### A Background Correction and Normalisation Framework for multiplex Immunofluorescence Spatial Proteomics

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Multiplex spatial proteomics enables simultaneous imaging of dozens of proteins within intact tissue sections, generating detailed maps of protein expression across thousands of cells. Recent advances now allow these measurements to extend across multiple tissue slices, producing large three-dimensional datasets. However, the raw intensity values produced by these technologies contain substantial technical noise arising from instrument effects, tissue autofluorescence, and non-specific antibody binding. These background signals introduce bias and make it difficult to distinguish true biological signal from noise. Current approaches to background correction and quality control rely largely on manual inspection or hard thresholding, which are subjective, variable and impractical when analysing hundreds of proteins across hundreds of samples.

We present bgnorm, a model-based framework for pixel level background correction using a 3 component Gaussian mixture model. Pixel intensities are modelled as arising from background noise, non-specific signal, or true biological signal. Using this model, we estimate and remove background contributions through probabilistic signal deconvolution. The framework also includes model based quality control to detect failed stains and a normalisation step to enable comparisons across samples and channels.

bgnorm improves separation between signal and background, enabling more reliable downstream spatial analysis of high dimensional imaging data

### Menopause-related heterogeneity in lipoprotein(a) effect on atherosclerotic cardiovascular disease: a sex- and age-stratified Mendelian Randomization study in the UK Biobank

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Atherosclerotic cardiovascular disease (ASCVD) risk rises in women during the menopausal transition, making postmenopausal women a key target for prevention. Lipoprotein(a) [Lp(a)] is a promising therapeutic target as it contributes to ASCVD risk and increases after menopause. However, whether its therapeutic potential could vary across menopausal stages remains unclear.

Mendelian randomization (MR) uses genetic variants associated with an exposure to estimate its causal effect on an outcome. While MR is well suited to assess the role of Lp(a) in ASCVD, stratifying analyses by menopausal status may induce collider bias since menopause can be influenced by Lp(a)-related variants and ASCVD risk factors. In contrast, conditioning on sex and age avoids this bias, as neither is affected by Lp(a) genetics or cardiovascular risk factors. Sex- and age-stratified MR can thus be used to investigate menopause-related heterogeneity in Lp(a) effects, conceptualized as age-dependent differences specific to women.

Using the UK Biobank, we evaluated the effect of Lp(a) on coronary and peripheral artery disease across sex and age strata. Lp(a) was associated with increased risk in both women and men, with no evidence of female-specific divergence across age strata. These findings support a consistent causal contribution of Lp(a) to ASCVD risk across the female life course and propose sex- and age-stratified MR frameworks for studying menopause–related heterogeneity in cardiovascular aetiology

### Income, Inequality, and Mortality: A Harmonized Comparative Framework Across Ecuador, Colombia, and Brazil

*Gabriela Sandoval, CISeAL-PUCE*

Inconsistent income measures and non-comparable covariate structures across national census systems often limit comparative mortality research across Latin America. We present a harmonized analytical framework based on census microdata from Ecuador, Colombia, and Brazil, designed to enable direct cross-country comparisons of income-mortality gradients. The estimates reveal meaningful heterogeneity in the strength of the income-mortality relationship across countries. This talk offers both a reusable methodological pipeline for researchers working with limited-income-data census contexts and substantive findings on cross-national mortality inequality patterns

### Towards continuous ancestry aware PRS via genetic distance kernel methods

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Polygenic risk scores suffer from well-documented portability failures across the genetic ancestry continuum, arising from several interacting sources: systematic differences in linkage disequilibrium patterns, misspecification of allele frequency normalisation, potential effect size heterogeneity, and GWAS discovery bias towards European-ancestry cohorts. To date, more than 87% of GWAS have been conducted in predominantly European cohorts, and the resulting PRS show substantially degraded performance in non-European individuals. Critically, this degradation is not confined to discrete ancestry group boundaries: Ding et al. demonstrated that PRS accuracy decays continuously with an individual's Euclidean distance from the training data centroid in PC space, establishing that portability is fundamentally a problem of genetic distance rather than of categorical ancestry misassignment. The prevailing methodological response of partitioning individuals into continental ancestry groups and estimating group-specific corrections temporarily improves performance within those strata but entrenches the conflation of biological and sociopolitical categories that the field has been called upon to abandon. A principled solution requires methods that operationalise ancestry as a continuous variable from the outset. Here we present a kernel formulation of PRS which subsumes previous continuous PRS methods and allows for kernel design choices that maximise portability directly.