The SCAnDi Project - Single-Cell Technologies for DNA Analysis

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Every cell leaves a trace

Cells can act as a vehicle by which our DNA is transferred from the individual to their surroundings - every day we deposit millions of cells through shedding, touch, injury and intimate contact. Each of these cells - if nucleated - contain DNA signatures that can identify us.

Reading out these signatures from individual cells could therefore represent a powerful tool in forensic science, using the cell as a "unit of transfer". Linking DNA profiles to individual cells could enable enhanced mixture deconvolution - where one cell could be linked to one contributor - and analysis of specimens where few cells remain. And going beyond "just" DNA, linking information about the type of cell transferred with the contributor of the cell could offer information relating to the nature of the transfer, in addition to the identity of the contributors.

There are, of course, significant challenges to the generation of DNA profiles from individual cells - from cell isolation to the sensitivity and interpretation of the analysis. The UKRI ESRC funded Single-cell Analysis for DNA Intelligence (SCAnDi) project aims to address many of these challenges, working closely with forensic practitioners to explore how the last decade's remarkable advances in single-cell technologies - which have transformed biomedical science - could translate to a forensic setting.

The challenge - unmixing the mixtures

As many as 45% of the DNA profiles generated in the UK are classified as "mixed" - consisting of two or more DNA profiles. At present, deconvolution of complex mixtures relies heavily on probabilistic genotyping software such as STRmix (Bright et al., 2016).

However, interpretation remains exceptionally challenging, especially when mixtures comprise four or more contributors.

Rather than further refining downstream interpretation alone, our team is addressing the problem at its source: the sample itself. By isolating, identifying and profiling individual cells, we aim to enable more reliable attribution of contributors, with the added potential benefit of providing contextual, activity-level information - not just identifying which contributor the DNA belongs to but, through identification of the cell-type-of-origin of the DNA, inferring information about the nature of the DNA transfer that has occurred.

Single-cell technologies - a rapidly advancing field

Single-cell genomics has been one of the most transformative new tools in biomedical science, and techniques for the isolation and profiling of genetic information from individual cells have proliferated dramatically over the last decade.

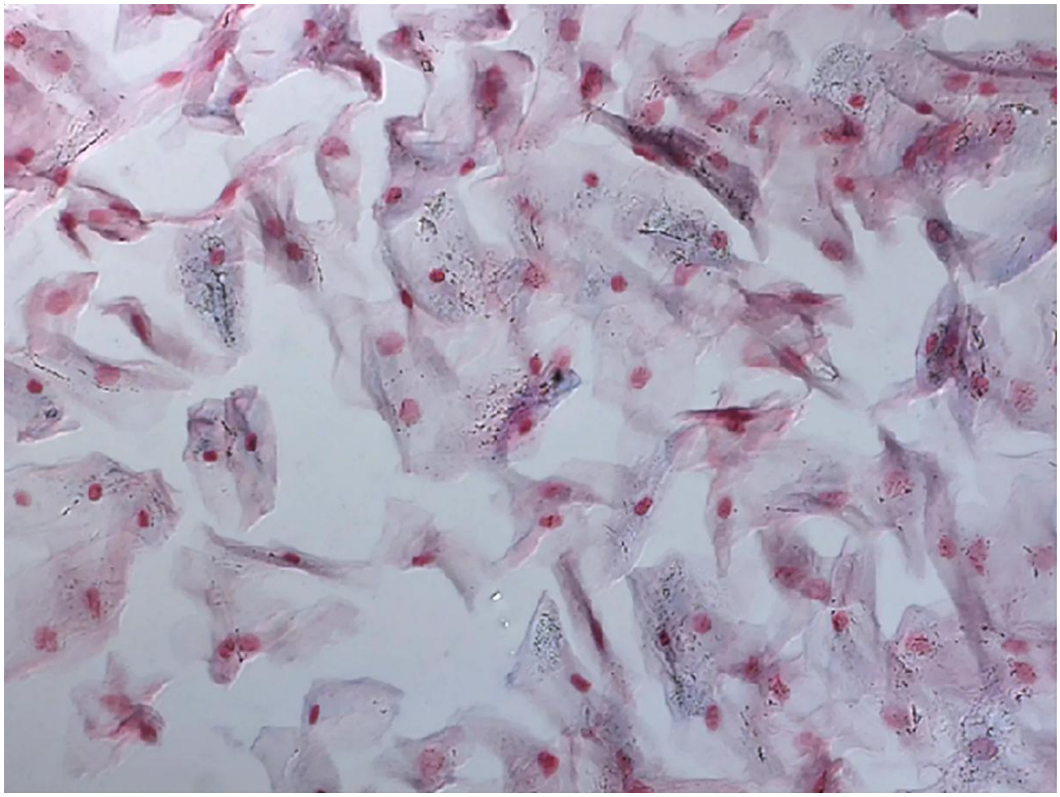
Forensic scientists were actively engaged with single-cell analysis long before the current technical revolution, including the UK's Forensic Science Service (to which the SCAnDi project can trace its ancestral roots). The rapid development of new technologies and approaches have created new opportunities for forensic DNA analysis, including the Deparray platform [Anslinger & Bayer 2019, Schulte et al 2024] and Laser Capture Microdissection (LCM) which, while not used in UK casework, demonstrate potential for mixture deconvolution [Dawnay & Sheppard 2023, Groombridge et al 2025, Dawnay & Sheppard 2025].

In the SCAnDi project, we have explored novel cell isolation technologies which can, in parallel, isolate and image individual cells. Imaging cell sorting is a new technology that does just this - allowing us to image cells and sort them, individually, into wells of 96-well plates for downstream processing. In the initial phase of the project, we worked with human cell lines to explore the logistics of cell sorting and compatibility with forensic DNA readouts.

In particular, we wanted to explore the ways in which whole-genome amplification (WGA) impacts upon this readout. Since a single diploid human cell contains just 6 pg of genomic DNA, a haploid cell just half that - far below the input requirements for current Short Tandem Repeat (STR) typing kits run on Genetic Analysers - we require a process that evenly amplifies the genome, preserving STR loci and alleles with high sequence and length fidelity.

Using this approach we generated proof-of-concept data that indicated that complete STR profiles - either using capillary electrophoresis or next-generation sequencing approaches - can be obtained from a single cell. However, the genomes of cell lines are highly unusual and often aneuploid - and thus do not represent an ideal model of a real-world sample. To move closer to a forensic specimen, while still allowing scope for technical development, we generated artificial mixtures of blood cells from six different

individuals. This allowed us to continue technical development while also assessing the feasibility of mixture deconvolution - all the while working towards a framework that could be applied to samples that more closely represent real-world specimens.



Getting the right samples

One of the biggest challenges currently facing UK forensic scientists is access to relevant biological materials for their research. Simple body fluids such as blood and saliva or biological traces such as fingermarks or touch DNA are relatively accessible, while other samples such as semen or post-coital swabs are extremely difficult to obtain [Speck & Hanson, 2019].

The initial focus in the SCAnDi project has been driven by the UK Government Mission relating to Violence Against Women and Girls (VAWG) [ref], which includes instances of sexual contact where mixed profiles are commonly obtained, and where support for competing activity-level hypothesis is unable to be provided using DNA evidence alone [Biedermann & Hicks, 2016].

As such, the key samples of interest for method development included pre- and post-coital swabs taken from consenting couples. Ethical approval for sample collection was obtained from Liverpool John Moores University, with these complex samples requiring dialogue with the University Research and Governance Team and the University Research

Ethics Committee and also project Stakeholders who advised on collection protocols and contexts of forensic interest. Detailed participant information and consent forms were required for the collection of such sensitive samples, and it was necessary to include information to safeguard against coercion and to signpost sexual assault support services to fully protect and inform volunteers.

Although limited by potential biases in collection and volunteer uptake, this pilot study successfully established a framework for a Forensic Research Participant Database (FoRPD) which allows us to notify those individuals of any ethically approved research research project currently seeking volunteers. In doing so, the database seeks to notify those individuals most likely to provide samples for research instead of promoting open calls with limited effect.

The FoRPD project has provided an essential platform to support not just the SCAnDi project, but also other UK forensic research including the Swab Out Crime Initiative [FCN, 2026] and several PhD studentship, with potential to widen participation across multiple UK Universities also being considered.

Doing the right science - the importance of stakeholder engagement

There is an incredible diversity of approaches and technologies that could be applied in the development of single-cell approaches for forensic DNA analysis, but the forensic science community has specific constraints on the translation of new technologies. Thus, the project was encouraged to engage with a dedicated community of stakeholders - practitioners in forensic science and its regulation, as well as representatives from across the justice system. This has been critical in framing the project in a real-world context, while still allowing space for speculative scientific research.

Through stakeholder engagement meetings and community building events, we've had the opportunity to co-develop aspects of the project - both broadening the focus in terms of unmet needs, but also refining the need for realistic solutions, especially in terms of generating data that would be compliant with the UK National DNA database.

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Furthermore this engagement highlighted the benefits single-cell technologies could bring to contested testimonies and activity- and offence-level propositions for the

scientist and court, respectively, using cell-of-origin data to bring context where mixed profiles cannot. It also brought attention to the need to explore approaches beyond the separation of sperm and epithelial cells, and the need to determine feasibility of application in other cell types and other situations where DNA is transferred.

In November 2025, together with the Trust and Triage projects which arose from the same UKRI funded sandpit, we hosted an event at the House of Lords to share outcomes and outlooks from the projects with our stakeholder communities. We have also connected with communities of researchers working on the forensic application of single-cell technologies across the UK, Europe and the US.

The general public are key stakeholders in the justice system, and we have run a number of accessible science events targeting both children and adults - including the Edinburgh Science Festival (available to view on YouTube Extracting Evidence | Edinburgh Science Festival 2025.), which will again be delivered at the Royal Institute in London in June 2026. We also developed a Lego themed murder mystery activity that introduces forensic science to a young audience [Dawnay et al 2025]. and have visited a number of schools and events, with the hope of inspiring the next generation of forensic scientists.

Members of the SCAnDi team.

Towards proof-of-concept: advances and limitations

From its inception, the project envisioned a 5-10 year timeline to delivery of a usable forensic tool. Currently at a proof-of-concept phase, we have generated data - currently in preparation for publication - that demonstrates the feasibility of routine generation of complete STR profiles from individual cells with >95% allelic matches to a donor derived reference. This approach has successfully been applied to deconvolute 6-contributor mixes, and we are optimistic that this will translate well to more realistic samples and eventually casework material.

However, several challenges remain and we are realistic about the barriers to translation - we have seen that whole genome amplification can have an impact on STR profiles, and even where reasonable profiles are obtained we can see poor inter-locus balance, loss of whole loci, poor heterozygote balance, and allelic dropout. Resolving this is now a major focus of our work.

Similarly, translation to casework applications will bring with its own challenges - from variations in sample collection, age and storage to DNA degradation; it is nearly impossible to replicate these samples for a research and development environment and so continuous improvement and bespoke approaches will almost always be required. Furthermore, there is much to consider in terms of governance, validation and regulatory requirements that would be associated with implementation of such an approach in the UK justice system.

Future technologies

Although delivering to current needs has been critical in the project's development, there is also a clear need to explore how emerging technologies can assist in the resolution of complex DNA mixtures.

Prof Michael Chen at the University of Edinburgh has been leading the development of single-use microfluidic devices for sperm cell separation from complex mixtures - with the aim of developing in-field tools for cell-type specific and single-cell profiling.

Artificial Intelligence (AI) is transforming many aspects of biological research, and within the SCAnDi project Prof Ardhendu Berhera at Edge Hill University has been exploring the potential of AI for automated cell type identification - particularly from images or other data arising from single-cell analysis.

We have also explored the application of alternative sequencing based approaches - which potentially would scale more appropriately if (as is likely the case), hundreds, or even thousands of single cells were to be profiled in parallel from a single sample. Such approaches would also enable the analysis of the cell's genome beyond STRs, including single nucleotide polymorphisms (SNPs) and mitochondrial DNA. To do this we have

explored existing forensic NGS approaches as well as long-read sequencing using Oxford Nanopore technologies.

Beyond DNA, we are also investigating the potential of other information that single cells could provide - including epigenetic information and RNA that may still reside in the cell. Although there are many challenges with both of these approaches, they offer additional routes to assign cell type identity to DNA profiles beyond imaging.

Future Outlook

The SCAnDi project has highlighted a national interest in the application of genomic technologies - including single-cell analysis - in forensic science, and we are optimistic that the project will not just deliver transformative science, but - and perhaps more importantly - leave a collaborative network of researchers as its legacy. In addition, aspects of the project such as the ForPD have the potential to support a much wider range of research programmes in forensic science.

There is such interest in this topic - from both researchers internationally, and their respective justice systems, that it is inevitable that single-cell approaches will move ever closer to operational use. While significant amounts of research and development still remain to be done, it represents an opportunity to resolve the challenge of complex DNA mixtures and ultimately provide greater context to DNA transfer events. This has the potential to increase the overall evidential value of DNA profiles and - hopefully - avert miscarriages of justice in the future.

Acknowledgements

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