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# Statistical needs for Exposome Analytics: an Illustrative overview

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## Résumé

The Exposome concept has been developed as a necessary complement to the genome to better understand the determinants of health and of the risk of chronic diseases. The external exposome combines a large range of external stressors (i.e. non-genetic) factors potentially impacting human health from conception onwards. These external exposures (i) are heterogeneous in nature, scale, and variability, (ii) feature complex correlation patterns and (iii) may operate as mixtures. The internal exposome can be defined as the way these exposures are embodied and its exploration relies on the screening and integration of high-resolution molecular data. While methods for omics data analyses are established, their application in an exposome context is raising specific methodological challenges including the analysis of complex and correlated exposures. Furthermore, the isolated exploration of an omic profile offers the possibility to capture stressor-induced biological/biochemical alterations, potentially impacting individual risk profiles, but this may only yield a fractional picture of the complex molecular events involved, therefore limiting our understanding of the effective mechanisms mediating the effect of the exposome. This defines three main methodological challenges in Exposome analytics: (i) reproducible and interpretable feature selection, (ii) data integration, and (iii) complexity reduction. Taking examples from real-world exposome projects we will illustrate the use of statistical and machine learning techniques to address these challenges and accommodate co-occurring exposures contributing to population stratification, explore the links between these and health outcomes, and investigate the (multi)-omic response to these sets of exposures.

**Mots-Clés:** Exposome, Omics Data, Stability selection, Graphical models

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