

Use of the “Exposome” in the Convergence of Toxicology and Epidemiology: A Primer on –Omic Technologies for Achieving Health Impact

Society of Toxicology
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Webinar Presentation Abstract

- The exposome has been defined as the totality of exposures individuals experience over the course of their lives and how those exposures affect health.
- The inherent value of exposomic approaches and data in toxicology and epidemiologic studies is that they can provide greater understanding of the relationships among a broad range of chemical and other risk factors and health conditions and ultimately lead to more effective and efficient disease prevention and control.
- Proof-of-concept studies will be described for the integration of different kinds of toxicological and epidemiological data, including biomarker measurements, and exposure data from other sources such as sensors, geographic information systems, and conventional tools such as survey instruments.



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Practice of Epidemiology

Use of the “Exposome” in the Practice of Epidemiology: A Primer on -Omic Technologies

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Background: NIOSH Exposure Assessment Program Goals

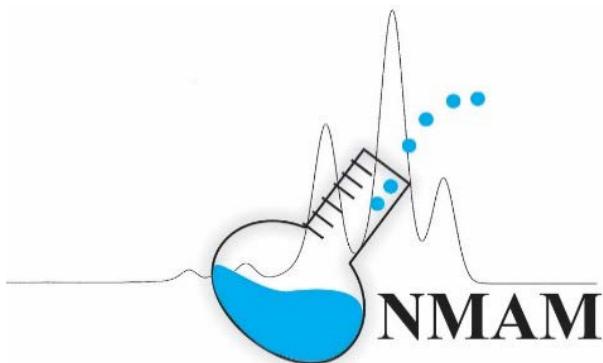
EXAP Strategic Goal 1

Foster research and provide guidance to develop and improve exposure assessment ***strategies***

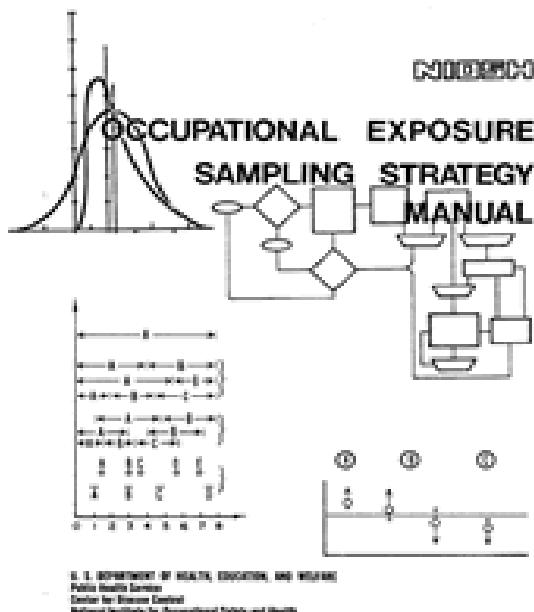
EXAP Strategic Goal 2

Develop and improve specific ***methods and tools*** to assess worker exposures to critical occupational agents and stressors

NIOSH Exposure Assessment Program Flagship Efforts



NIOSH Manual of Analytical Methods



Direct Reading Exposure Assessment Methods

The Exposome: Exposure to Disease

Our Exposures

Our Unique
Characteristics

Disease

NIOSH Exposome and Exposomics Webpage

The National Institute for Occupational Safety and Health (NIOSH)

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Promoting productive workplaces through safety and health research



Exposome and Exposomics



The Exposome: Exposure to Disease



Overview

What is the exposome?

Success in mapping the human genome has fostered the complementary concept of the "exposome". The exposome can be defined as the measure of all the exposures of an individual in a lifetime and how those exposures relate to health. An individual's exposure begins before birth and includes insults from environmental and occupational sources. Understanding how exposures from our environment, diet, lifestyle, etc. interact with our own unique characteristics such as genetics, physiology, and epigenetics impact our health is how the exposome will be articulated.

Exposomics is the study of the exposome and relies on the application of internal and external exposure assessment methods. Internal exposure relies on fields of study such as [genomics](#), [metabonomics](#), [lipidomics](#), [transcriptomics](#) and [proteomics](#). Commonalities of these fields include 1) use

On this Page

- Overview
- NIOSH Contacts
- NIOSHTIC-2
- Exposure and Biomonitoring Links
- Other NIOSH Resources

Context of NIOSH Views on the Occupational Exposome

Decker, J.A., D.G. DeBord, A. Weston, and M.D. Hoover: **Exploring the Exposome - A Focus on Totality of Exposures Could Mean New Opportunities for Industrial Hygienists**, The Synergist, 21(6): 32-33, 2010.

Hoover, M.D.: **Welcome and Charge to the Group, NIOSH Exploring the Exposome Workshop**, Cincinnati, OH, September 22-23, 2010.

Howard, J.H., D.G. DeBord, and M.D. Hoover: **The Future of Industrial Hygiene**, The Synergist, 75th Anniversary Supplement, 25(8):7, 2014.

DeBord, D.G., T. Carreón, T.J. Lentz, P.J. Middendorf, M.D. Hoover, and P.A. Schulte: **Use of the “Exposome” in the Practice of Epidemiology: A Primer on –Omic Technologies**, Am J Epidemiol. 184(4):302–314, 2016.

NIOSH Priority areas for Exposure Assessment

- Investment in and exploration of new technologies and tools to measure internal and external exposures
- Molecular epidemiology studies to determine associations between exposures and disease
- Development and validation of biomonitoring techniques for both legacy and response monitoring
- Making occupational exposure information publicly accessible

NIOSH Research Needs for the Exposome

- Fill information and data gaps by
 - Conducting more expansive exposure assessments using biomarkers
 - Developing new tools
- Develop reliable measures of exposure history that
 - Account for variability and individual differences
 - Can be evaluated by “high-throughput” methods
- Improve models to comprehensively assess relationships among health outcomes and the many factors of exposure
- Develop and use of databases to share information

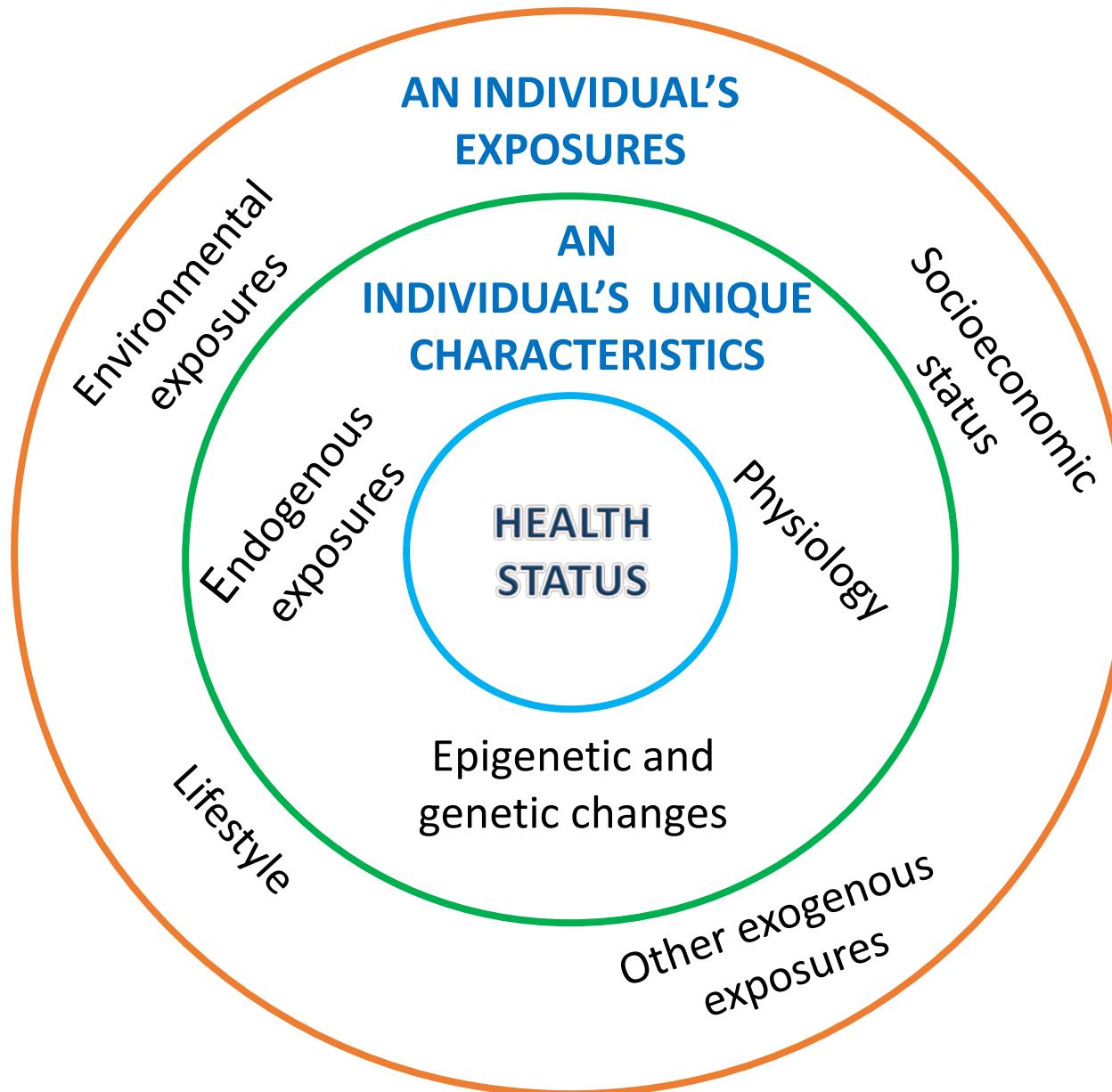
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The exposome has been defined as the **totality of exposures** individuals experience over the course of their lives and how those exposures affect health. Three domains of the exposome have been identified: internal, specific external, and general external. **Internal factors** are those that are unique to the individual, and **specific external factors** include occupational exposures and lifestyle factors. The **general external domain** includes sociodemographic factors such as educational level and financial status. Eliciting information on the exposome is daunting and not feasible at present; the undertaking may never be fully realized. **A variety of tools** have been identified to measure the exposome. **Biomarker measurements** will be one of the major tools in exposomic studies. However, exposure data can also be obtained from other sources such as **sensors, geographic information systems, and conventional tools such as survey instruments**. Proof-of-concept studies are being conducted that show the promise of exposomic investigation and the **integration of different kinds of data**. The inherent value of exposomic data in epidemiologic studies is that they can provide greater understanding of the relationships among a broad range of chemical and other risk factors and health conditions and ultimately lead to **more effective and efficient disease prevention and control**.

Keywords: biomarkers; environmental exposures; epidemiologic methods; occupational exposures

The Exposome Concept



What is the Exposome?

Totality of exposure individuals experience

- From conception until death
- Includes:
 - toxicants in the general environment
 - toxicants in workplaces,
 - diet,
 - lifestyle choices
 - socioeconomic status

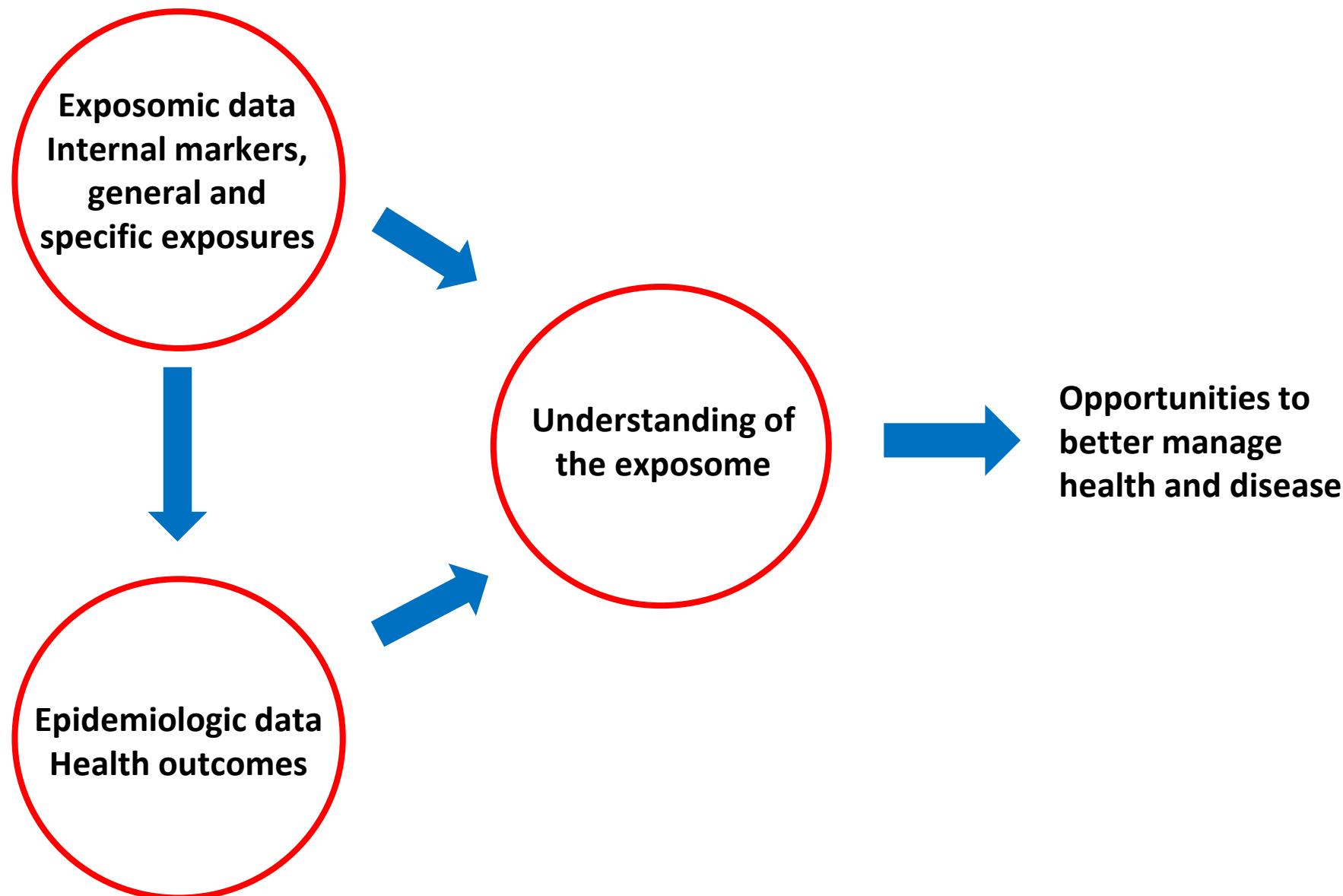
Why should we study the exposome?

- One of the promises of the human genome project was that it could revolutionize our understanding of the underlying causes of disease and aid in the development of preventions and cures for more diseases.
- However, genetics has been found to account for only about 10% of diseases, and the remaining causes appear to be from environmental causes.
- To understand the causes and eventually the prevention of disease, environmental causes need to be studied.

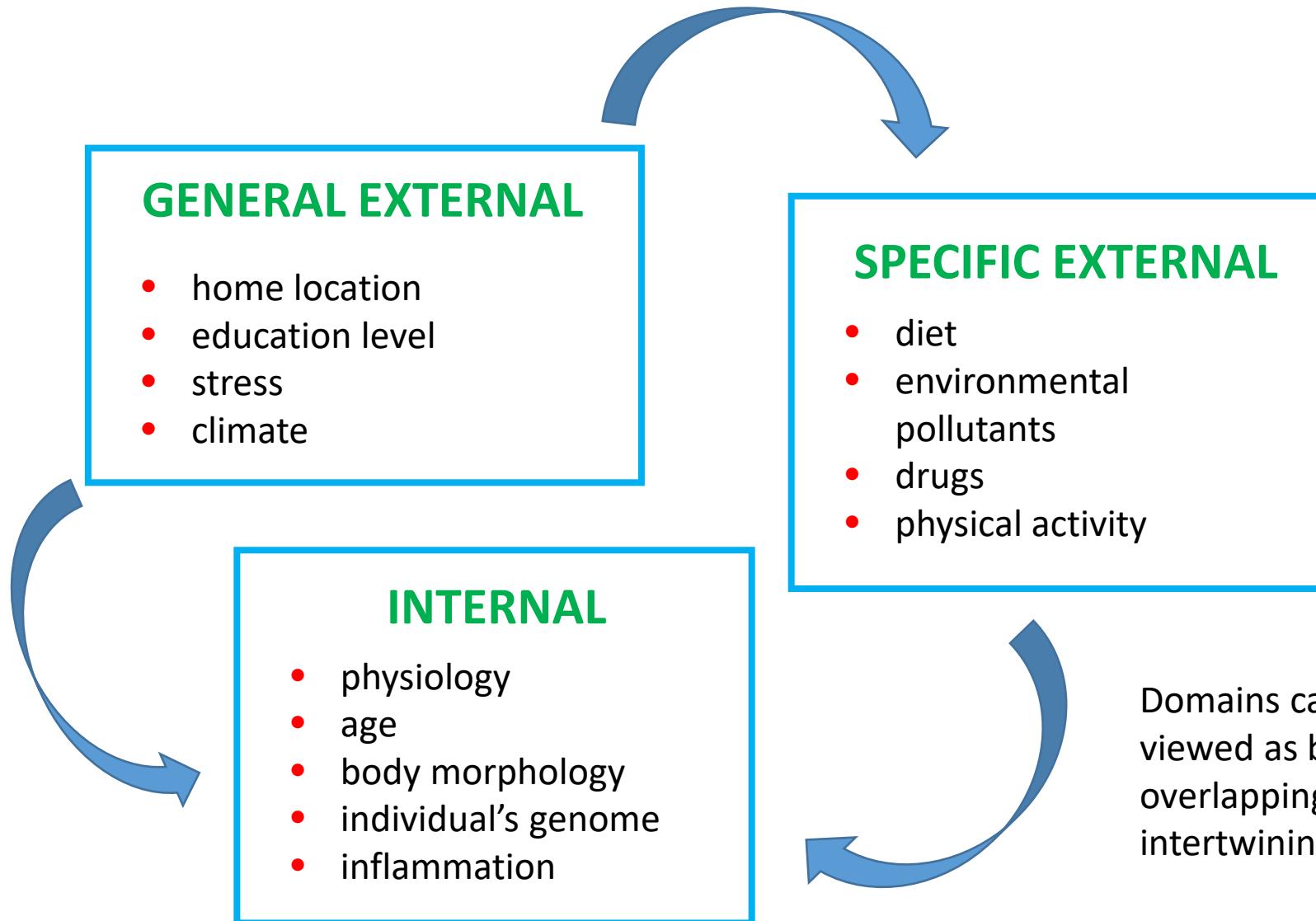
The Exposome is Dynamic

- Exposures vary on an hourly to yearly basis
- A given exposure or dose will not have the same effect during the various developmental periods
- Measurement of the exposome at one given point in time would not be sufficient to characterize all health impacts of the environment
- One way forward would be to start developing the exposome at certain key points in exposure experience or disease development – **exposomic approach**

Exposome-Informed Epidemiologic Research

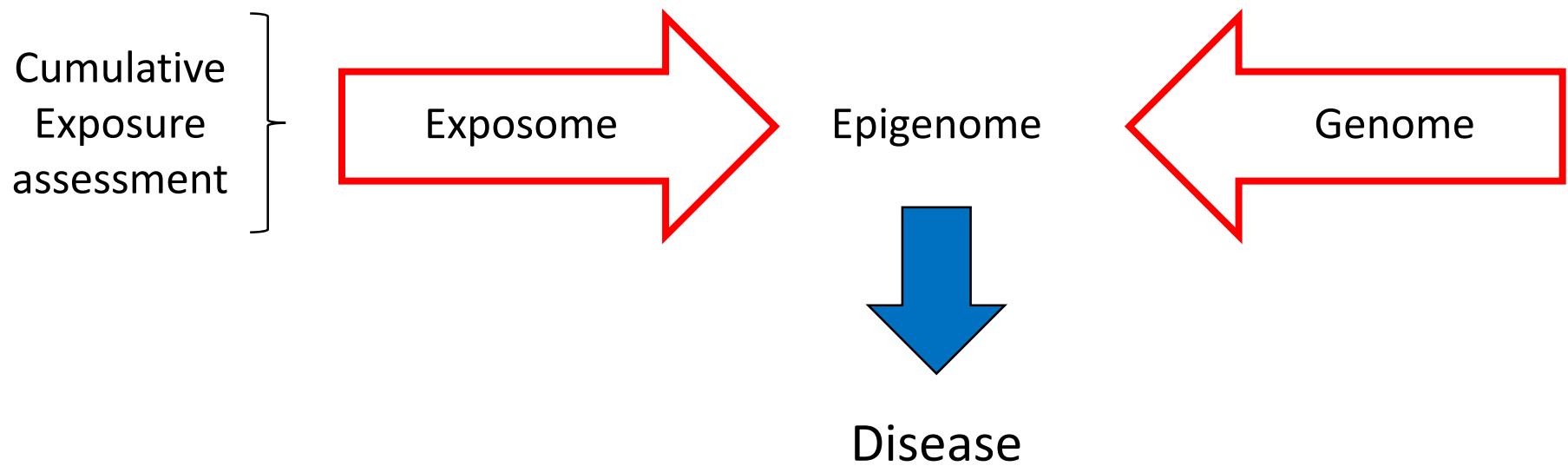


Domains of the Exposome



Domains can be viewed as both overlapping and intertwining

Example of an Exposome-Genome Interaction



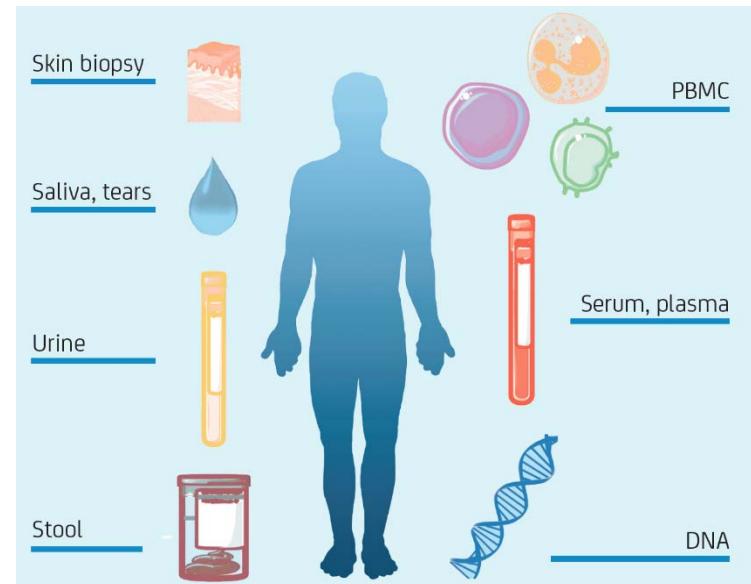
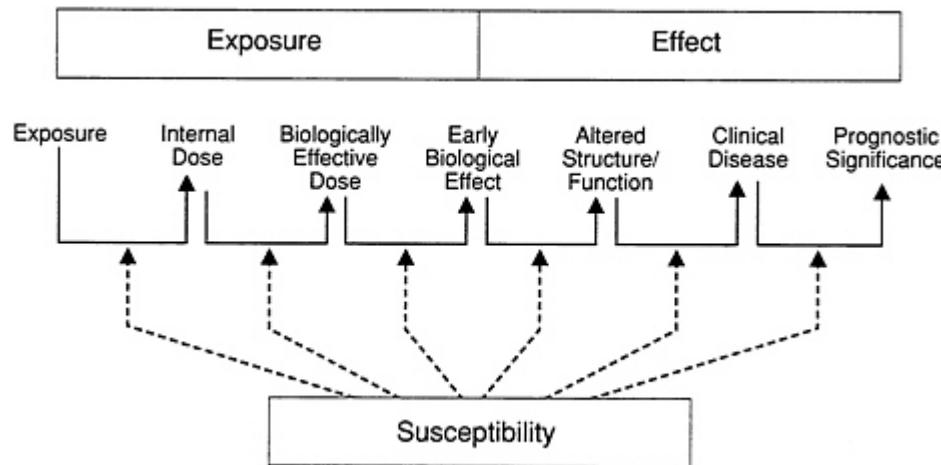
Health status is influenced by the interaction of an individual's environmental and genetic factors from conception to death

Potential Tools to Measure the Exposome

Tool	Domain
Biomonitoring and biomarker data from omics or other techniques	Internal
Sensors for environmental or personal monitoring	Specific external
Geographic Information Systems	General external
Conventional methods such as survey instruments or job-exposure matrices	Specific external
Reality mining from social networks or other sources	General external

Biological Monitoring

- Measurable event occurring in a biological system, such as the human body
- Reflects an event or sequence of events that occur somewhere in the causal chain between an exposure and a related adverse effect



Omic Technologies

Epigenetics

The study of the totality of all heritable changes in gene expression and chromatin organization that are independent of the DNA sequence itself and that can be inherited in a stable manner over cell divisions

Transcriptomics

The study of the sequence of an RNA mirrors the sequence of the DNA from which it was transcribed. By analyzing the transcriptome, researchers can determine when and where each gene is actively expressed at any given moment

Proteomics

The study of the full set of proteins encoded by a genome is known as proteomics and involves the identification, characterization and quantitation of expressed proteins in biological samples

Metabolomics

The study of low molecular weight metabolites present in a biological sample

Adductomics

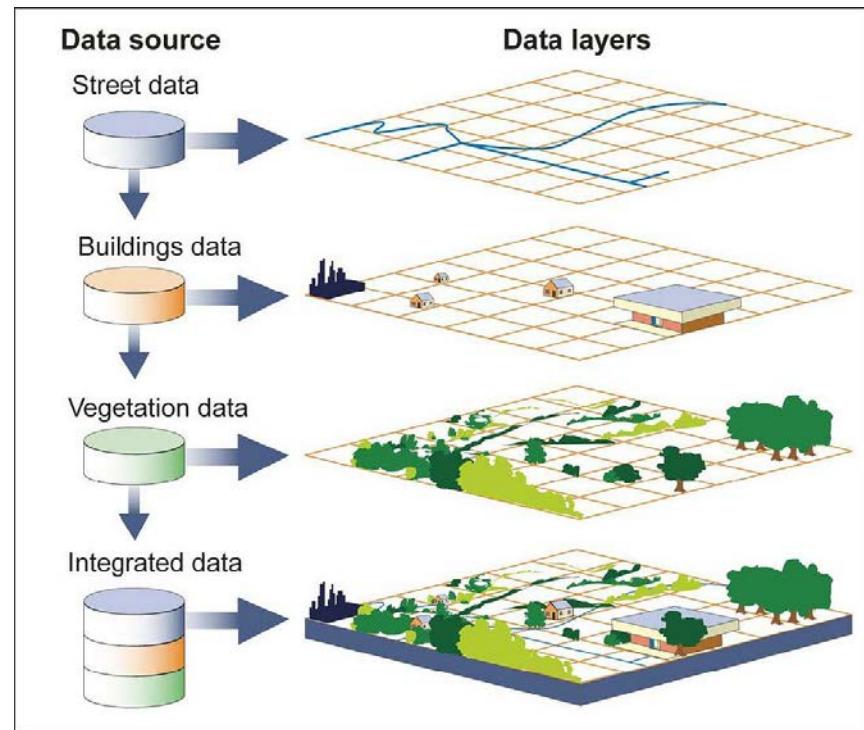
The study of macromolecular adducts in the context of an entire genome

Genomics

The study of genes or their function

Geographic Information Systems (GIS)

- For mapping a variety of data, for example environmental, topographical or health-related, to understand trends and patterns
- Enhance exposure assessment because they provide information on broad environmental contaminant levels or to define a population



Source: GAO.



Exposome Informatics

- Development of new biostatistical methods for quality control, imputation, and analysis issues such as multiple hypothesis testing
- Need for evaluating the interrelationships among phenotype, genotype, and exposure data
- Closely related to the concept of 'reality mining,' which refers to the analysis of behavioral and self-reported data extracted from social networks and handheld devices such as mobile phones and applications



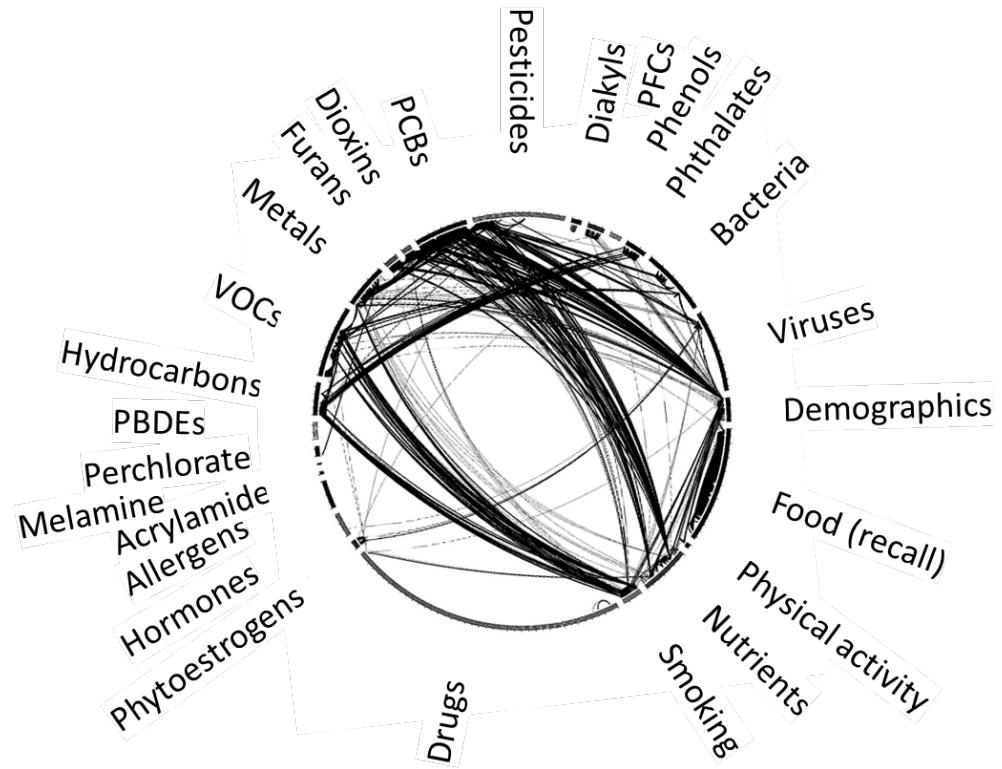
Nanoinformatics

(a working definition)

- The *science and practice* of determining *which information is relevant* to meeting objectives of the nanoscale science and engineering community,
- and then developing and implementing effective mechanisms
- to *collect, validate, store, share, analyze, model, and apply the information, and then to confirm achievement of the intended outcome* from use of that information,
- and then *conveying experience to the broader community, contributing to generalized knowledge, and updating standards and training.*

Environment-Wide Association Studies

- Comprehensive display of replicated correlations between individual exposures of the exposome
- Visual depiction of the network of replicated correlations between individual exposures of the exposome



Study Design in Exposomic Studies

- The best approach would be to use a longitudinal (prospective) cohort study design
- Two strategies have been identified for characterizing the exposome:
 - ‘**Bottom-up**’ strategy in which all the exposures in a person’s exposome are measured at set time points
 - ‘**Top-down exposomics**’ in which a combination of omic endpoints and legacy biomarkers are measured in repeated blood specimens. This data-driven (or “agnostic”) approach lacks specific hypotheses

Challenges in Study Design

- Large quantity of variables in exposomic studies may require approaches that are different from traditional epidemiology
- Multiple challenges have been identified
 - Reverse causality
 - Testing multiple variables for associations
 - Correlation among variables
 - Variability over time and between subjects
 - Variability of exposure data
 - Analytical measurement error and other measurement challenges
 - Multi-level analysis

Ethical and Policy Challenges

- Correct application of research
- Confidentiality and privacy
- Language of informed consent forms
- Appropriate feedback
- Sample archiving
- Protection from commercial interests
- Regulatory implications of research findings

**What is the status and
what are we learning
from other funding initiatives and resources?**

Funding Initiatives and Resources: Health and Exposome Research Center: Understanding Lifetime Exposures (HERCULES)

- At Emory University funded by the National Institute of Environmental Health Sciences (NIEHS)
- Goal: understanding lifetime exposures
- Main aims of HERCULES:
 - Provide greater access to exposome-related approaches
 - Facilitate communication of the importance of environmental factors in disease using exposome principles
 - Expedite translation of novel scientific findings to develop novel sustainability, prevention or treatment strategies in humans

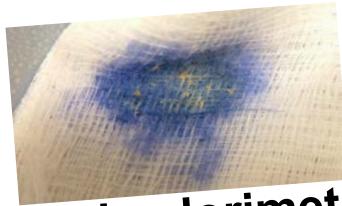
Funding Initiatives and Resources: Human Early-Life Exposome (HELIX)

- Proof of concept study to characterize children's exposomes as they progress through early life
- 13 partner institutions using data from ongoing prospective European birth cohorts: 32,000 mother-child pairs
- Use traditional exposure assessment methods as well as biomarker and omics measures
- Will measure environmental exposures to food, water, air pollution, pesticides, noise, and ultraviolet radiation, as well as growth, development, and health of the children, including birth outcomes, postnatal growth and body mass index, asthma and lung function, and neuro-development

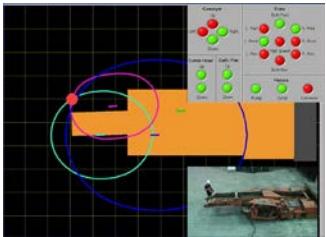
Funding Initiatives and Resources: Health and Environment-Wide Associations Based on Large Population Surveys (HEALS)

- Objective is to refine a methodology that integrates and applies analytical and computational tools for performing environment-wide association studies (EWAS)
- Will use a series of population studies across Europe including twin cohorts (335,000 individuals of different age, gender and socio-economic status groups)
- External exposome will be estimated by integrating environmental, occupational and dietary data into exposure models
- Internal exposome will be estimated at the individual level by integrating omics derived data and biomonitoring data

NIOSH Center for Direct Reading and Sensor Technologies



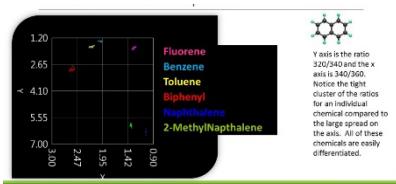
Lead colorimetric detection



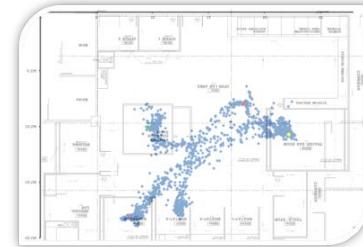
Intelligent Proximity Detection Systems



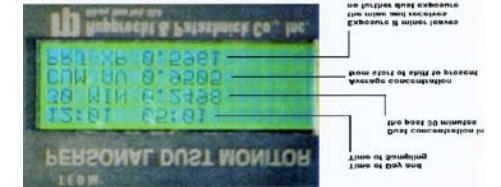
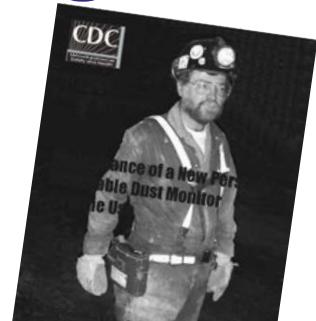
Nanoparticle Sizing



Naphthalene and PAH sensing



Chemical Hazard Mapping



Personal Dust Monitor



Smartphone Noise app



The Helmet-CAM and Enhanced Video Analysis of Dust Exposure (EVADE) software



Methamphetamine



Coal Dust Explosibility Meter



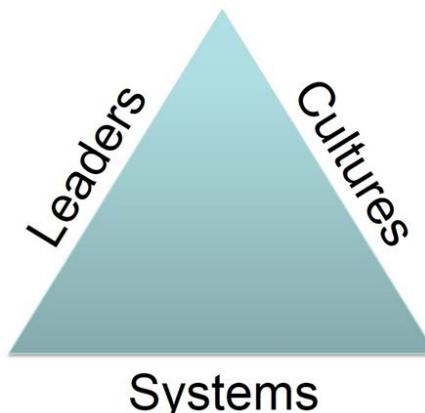
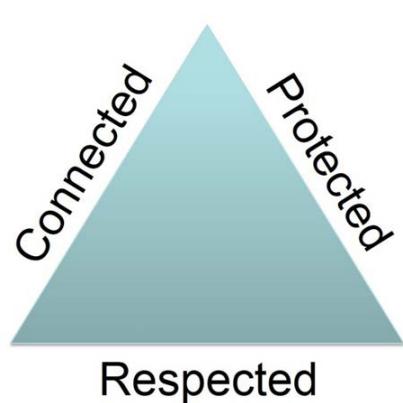
A sensor revolution is underway



Right Sensors used Right: Goal

NIOSH Center for Direct Reading and Sensor Technologies

Make it easier for everyone to get the right things done right for health by helping to build and sustain connected, protected, and respected communities with leaders, cultures, and systems that have all the tools, training, and experience needed to anticipate, recognize, evaluate, control, and confirm protection of safety, health, well-being, and productivity *in all the places we live, learn, work, and play.*



They must be built and sustained.

NIOSH Workplace Monitors to Improve Health and Safety

- **Personal Dust Monitor** (to protect respiratory health)
- **Coal Dust Explosibility Monitor** (to prevent mine disasters)
- **NIOSH Intelligent Proximity Technology** (to prevent traumatic injury)
- **Portable Aerosol Mobility Spectrometer** (to characterize airborne hazards from nanoparticles)
- **Aerosol Spark Emission Spectrometer (ASES)** (to characterize airborne metals)
- **Photoionization Contour Mapping** (for volatile organic compounds)

Future Prospects

- The benefits of the exposome are many for both individual and population health research
- The exposome can aid in identifying modes of action of stressors, identifying unknown exposures and improving our understanding of disease
- This can lead to better risk assessments, better translation of science into practice and ultimately to disease prevention

Questions and Discussion



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