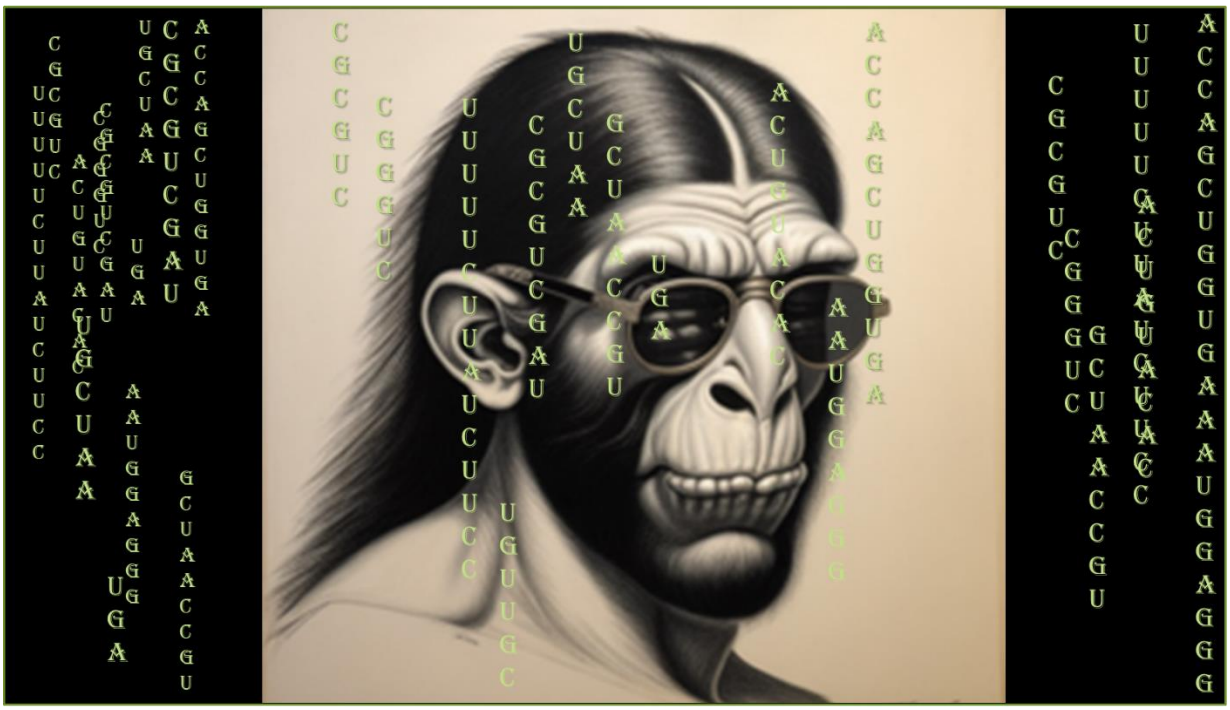
I & Vision Research Centre

Data Enormity: Biobanks in Biomedical, Psychopathological, and Paleogenetic Research



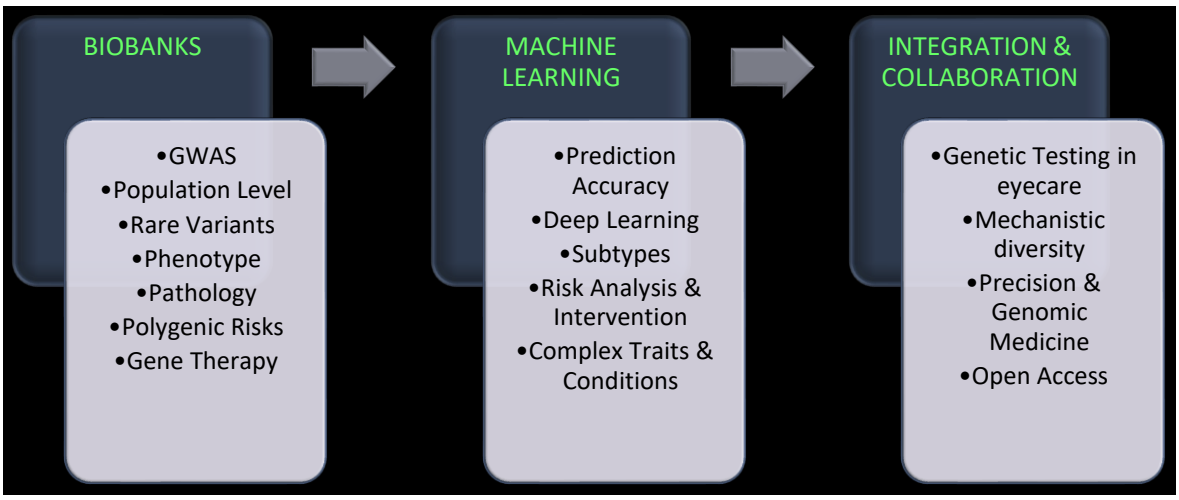
Neanderthal genes: Vulnerability to contemporary circadian rhythm disruptions, prone to sunburn, resistant to ancient European viruses (Hotpot AI, edited)

Posted 20 April 2023: https://www.linkedin.com/pulse/data-enormity-biobanks-biomedical-psychopathological

Two studies published this year are great examples of the new directions in health research and vision science: large datasets, machine learning, and molecular medicine.

Currant *et al.* (2023) performed the largest (for now) genome-wide association study (GWAS) of genes underlying photoreceptor cell multi-layer morpohology, discovering 27 new regions in addition to 111 loci with prior associations to ocular disease. Genetic data from the UK Biobank and optical coherence tomography (OCT) was used to unveil how common and rare genetic variations near PRC thickness loci may influence retinal dystrophies, including retinitis pigmentosa.

Cellular level imaging (OCT), polygenic risk scores, as well as genetic counselling are becoming a new standard of care in optometric and ophthalmic practice. Biomarker-based research and healthcare utilising eye scans, blood tests, and proteomics is advancing fast, similarly driven by changes in biological data availability and technology.



That's not all that Biobanks are being used for. At one end of the timeline, the data can be used to uncover neural substrates and morphology related to the recent trend of 'singular living' as one aspect of a global epidemic of loneliness and perceived isolation. Research in population-level neuroscience then allows identification of issues and planning for public health and urban policy of the future if the number of single-person households continues to increase (Noonan *et al.*, 2023).

At the other end of the hominid timeline, several years ago the enormous UK Biobank – which is accessible to all researchers – made a connection with the field of paleogenetics. Thanks to a fortuitous professional encounter at Oxford in 2013, 6000 rare Neanderthal gene variants were included in a chip designed to analyse blood samples, enabling detection and an idea of the proportion of carriers in the population (See Gibbons, 2019).

Thanks to other kinds of fortuitous encounters 70,000 years ago (give or take), we were able to reap the benefits of Neanderthal DNA (introgression) which made our species more resistant to several viruses (Enard & Petrov, 2018) and miscarriages (Pääbo in Connolly, 2023). Downsides of that for some populations included behavioural trade-offs like preferring evenings, feeling isolated, higher frequency of unenthusiasm and disinterest, and smoking, while for appearance it was simply not being a redhead based on the sample (Dannemann & Kelso, 2017).

The second study we would like to point out is one by Babenko *et al.* (2023). This relied on fundus photography (anterior segment imaging) of 9 types of ocular sequelae recognised as biomarkers in systemic disease. A deep learning system as well as explainability experiments were used to investigate the viability of fundus photography or in future, perhaps even smartphone photography, to detect things like kidney disease for remote and/or low income healthcare. With personal devices, timely gathering and phenotypic modelling would be another layer of data to build our understanding of how lifestyle factors and daily physiological variations influence disease progression and even eventual neurobiology.

For the population neuroscience study on solitary living, the largest impact on brain gray matter volume were factors such as time spent watching tv as well as drug and alcohol use, described as 'self-medicative behaviours' (Noonan *et al.* 2023). For self-report data, especially if looking at lifestyle and subjective states (e.g. emotion, mood) with high

explanatory power, the accuracy of the profile and analytical insights could potentially be improved through instant reporting on a personal device.

Rather than statistical techniques which are typically meant for making inferences, machine learning emphasises prediction accuracy, with the subset 'deep learning' based on artificial neural networks that can learn – like a brain. Although not quite like a brain, as the human brain has a certain array of anatomical and other biases, quite famously for the visual system. The inevitability of optical illusions based on light or colour contrasts and sneaky cortical assumptions is just one aspect. As such, many elements of a diagnosis that an artificial intelligence might be able to pick up may not be visible to or not yet consciously perceived by the human eye. The example in Babenko *et al.* (2023) was detection of novel signals for anaemia, beyond the current clinical examination of conjunctiva colour.

In other research, machine learning can be used for delineating unique biomarkers and subsets of psychopathology for risk analysis and intervention, like the 'hikikomori discrimination model' (Setoyama *et al.* 2021). This is more important when the condition is complex, spreading across multiple disparate contexts / from polygenic risks, with a variety interactive factors and characteristics that may be many-to-one. Different forces and underlying pathological mechanisms may be yielding the same behaviour or label, hence a lot of traditional diagnoses are being rewritten or subtypes coded to reflect this wealth of new biological knowledge. Innovations are accordingly taking place in terms of proteomic and molecular medicine to match patients with applicable but off-label drug use.

Eventually, once biomarkers and monitoring techniques (including personal medical devices/apps) are refined, this could reduce the demand and manpower requirements for clinical training relative to the number of patients under this mode of care. Hopefully, quality and efficacy of care and patient outcomes will not just be maintained but significantly improved.

A major value of this trajectory are the reigning principles of collaboration, data accessibility, and sharing. ARVO 2023 in New Orleans next week for example boasts a 'diversity of vision scientists' to handle the diverse mechanisms of ocular disease, and accordingly the range of new techniques, talent, and approaches in studying eye health and patient care.

As for accessibility and sharing, aside from Biobank datasets and the open GWAS Cohort… Would you like to explore Mars?

You can now! https://murray-lab.caltech.edu/CTX/V01/SceneView/intro_c.html

Funnily enough, it is presently easier to virtually roam the surface of another planet than to figure out whether Neaderthals were big game trophy-hunters capable of symbolic intent and behaviour. Besides ethnographic examples suggested by Baquedano *et al.* (2023), maybe at some point there will be a GWAS to help address that question.

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Disclaimer: *The material presented is for informational and entertainment purposes only, in summary of recent news and events. It neither reflects the views nor constitutes professional advice of the organisation. The major sources used are referenced below.*

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