

Methylation Detection with PacBio HiFi Sequencing - ASHG 2021

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In this talk, Dr. Aaron Wenger describes how PacBio HiFi reads (15 kb - 25 kb, & greater than 99.9% accuracy) provide the most complete view of human genetic variation, including small variants in difficult-to-map regions and structural variants genome-wide. Further, PacBio sequencing simultaneously detects epigenetic modifications without requiring a specialized library preparation step like bisulfite conversion. This ability is commonly used to characterize epigenetic marks in bacterial genomes. Recent improvements in read length and data analysis have extended the ability to include the 5mC methylation that is present at CpG sites in human genomes. Using a deep learning model that integrates sequencing kinetics and base context, the accuracy of 5mC detection in humans for individual HiFi reads is around 80%. Combining multiple reads, the concordance to EMseq and bisulfite sequencing reaches around 90%. The single-molecule resolution of methylation, together with phasing from accurate long reads, allows the detection of allele-specific methylation patterns such as parental imprinting. This ability to detect bases and modifications allows HiFi sequencing to provide the most complete genome and epigenomes with a single technology and library preparation.

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Transcript

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@cemanthad · 7 years ago

Hi Aaron, Does the training data have to be from the same genome? In other words, can you train the algorithm using a human data training set and then apply it to a different organism's (non-human) genome?

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S @soulsqueezer4022 · 7 days ago

Hello, I am not Aaron but yes and no. If you train a model from a human genome and then apply it to mouse data, things should go pretty well. If for example you try to apply it to an insect or even a plant, where the genomes and epigenomes substantially differ, this would not be suitable. So, in principle you would want to use a closely related organism, but that of course also depends on your research question.

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 **@camenthead** 2 years ago
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 1  Reply



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 **@xkm1948** 2 years ago
Would be very cool to have asymmetrical modified base detection. mCH is prominent in neurons and this method wont be able to capture that.

 3  Reply



 **@PacificBiosciences** 2 years ago
Symmetry is a design choice of our current algorithm, but it could be extended in the future to consider strands separately. Thanks for the comment!

 1  Reply

 **@soulsqueezer4022** 7 days ago
Is it possible to detect 5hmC together with 5mC? Also, in non-CpG content (for 5mC). Is there an update to this video coming? This video is still linked to PacBio's website when looking into epigenetic detection with PacBio.

  Reply

URL

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