Propositions

I. Current large-scale genome-wide association studies (GWASs) are able to gradually uncover the genetic architecture of social-scientific traits and – with further increasing sample sizes – are likely to attain sufficient predictive accuracy in the near future to become relevant to the social sciences as a whole (Chapter 2).

II. Studies of social-scientific traits tend to induce little societal tension in case the correlates of interest are perceived to be malleable. However, GWAS results yield predictors that partially explain trait variation and which are immutable, in the sense that they are a function of the genes we are endowed with. Although such traits are not 'determined' by these genetic predictors, GWAS results contest the view of man as a *tabula rasa* to an extent hitherto unseen; in addition to the existing challenge posed by heritability estimates, the blank slate theory is now contested by individual-level genetic predictors. Ensuing tensions warrant open and pluralistic discussions across society regarding the philosophical implications and the ends to which knowledge of the genetic architecture of social-scientific traits should be used.

III. In meta-analyses of GWAS results from different studies, statistical power to detect trait-associated single-nucleotide polymorphisms (SNPs) is attenuated in case of cross-study heterogeneity in the genetic architecture of the trait of interest. Despite this attenuation, such meta-analyses are typically still well-powered provided the total sample size is large enough (Chapter 2).

IV. In case a classical polygenic score (i.e., a weighted sum of SNPs with weights based on GWAS results) is highly predictive in a hold-out sample, this does not necessarily imply that the underlying GWAS was well-powered, nor does the converse necessarily hold (Chapter 2).

V. Although outcomes of reproductive choices (e.g., number of children ever born) may be informative proxies for an individual's fitness, natural selection has left such outcomes moderately heritable. Consequently, SNPs that are robustly associated with these outcomes can be found using a large-scale GWAS (Chapter 3).

Abbreviations: genome-wide association study (GWAS), linkage disequilibrium (LD), single-nucleotide polymorphism (SNP)

VI. When partitioning SNP-based heritability according to functional categories of SNPs (e.g., coding regions), owing to linkage disequilibrium (LD) between SNPs, a dense set of SNPs is required to prevent misattribution of the explained variance amongst categories. Even in a set of one million SNPs there is misattribution. Hence, at least several million SNPs are needed to address this issue (Chapter 4).

VII. In addition to improving the predictive accuracy of classical polygenic scores, increasing GWAS sample sizes boost the gain in predictive accuracy of more advanced methods (e.g., using ridge-regression estimates of SNP effects or `LDpred`) when compared to the performance of classical polygenic scores (Chapter 5).

VIII. When estimating genetic and environment (co)variance components for multiple traits, the computational complexity of a naïve approach increases strongly with the number of traits and the sample size per trait. However, when these traits are observed in the same set of individuals, the complexity can be reduced to the same order as that of estimating components for only one trait (Chapter 6).

IX. Each parameter that can be estimated by applying LD-score regression to a single set of GWAS results can also be estimated directly from individual-level data. Differences in estimates from individual-level data and summary statistics are a result of (i) the use of different underlying samples (including those used for constructing LD scores), (ii) non-uniform procedures, and (iii) sampling variance (Chapter 7).

X. Life is like a ‘Rube Goldberg machine’; advanced biochemical mechanisms are needed even for seemingly easy tasks.

XI. Occam’s razor, though useful, is nothing more than a conservative heuristic. It does not tell the truth; it merely helps keeping one’s sanity.

XII. Believing “*as many as six impossible things before breakfast*,” as Lewis Carroll put it, is a laudable goal for a scientist, provided those beliefs are subjected to dispassionate scrutiny after breakfast.