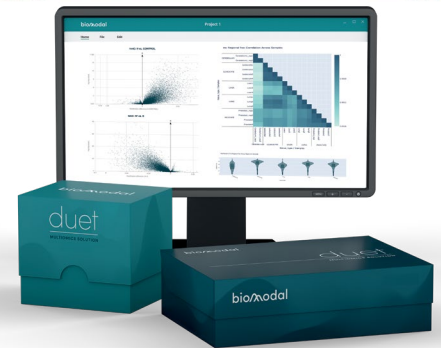


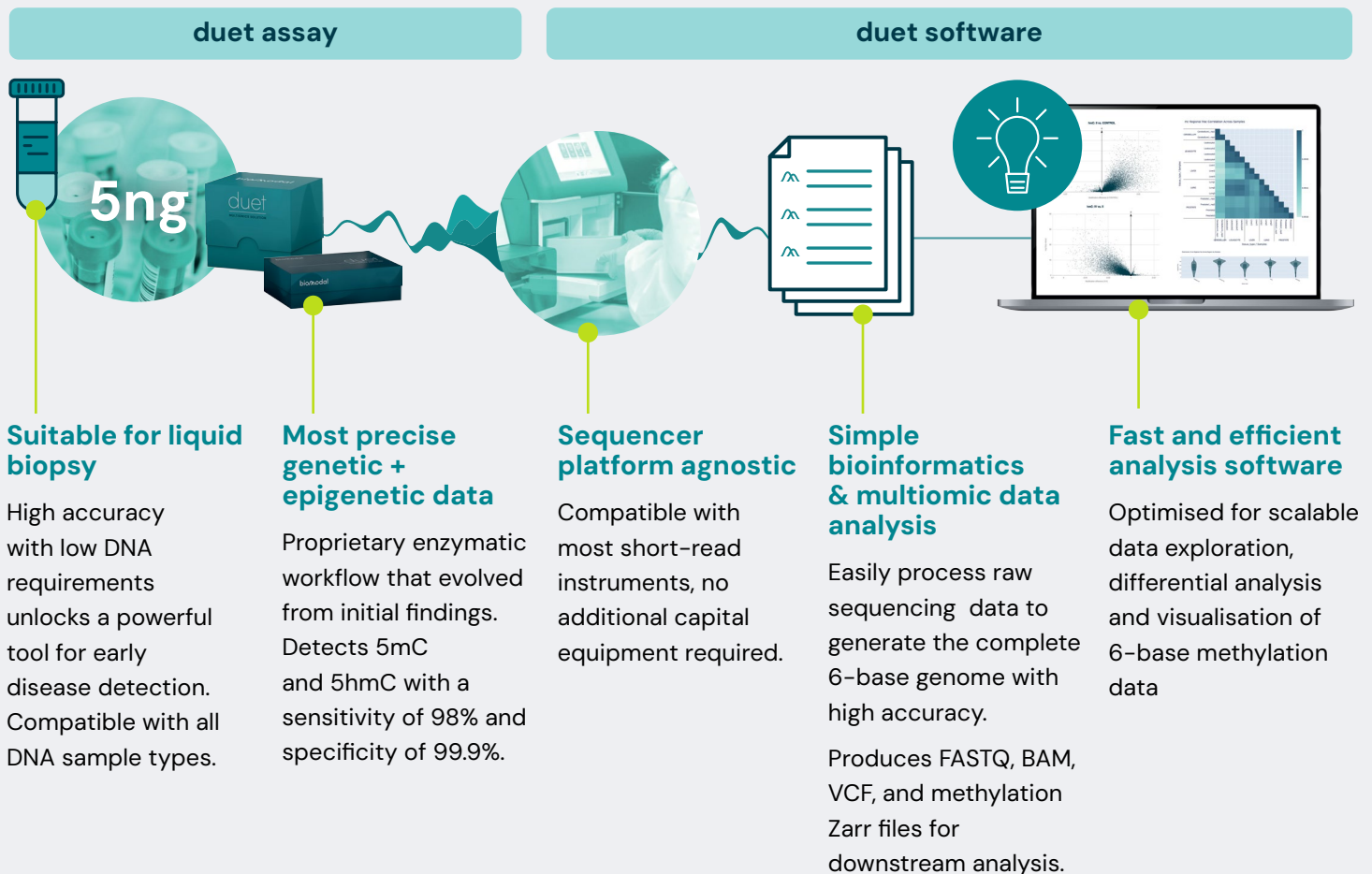
duet multiomics solution evoC

DNA mutations alone rarely tell the full story of disease. While genetic variation can drive pathological processes, it's often the regulatory systems beyond the genome— the epigenome— that shape cell behavior. Among these, DNA methylation at cytosine bases is a key player, influencing gene expression and cell identity. Aberrations in methylation patterns, particularly at 5-methylcytosine (5mC) and its oxidized form, 5-hydroxymethylcytosine (5hmC), are increasingly recognized as early indicators of disease.

To fully understand disease progression and harness methylation patterns as biomarkers for early detection, researchers need tools that provide a comprehensive view of these epigenetic marks. biomodal's duet multiomics solution evoC enables simultaneous detection of DNA sequence, 5mC, and 5hmC on a single molecule, offering unprecedented insights into the interplay between genetics, epigenetics, and disease development.

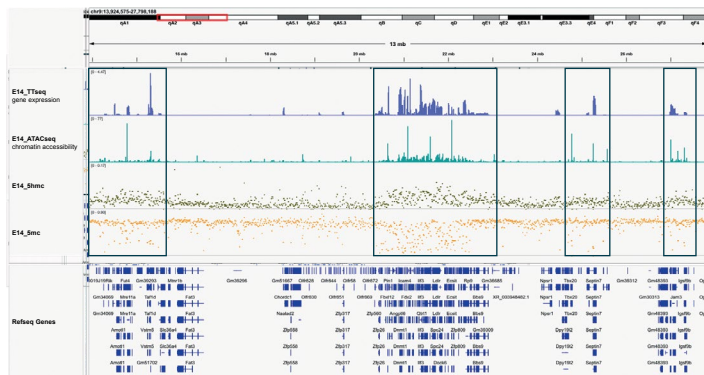
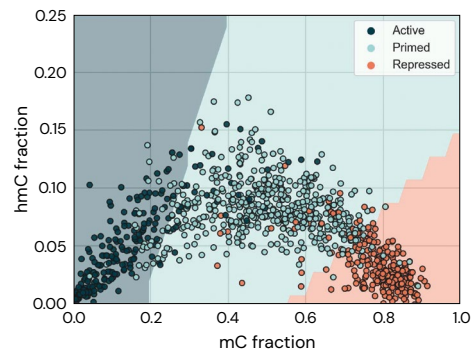


One sample. One workflow. One solution. One standard method to interrogate all samples.



The 6-base genome provides insight into the dynamics of the genome, providing an early window into biological change

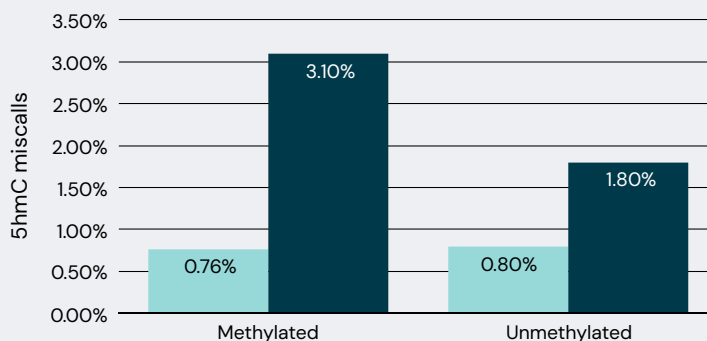
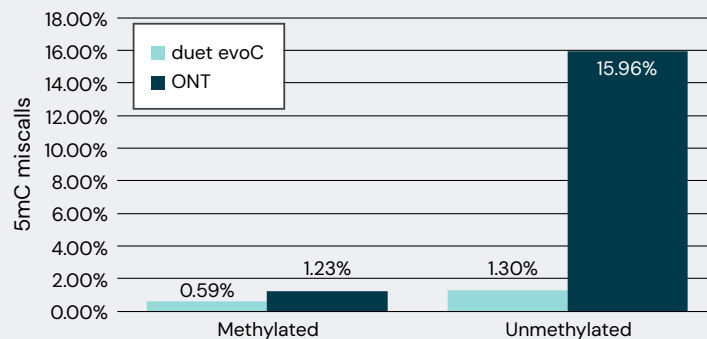
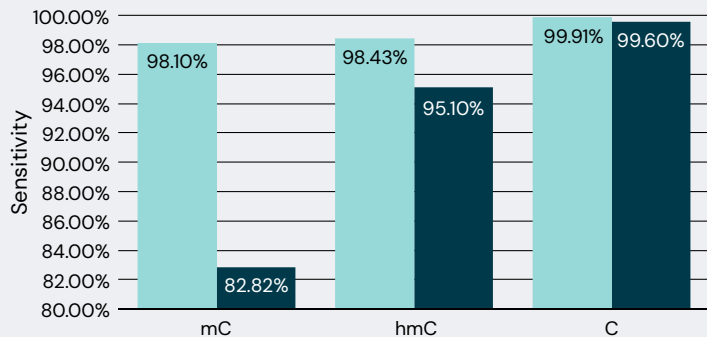
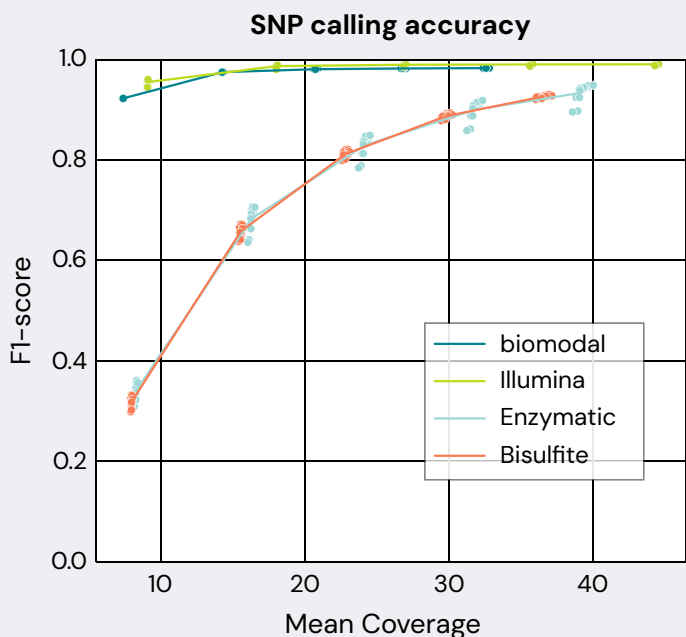
The 6-base genome can provide insight into genome dynamics focussed on enhancer regions that regulate expression of distal genes. Enhancers can be repressed, primed, or active. Here we plot 5mC and 5hmC levels at enhancers across the genome. The dot colour indicates histone-derived enhancer state and background shading is a prediction based on 6-base data. The data show that an increase in 5hmC identifies regions that are committed to an activating trajectory as they move from high 5mC inactive state to an unmethylated active state.



Using the model E14 mouse embryonic stem cell system nascent gene expression (blue), chromatin accessibility (green), 5hmC (brown), and 5mC (orange) levels are plotted for a region of the genome. Boxes highlight regions where gene expression, chromatin accessibility, and increased 5hmC levels are aligned with a reduction in 5mC levels. The data show that 6-base data can be used to infer gene expression and chromatin accessibility, providing insight into genome dynamics that would otherwise be lost in a conflated traditional modC readout.

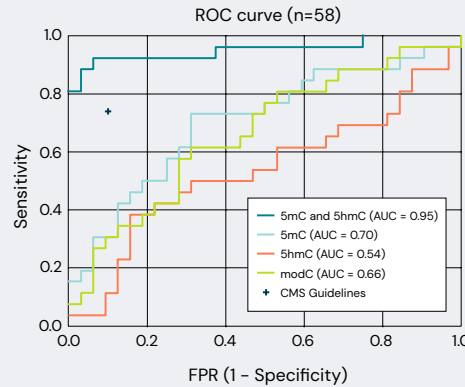
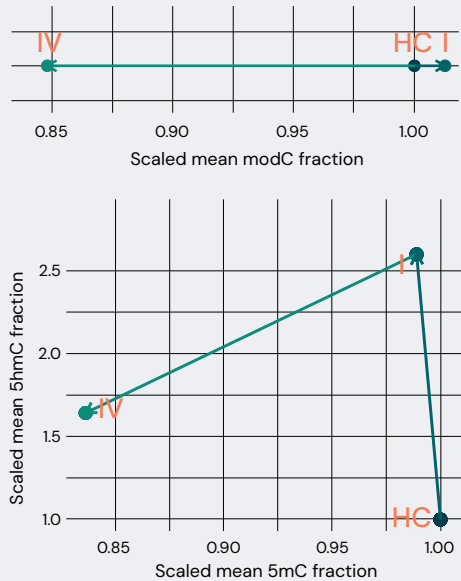
duet evoC delivers accurate genetic and epigenetic information

duet evoC delivers genetic data that enables SNP calling accuracy greater than or equal to current genetic and epigenetic sequencing technologies. In the same dataset and from the same DNA molecule duet evoC provides complete single-base resolution methylation information, distinguishing 5mC from 5hmC.



5mC and 5hmC are synergistic biomarkers for early CRC detection

Highly accurate 6-base sequencing enables dynamic multidimensional examination of epigenetic changes across the genome. For example, the top left figure shows the 5-base methylation difference detectable at an enhancer region does not differentiate healthy controls from stage I. By using the second dimension provided by 6-base data at this enhancer, the true biological picture is revealed and it becomes possible to distinguish between healthy, stage I and stage IV CRC from cfDNA. By examining multiple regions across the genome in samples, biomarkers can be discovered and used to identify the CRC-specific early-activating regions that can be used to build effective disease classifiers to detect stage I CRC samples.



- Top-right figure: The further a ROC curve is to the top left, the better a classifier's performance
- Using a combination of 5mC and 5hmC biomarkers to detect stage I CRC increases classifier performance compared to using 5mC, 5hmC or modC biomarkers alone (top-left figure)
- 5mC and 5hmC classifier performance compares favourably to US CMS guidelines

Integrated analysis software accelerates 6-base sequencing data to biological insights

Unlock the full potential of 6-base sequencing data with a versatile analysis software designed to fast-track raw multiomic datasets to meaningful biological insights, in one workflow.

modality XPLR is a powerful analysis tool designed to help visualise multiomic data, enabling researchers to extract publication-ready insights, without the bottlenecks. Consuming raw outputs from the duet pipeline, modality XPLR empowers users to explore complex datasets and uncover biological patterns. Through biological QC, users can quickly explore the biological characteristics of their data with interactive PCA, and violin plots before moving on to customisable DMR analysis and visualisations. (Figures 1-4).

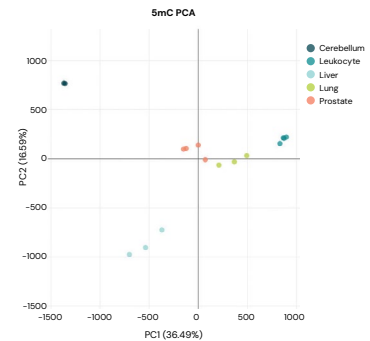


Figure 1: Principal Component Analysis for 5mC between tissue samples. These plots can be used to observe sample relationships for 5mC and 5hmC, and are included in the modality XPLR Biological QC report as standard.

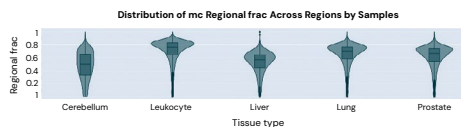


Figure 2: Violin plot showing the distribution of 5mC fractions over gene bodies by tissue type, indicating tissue-specific differences in methylation profiles.

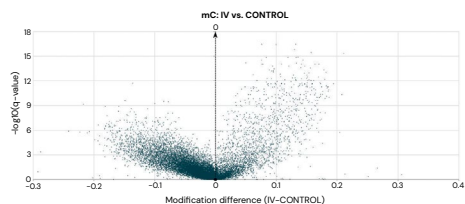


Figure 3: Volcano plot showing 5mC DMRs for Healthy Control and Stage IV CRC cfDNA samples, using TCGA tissue-derived DMRs as biological priors.

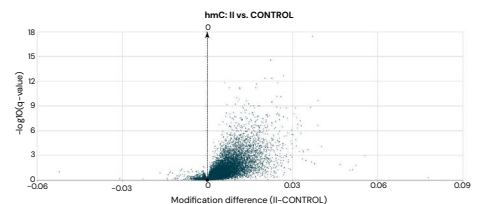


Figure 4: 5hmC DMRs between Healthy Control and Stage II CRC cfDNA samples, showing a trend early-stage 5hmC hypomethylation. 5hmC is an intermediate mark on the TET-mediated demethylation pathway, and is indicative of later gene activation.

duet evoC software and assay specifications

Input requirements	cfDNA 5–30ng gDNA 10–80ng
Assay time	Approx. 18 hours
Assay hands on time	Approx. 10 hours
Shelf-life	Minimum 3 months

duet software file output

Resolved FASTQ	Unaligned 6-base data
6-base BAM	Aligned 6-base data for downstream analysis
VCF file	Germline variant calls
QC reports	csv and html reports
Zarr store	6-base methylation analysis

Ordering information

Catalogue number	Product name	Product description
6205	duet multiomics solution evoC 8x reaction	Pre-sequencing workflow + post sequencing software for 8 reactions
6206	duet multiomics solution evoC 24x reaction	Pre-sequencing workflow + post sequencing software for 24 reactions
4103	UDI 8x reaction	UDIs for 8 reactions
4102	UDI 24x reaction	UDIs for 24 reactions
4104	UDI 96x reaction	UDIs for 96 reactions

Disclaimer

The duet multiomics solution is for research use only.



biomodal

Chesterford Research Park
Cambridge, UK
CB10 1XL

+44 (0) 1223 800 700
biomodal.com
info@biomodal.com

biomodal