Computational Analysis of Methylome Sequencing Data

Master Thesis Bioinformatics

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Outline

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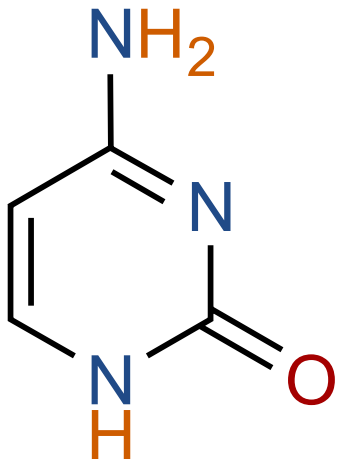
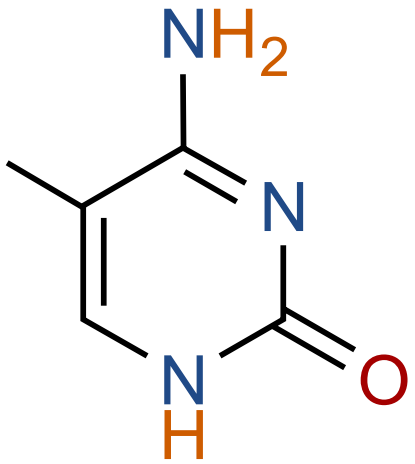
- Entirety of **methylated nucleotides** (e.g. cytosines) in the *DNA*
- Addition of a methyl group converts cytosine into **5-methylcytosine**





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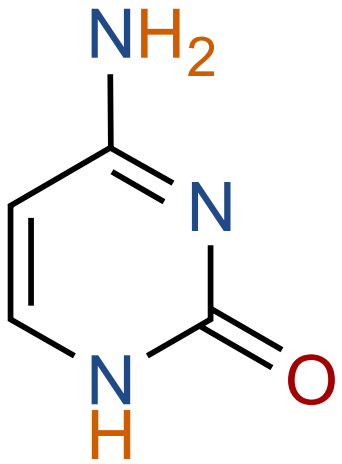

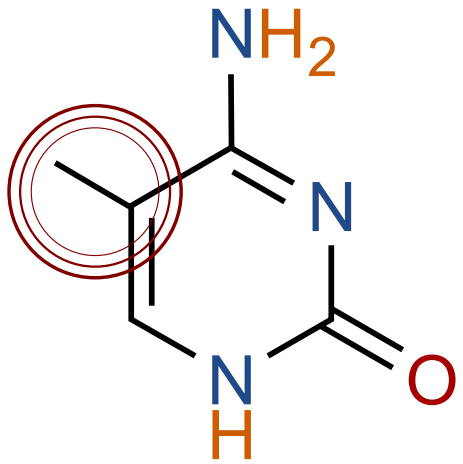

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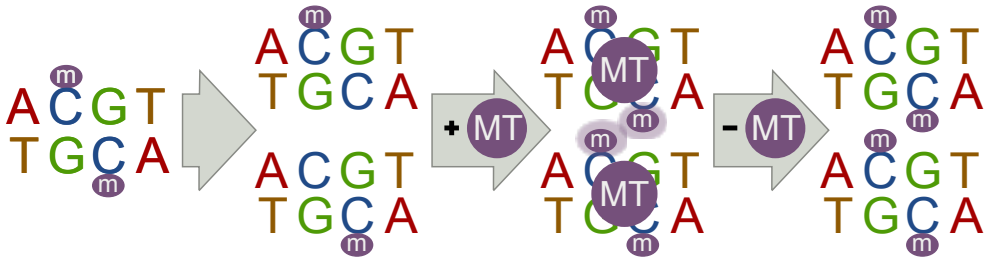

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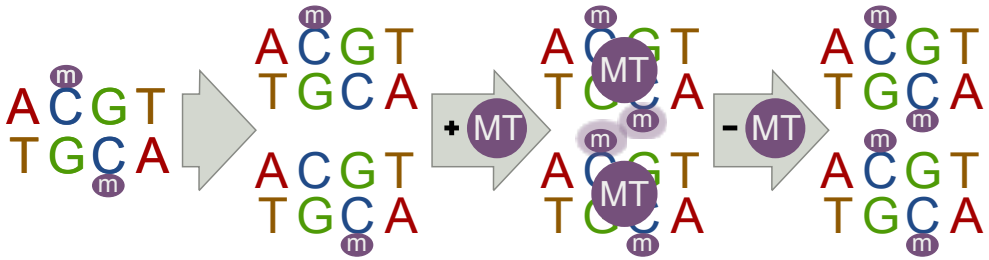

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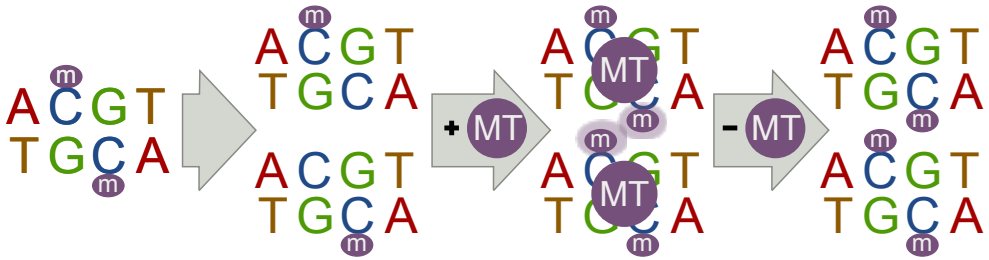

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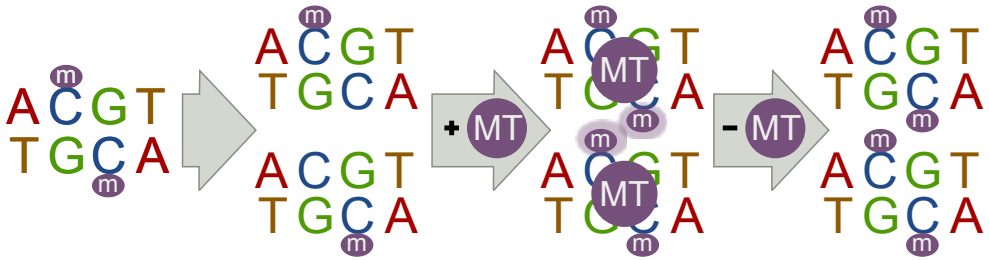

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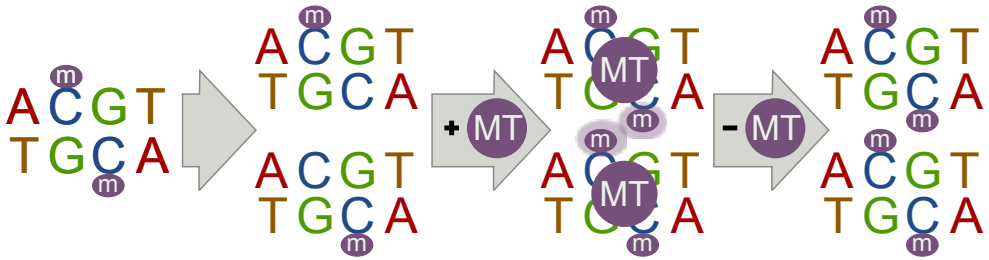

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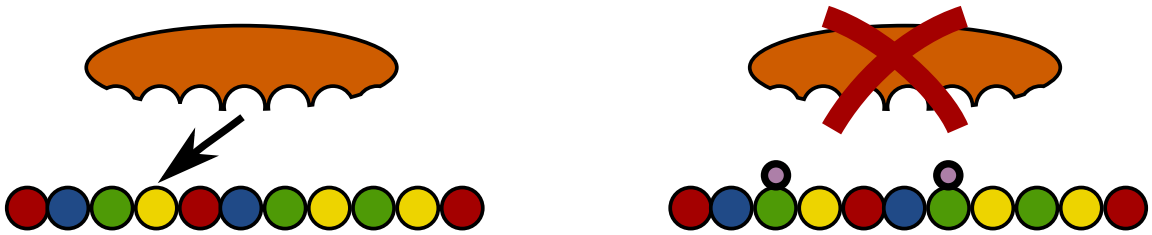

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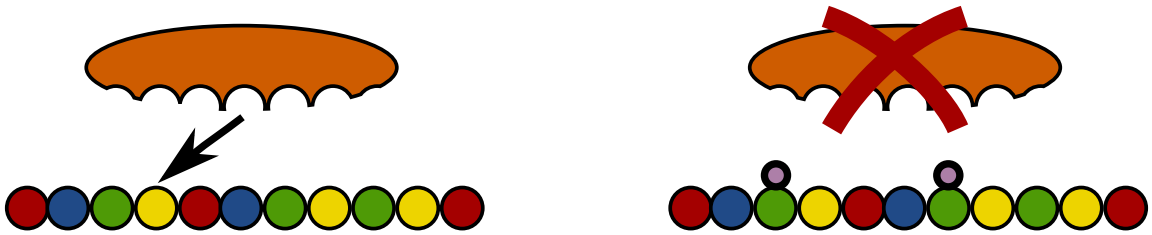

- Relevance for different research fields:
  - **Developmental biology** (e.g. for association studies)
  - **Medicine** (e.g. for tumorgenesis)
  - **Ecology** (e.g. documentation of environmental changes)
  - ...

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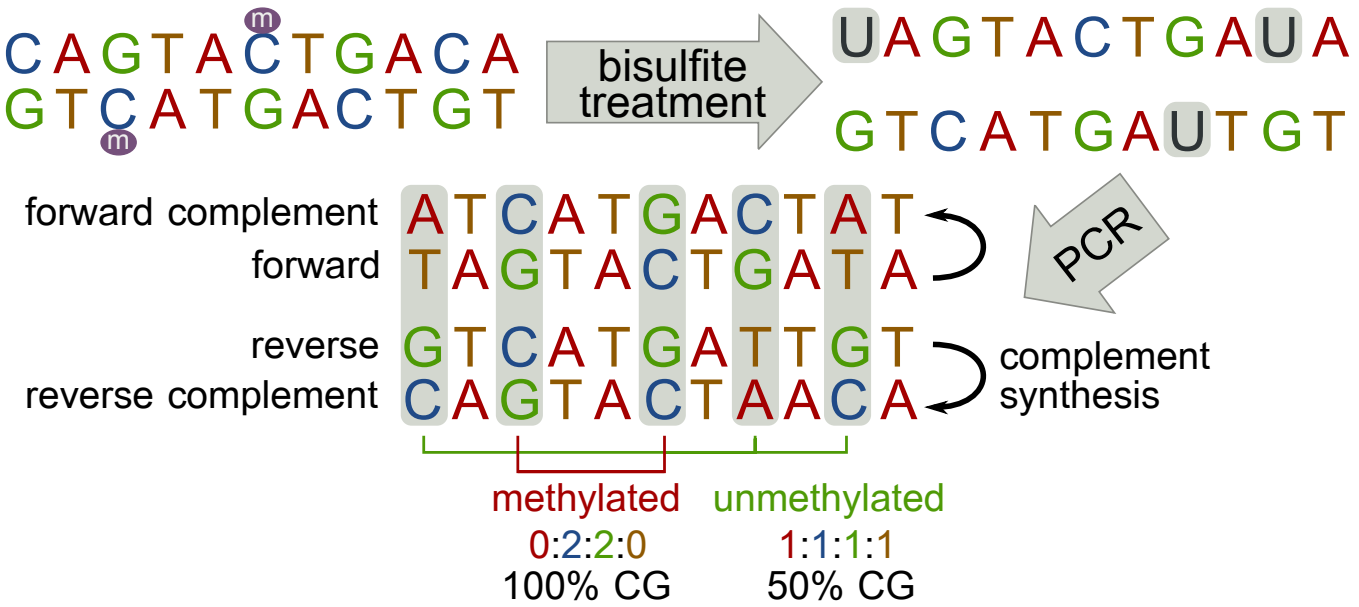

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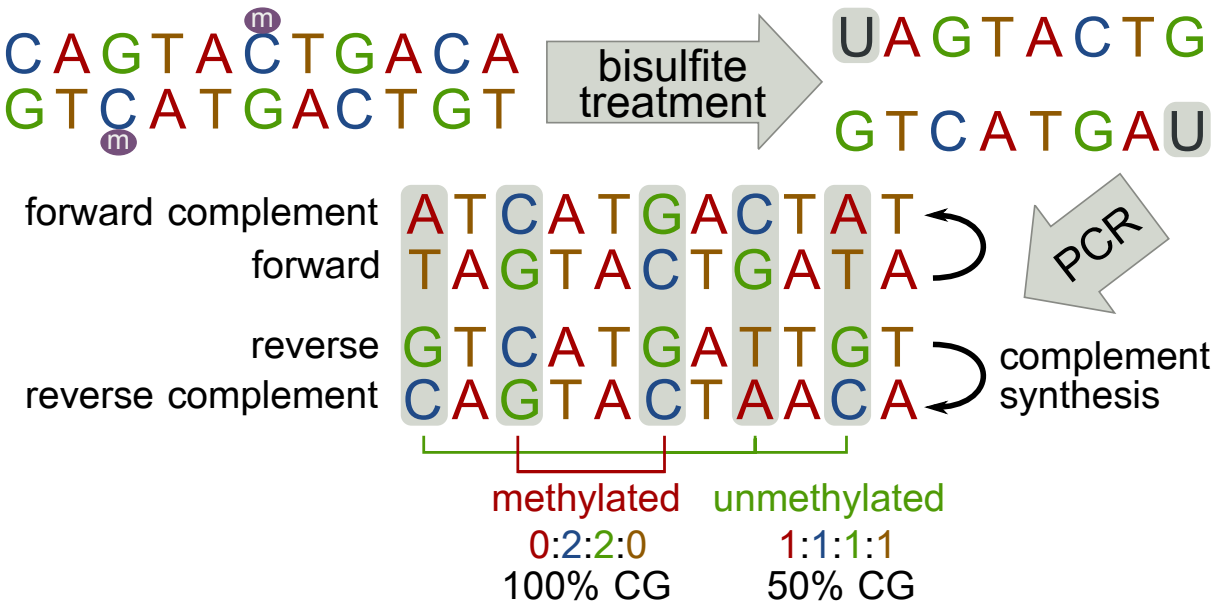
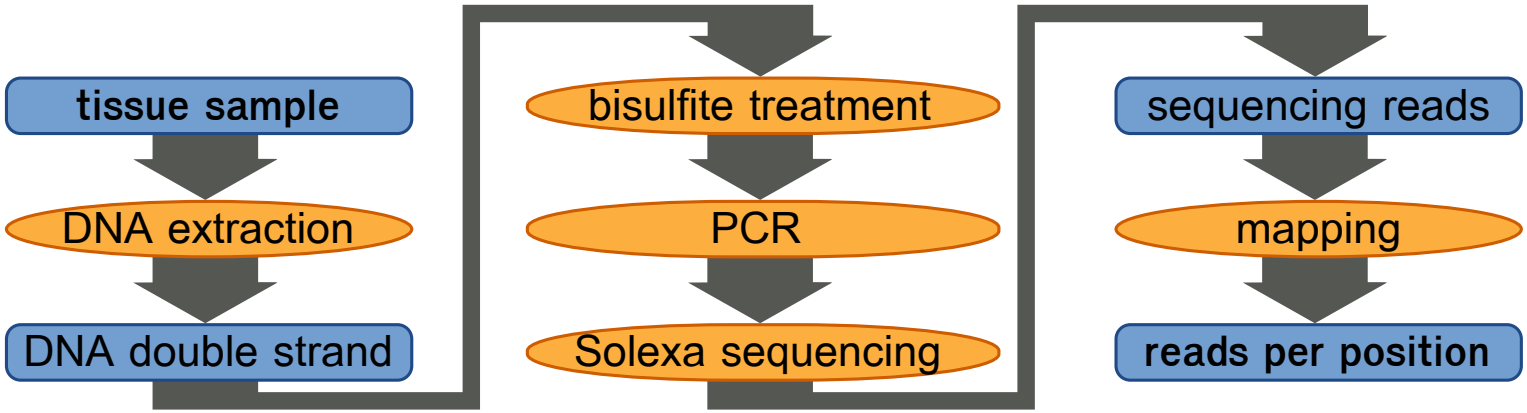


- Sequencing now reports only **methylated cytosines**

Sequencing Protocol

- Bisulfite treatment inserted into the **sequencing protocol**



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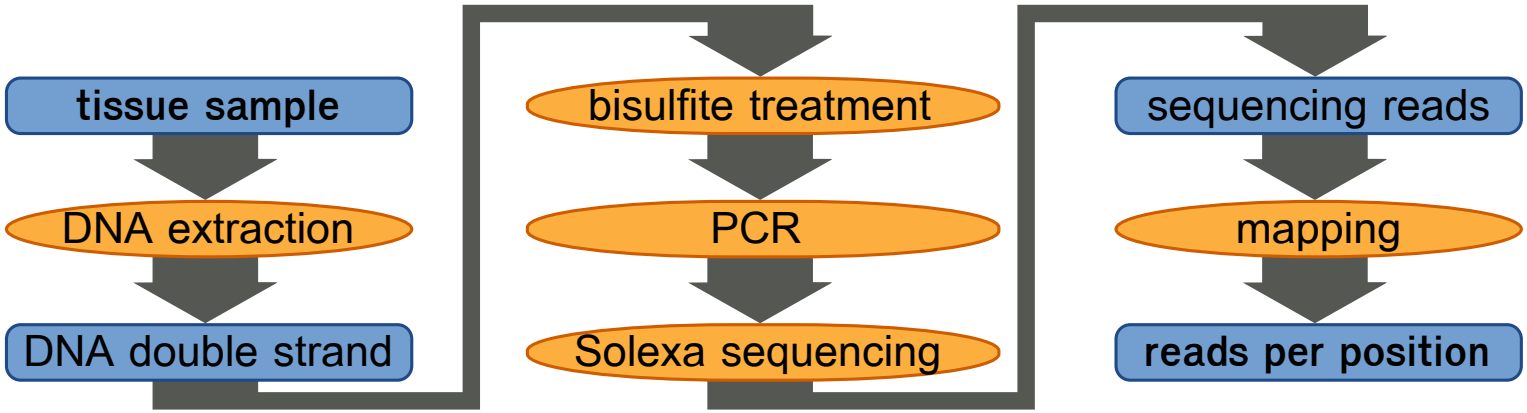

- **Methylation rates** calculated from the read counts per position

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Mapping

Problematic due to repetetive regions and reduced sequence complexity.

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Idea

Use machine learning to obtain an additional **confidence measure** based on sequence patterns.

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- Quantification of the **likelihood** for candidate nucleotides to be methylated

⇒ **Confidence score** between 0.0 and 1.0

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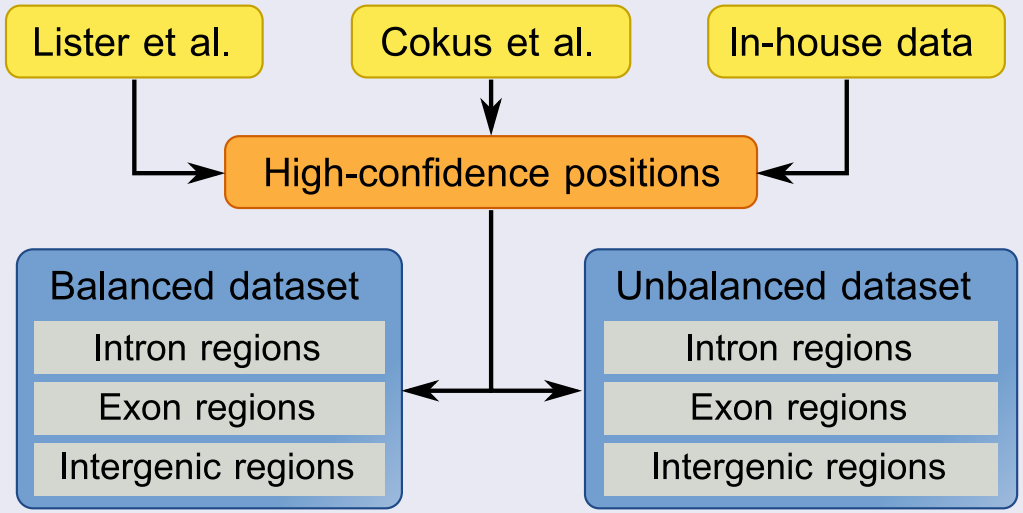
Solution

Manual creation of a **high-confidence dataset**



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- Prediction of methylations on **whole genome** with best classifiers

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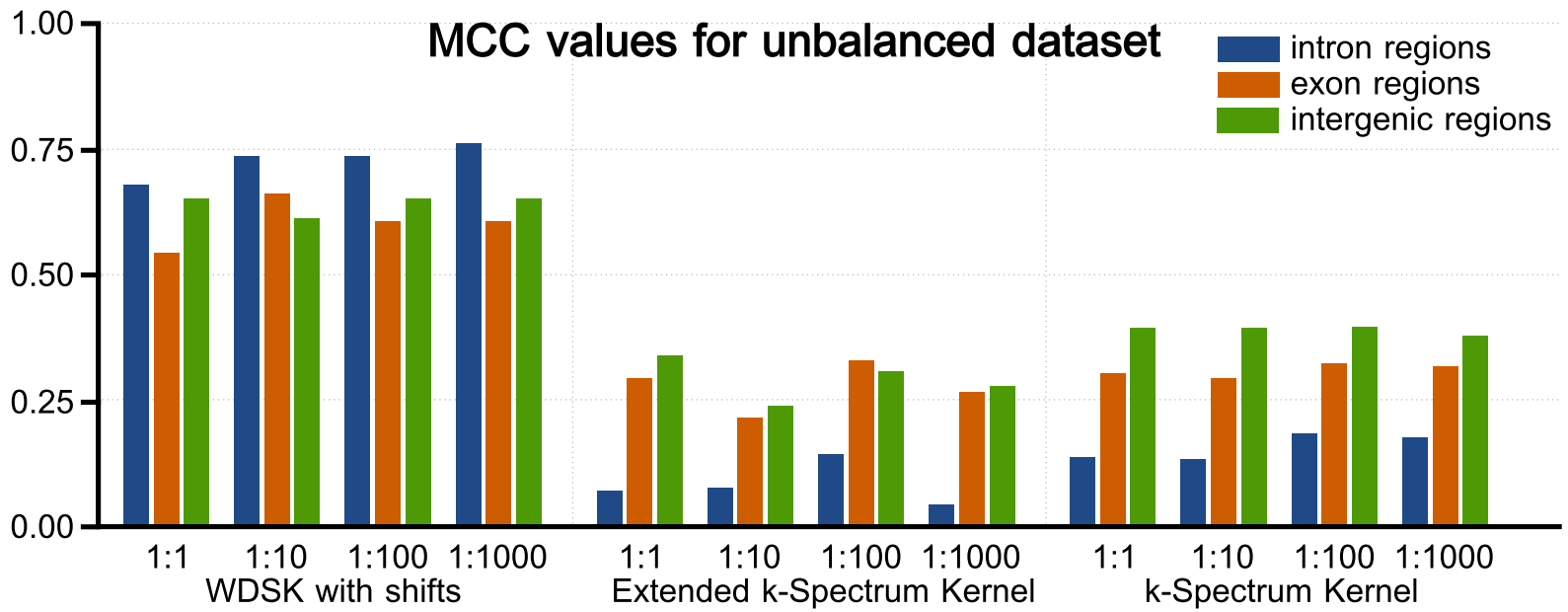
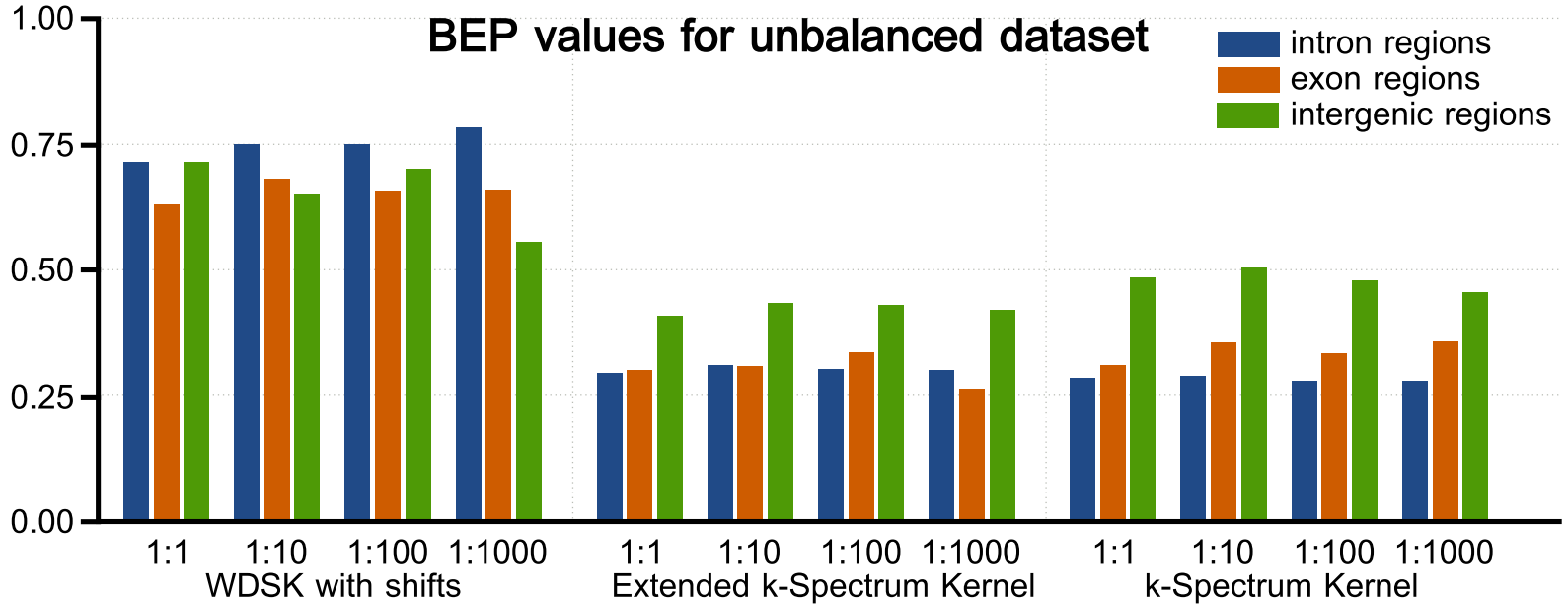
Performances on Unbalanced Dataset





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- **However:** Few reported methylated positions occur in original datasets

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- Application of supervised learning methods requires **more reliable datasets**
- **Unbalanced data** is more realistic but leads to additional complexity

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- **Unsupervised** learning methods
- **Recent research** promises methylome data as byproduct of standard sequencing

Thank you for your attention!

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- Dr. Karsten Borgwardt
- MLCB group
- WeigelWorld
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Most important sources:

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