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Utilizing signatures of age in the urine metabolome to construct metrics of biological age on the basis of the concept of individualization
(présentation en anglais)

Résumé

Myriads of methods have been proposed to measure biological age with the goal of enabling a personalized prognosis of age-related health issues and tailored treatments. However, it is highly unclear which method best suits the goal of measuring biological age in the context of a given dataset. Here, we present a new statistical definitional framework for quantifying biological age, generalizing recently published work on individualization. We explicate the statistical prerequisites for the meaningful differentiation of two individuals of the same chronological age regarding their true biological age by supervised methods, namely that each contributing variable must be stochastically independent of chronological age given the true biological age. If this specific condition is not fulfilled, we reveal that unsupervised methods will often outperform supervised methods. As a consequence, we prove that the most commonly applied predictor selection methods based on maximizing the correlation to chronological age lead to a heavy loss of biological and clinical information in a wide range of scenarios. Finally, by using data from the large prospective cohort Study of Health in Pomerania (n=4308) with extensive follow-up and baseline phenotyping, we demonstrate how to construct metabolomic measures of biological ageing from urine metabolome data, showing the advantages and disadvantages of the different approaches. On our way, we describe the complex nature of the impact of age on the metabolome and reveal sex-specific non-linearity, leading to the need for sex-specific measures of biological age. In conclusion, by reframing the measurement of biological age as a problem of individualization, we derive an applicable and theoretically sound statistical framework that permits the construction of biological age metrics tailored to the particular dataset.