Discussion of

XL Meng "A Multi-resolution Theory for Approximating Infinite-p-Zero-n"

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Multi-resolution theory and precision medicine practice

Li and Meng's sophisticated infinite-p-zero-n theory is conceptually attractive

However, applications to precision medicine need to face additional sources of variation not (yet) considered in Li and Meng's work, notably:

- measurement errors in the predictors
- heterogeneity in the training population
- occasion-to-occasion variability

Handling these "complications" is often already difficult in much more standard settings than Li and Meng's. . .

Measurement errors

As the number of predictors grows we might expect some deterioration of their quality

The impact of measurement errors could be important in those predictors considered at higher resolutions to refine the model and make it more "personalized"

What about the rate at which measurement errors cumulate?

Additional difficulties from the presence of correlation between the (miss-measured) predictors

The ordering of the predictors should not avoid to consider measurement errors and intercorrelations

Heterogeneity in the training population

Precision medicine: Each of us is unique ("$n = 0$")

but every unit of the training population is also unique!

Assuming homogeneity in the training population might "dilute" important effects for the target subject

No problem when "all" the relevant predictors are available and are measured/observed with good quality

In a more realistic world, it is important to correct the lack of homogeneity: random effects?

Occasion-to-occasion variability

Physiological fluctuations are a key aspect to consider for precision medicine

Stephen Senn "Statistical pitfalls of personalized medicine" (Nature, 2018):

> *'response' is not a permanent characteristic of a person receiving the treatment; rather, it varies from occasion to occasion.*

Need more N-of-1 trails where one (or more) treatments are repeatedly tested on the same person

. . . or at least repeated observations in the training population