1. Introduction: The utility of the exposome research framework

Diverging from conventional approaches that link a singular exposure to a specific health outcome, the exposome introduces a novel perspective. In encompassing the totality of our environmental exposures, it provides an original conceptual framework for the study of a myriad of environmental factors, including urban settings, chemicals, lifestyle choices, and social dynamics, that converge to shape our health. This more refined framework is not simply concerned with dissecting individual hazards, rather it seeks to comprehend the complex interplay of multiple exposures and their collective, potentially cumulative impact (Figure 1).

Environmental health policy areas that are set to benefit from an exposome approach include those required to deal with processes of priority setting and which, hence, demand a systematic approach to a range of suspected environmental risk factors. Policy areas that should profit most are those that tackle more than one risk factor or pollutant at a time and which require knowledge of how such factors act together to influence health: ranging from chemical regulations (e.g. relating to endocrine disruptors, chemical mixtures, pesticides, food contact materials, cosmetics, and air quality) to strategies for enhancing urban management (e.g. the EU's Thematic Strategy of the Urban Environment) and disease-specific prevention policies (e.g. the EU's initiative on the prevention of NCDs). It is becoming increasingly clear that approaches that do not examine complex multi-factor effects can be ineffective in explaining, let alone preventing, the onset of most common diseases. Here it is important to recognise the interplay of multiple exposures and the complex "system" in which efforts to reduce the harmful exposome are made (encompassing individuals, communities, organisations, the natural and built environment, and economic and political forces) (Barton & Grant, 2006). This particular vision – that afforded by the "system" – is

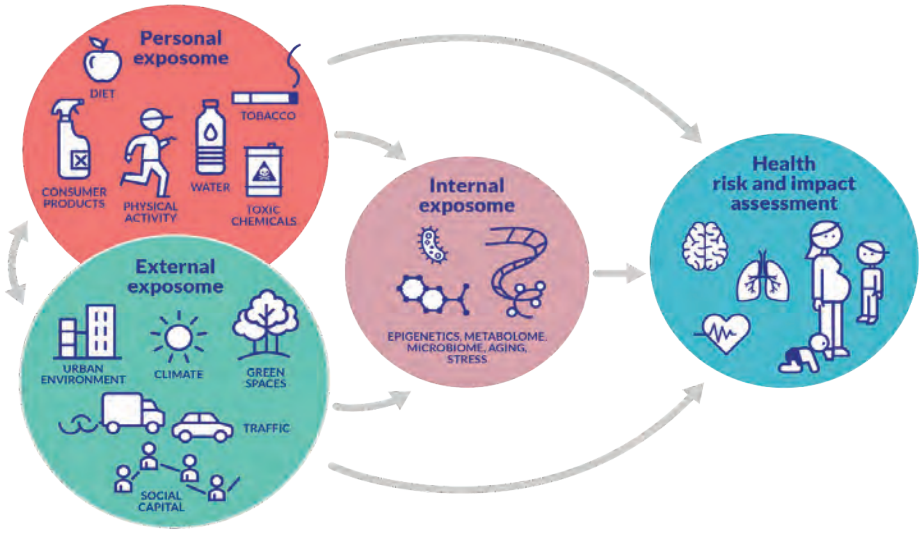

FIGURE 1. The three overlapping domains of the exposome.
SOURCE: Image extracted and adapated from the ATHLETE Project website, https://athleteproject.eu/.

further developed in the last section of this report, "Exposome and planetary health".

As an integral part of the exposome, internal biological responses to exposures can be measured at the molecular level using high-throughput omics techniques: metabolomics, proteomics, transcriptomics, and epigenomics, which have great potential for the broad and powerful characterisation of complete sets of biological molecules. Of particular interest is the identification of biological responses and pathways that respond to and interact with the exposures, resulting in adverse health, i.e. early pathway perturbations. This information may be used to improve biological plausibility of associations, to understand how different exposures may act on common pathways, and, ultimately, to predict environmental health related disease. Similar to developments in the fields of toxicology and pharmacology, the identification of perturbed pathways of well characterised exposures may facilitate the prediction of the public health burden of more recent, less characterised exposures.

The early part of the life course is a particularly important period in which to study early pathway perturbations: exposures during vulnerable periods may have pronounced effects at the molecular level but may remain clinically undetectable until adulthood. Each child is made up of a unique molecular profile at the methylome, transcriptome, proteome, or metabolome levels, as the result of

the interaction between his or her genome and early life events partially captured in the external exposome. Children may also display differences in susceptibility to their environment and in the era of personalised medicine, a personal exposome assessment should consider molecular susceptibility. For example, the toxicity of arsenic, a ubiquitous metal whose exposure occurs mainly through the consumption of fish and crustaceans, will depend heavily on the capacity of the liver and potentially gut microbiota to methylate arsenic species (Claus et al., 2016).

FIGURE 2. Key traits of the exposome.
SOURCE: Created by Léa Maitre.