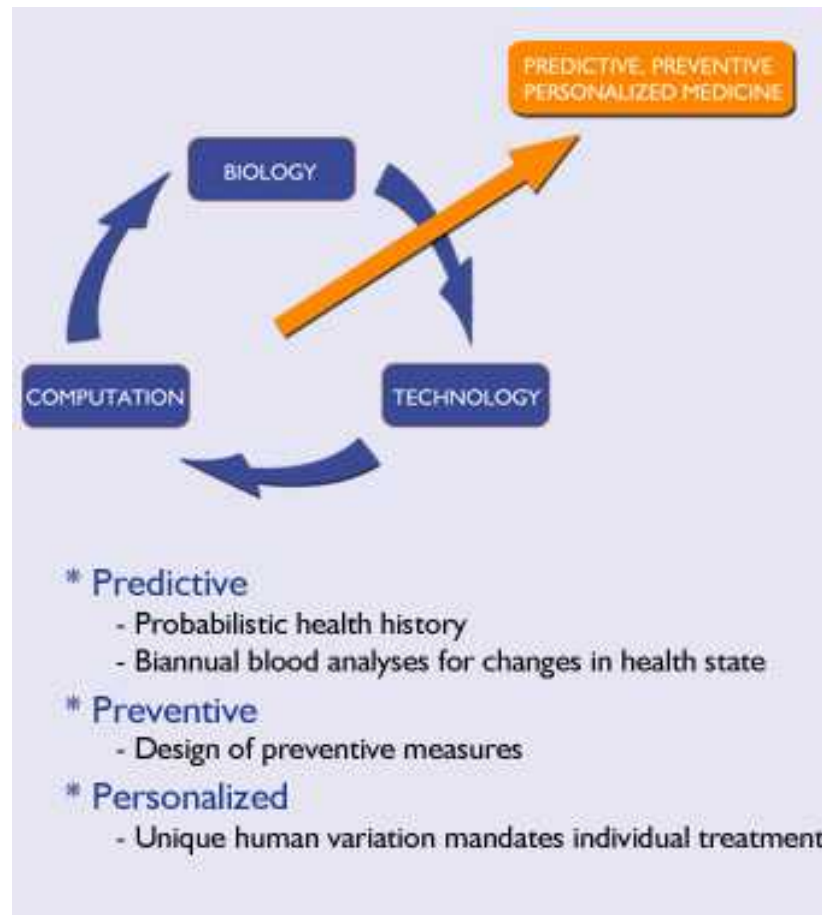


Framework: Cumulative Risk and Vulnerability

- “The propensity of social or ecological systems to suffer harm from external stresses and perturbations. (Kasperson *et al.* 1995)
- Four categories
 - Susceptibility
 - Differential Exposure
 - Differential Preparedness
 - Differential Ability to Recover
- Impacts Environmental Justice efforts



Revolution in Biology



“The Human Genome Project has Catalyzed two paradigm changes in contemporary biology and medicine—systems biology and predictive, preventive and personalized medicine. “

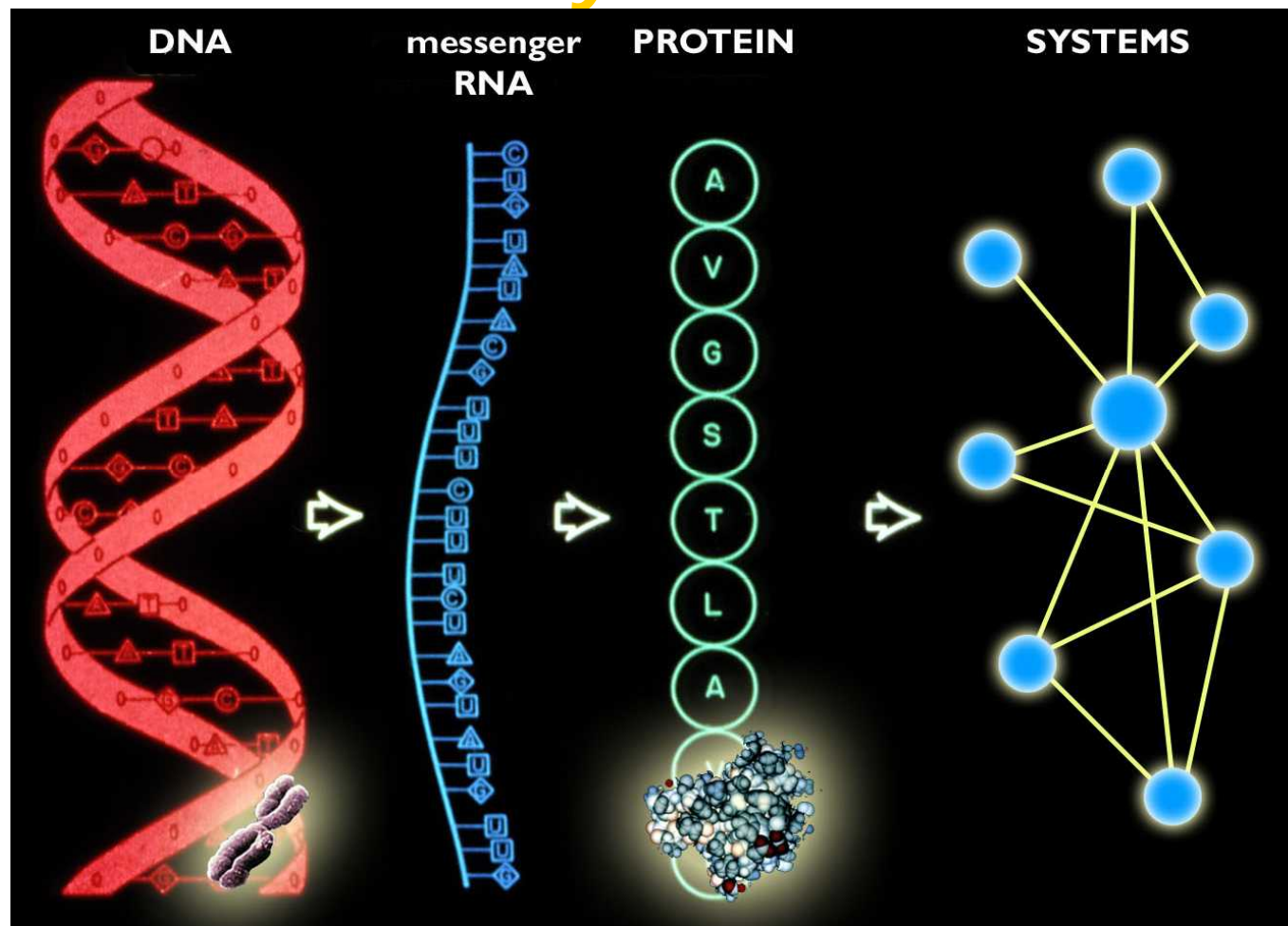
Graphic and text from the Institute for Systems Biology
<http://www.systemsbio.org/>



RESEARCH & DEVELOPMENT

Building a scientific foundation for sound environmental decisions

DNA to RNA to Protein to Systems



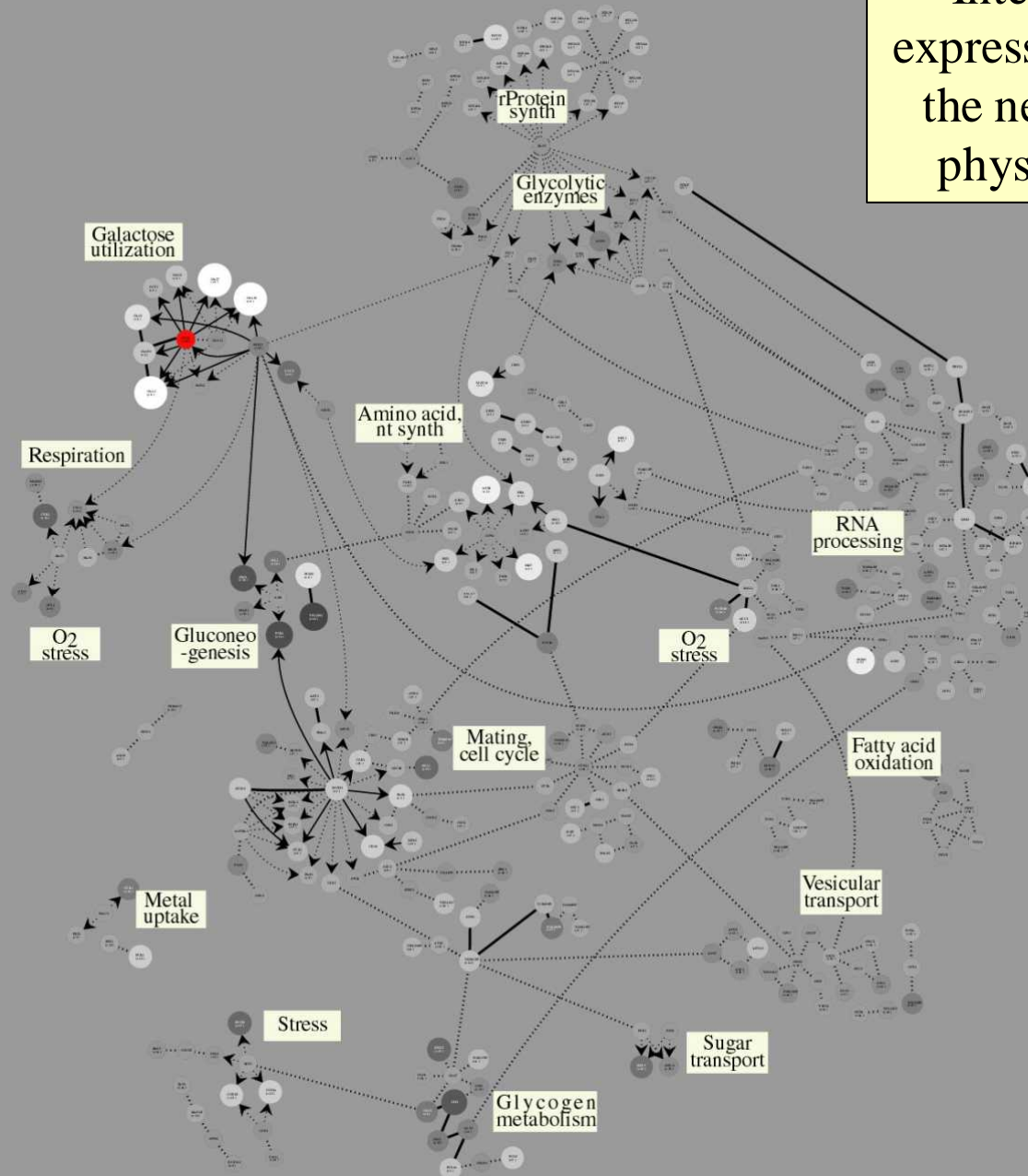
From a presentation by Dr. Lee Hood, Institute of Systems Biology



RESEARCH & DEVELOPMENT

Building a scientific foundation for sound environmental decisions

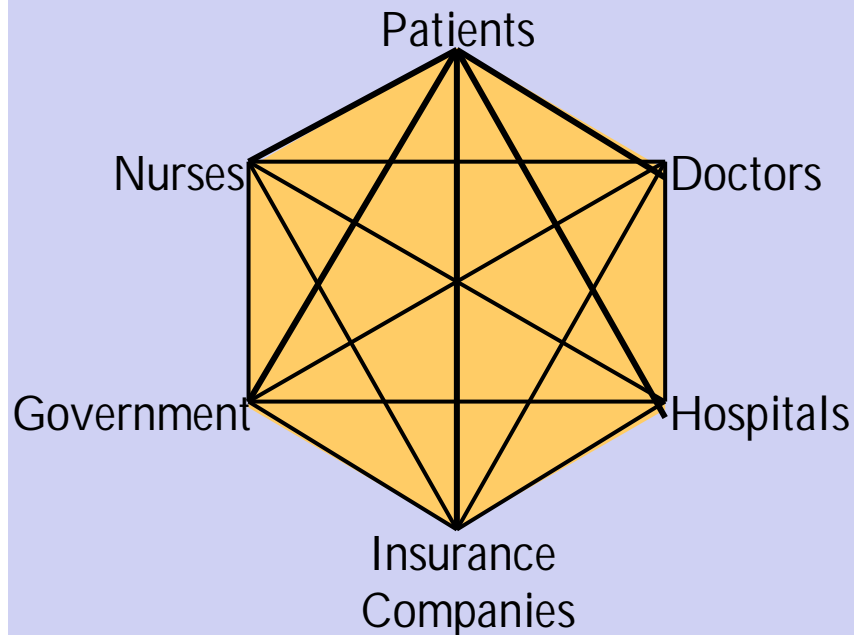
Integration of gene expression response with the network of known physical interactions



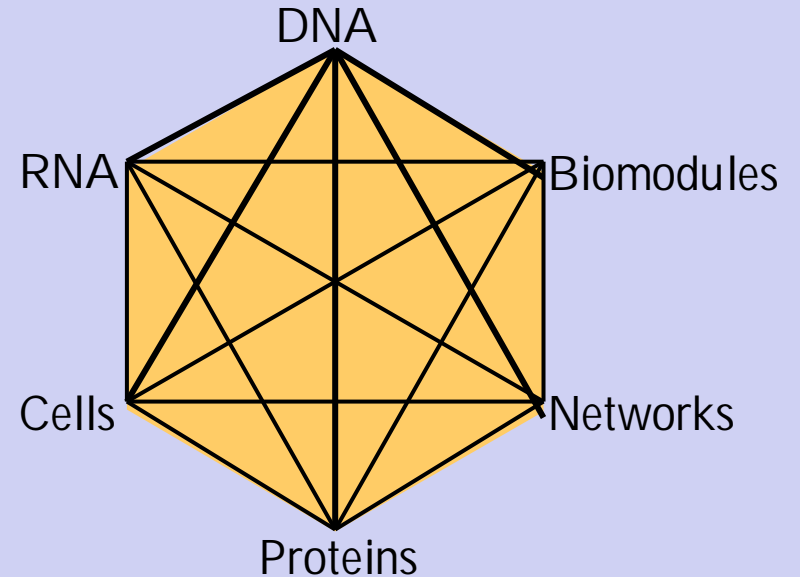
From a presentation by Dr. Lee Hood, Institute of Systems Biology

What Is Systems Biology?

Healthcare System



Biological System



From a presentation by Dr. Lee Hood, Institute of Systems Biology



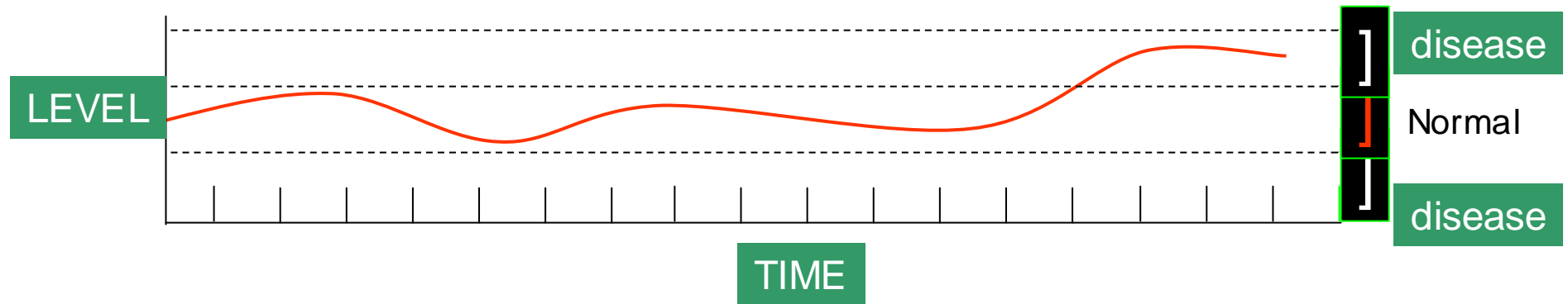
RESEARCH & DEVELOPMENT

Building a scientific foundation for sound environmental decisions

Preventative Medicine

Macrophage window to other physiological systems
(heart, brain, immune system)

- Measure 1000 mRNAs (1000 proteins) once/6 months - reflect differences in many informational pathways



- Instantaneous predictor of health status

From a presentation by Dr. Lee Hood, Institute of Systems Biology



RESEARCH & DEVELOPMENT

Building a scientific foundation for sound environmental decisions

Predictive, Preventive, and Personalized Medicine

- Predictive:
 - Probabilistic health history--DNA sequence
 - Biannual multiparameter blood measurements
- Preventive:
 - Design of preventive measures via systems approaches
- Personalized:
 - Unique human variation mandates individual treatment

From a presentation by Dr. Lee Hood, Institute of Systems Biology

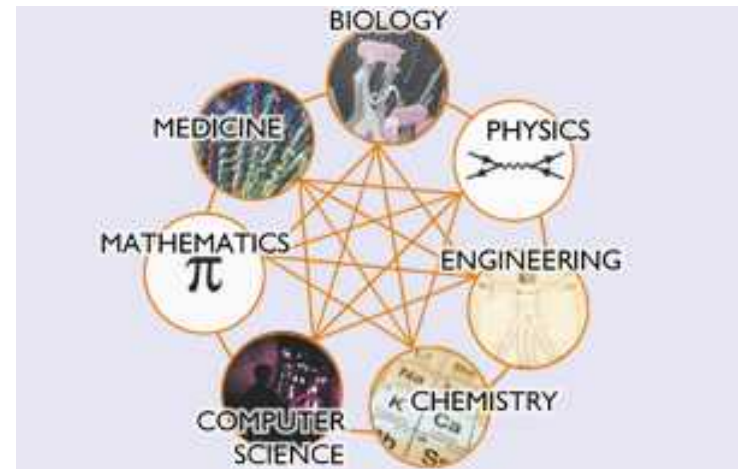


RESEARCH & DEVELOPMENT

Building a scientific foundation for sound environmental decisions

Cumulative Risk: Conclusion

- Complex problem
 - Really still in beginning stages of understanding
- Must be in a position to exploit advances in technology, information science and approaches like systems biology



Graphic from the Institute for Systems
Biology
<http://www.systemsbiology.org/>



RESEARCH & DEVELOPMENT

Building a scientific foundation for sound environmental decisions