

ideas for research on **the mathematics of selecting, based on a polygenic score, between chromosomes produced by crossover**

I've written about this some, here:

https://berkeleygenomics.org/articles/Methods_for_strong_human_germline_engineering.html#appendix-best-crossover

And here:

https://berkeleygenomics.org/articles/Methods_for_strong_human_germline_engineering.html#method-chromosome-selection

Some of the main questions:

- * In the continuum model (Brownian Bridge), what's the expected best single-crossover chromosome, given a fixed set of two chromosomes? What about best k-crossover chromosome? (Both in terms of the conceptually precise mathematical analysis, and in terms of simulation.)
- * What about if you can only measure SNPs at a few loci?
- * How does this affect the selection power of genome-wide chromosome selection of a haploid genome from chromosomes produced by meiosis from a single diploid genome?

I think there are several interesting angles on this question:

- * Nontrivial mathematics:
 - * In terms of abstract probability theory, the question touches on e.g. the theory of brownian bridges, as addressed by Kolmogorov and others.
 - * In terms of practical CS, there's useful simulations to run (especially for modeling cases where you can cheaply sense only 5 or 10 SNPs spread across a chromosome, and so have to guess at crossovers points).
- * Nontrivial biology:
 - * E.g., factoring in the distribution of loci of crossover points, and the distribution of trait-relevant variants across chromosomes.
 - * E.g., factoring in the number of crossover points in chromosomes (which varies significantly depending on the sex of the gametes and on the chromosome index).
- * Surprising results: based on my preliminary simulations, you can get >6 SDs of total selection power, just by selecting from chromosomes of one man's gametes and separately one woman's gametes. I think this is pretty surprising and interesting.

(None of this refers to anything that's currently biotechnologically feasible, as even chromosome transplantation in culturable cells is barely feasible, using arduous methods like MMCT.)