

## METHODS

# Methods for discovering genomic loci exhibiting complex patterns of differential methylation; Supplementary Materials

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## Simulation studies

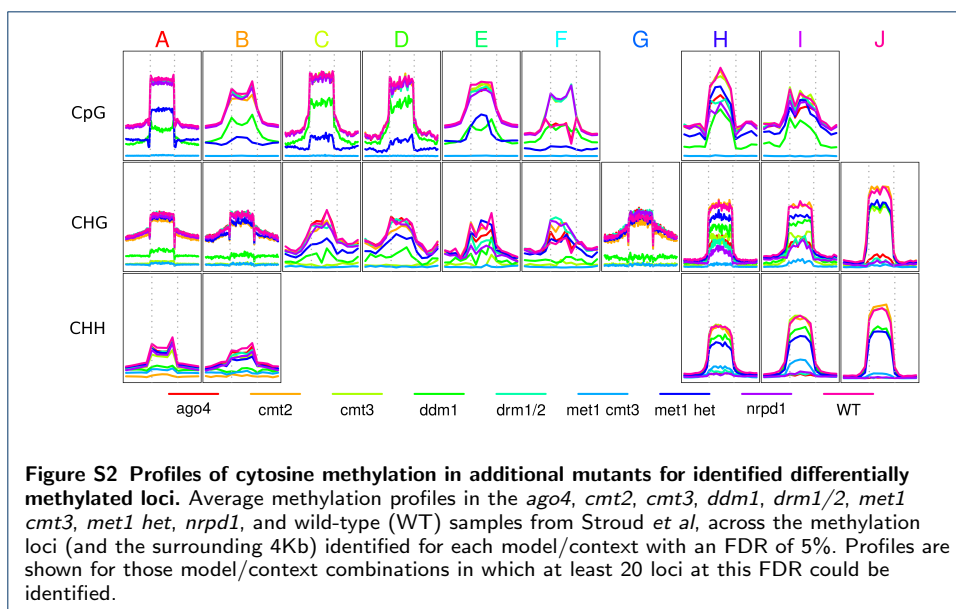
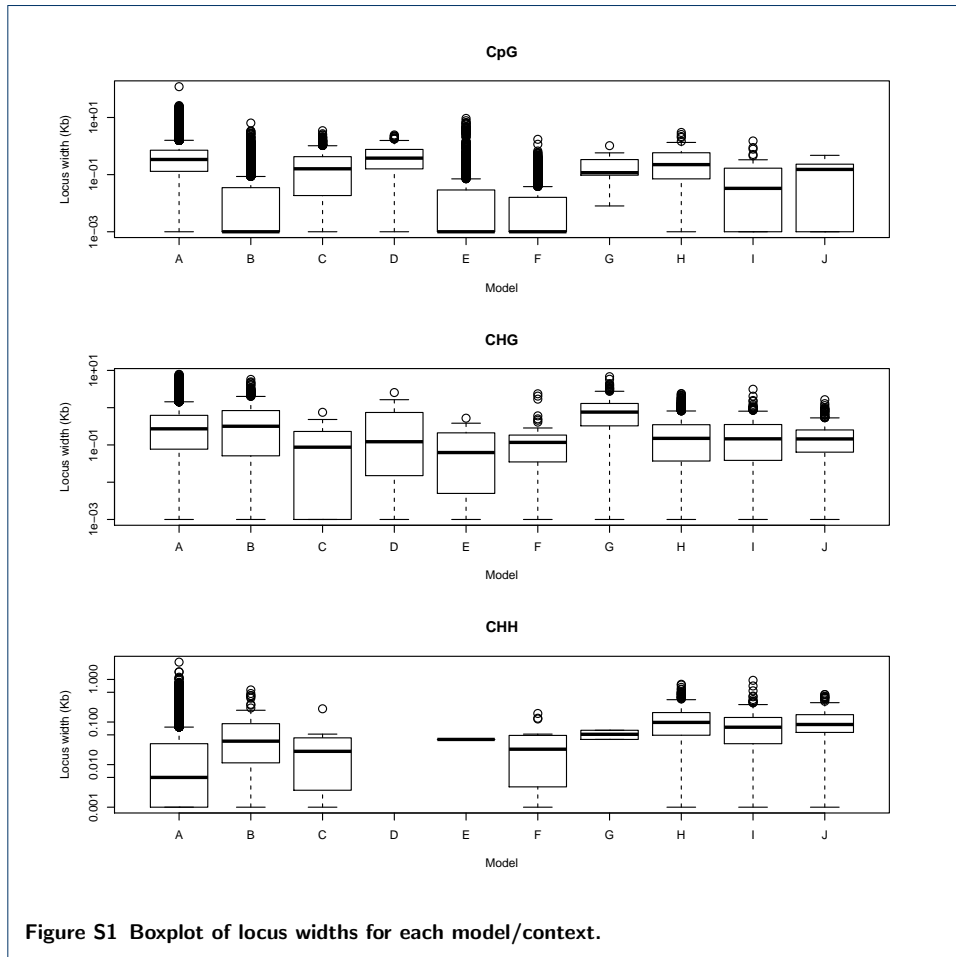
Data are simulated using WGBSSuite version 0.4, modified to include the effect of non-conversion rates by introducing a binomially distributed error in the number of methylated cytosines reported at each site. Plant-representative parameters were estimated by applying the `analyse_WGBS.R` script provided by WGBSSuite to the first million CpG cytosines on chromosome 1 of a single wild-type sample and the *dcl2/3/4* triple mutant in the Stroud *et al*[?] dataset. Data were then simulated for one hundred thousand cytosines using the following command, where XXX and YYY are placeholders for the number of samples in each replicate group and the magnitude of difference in the proportion of methylation respectively.

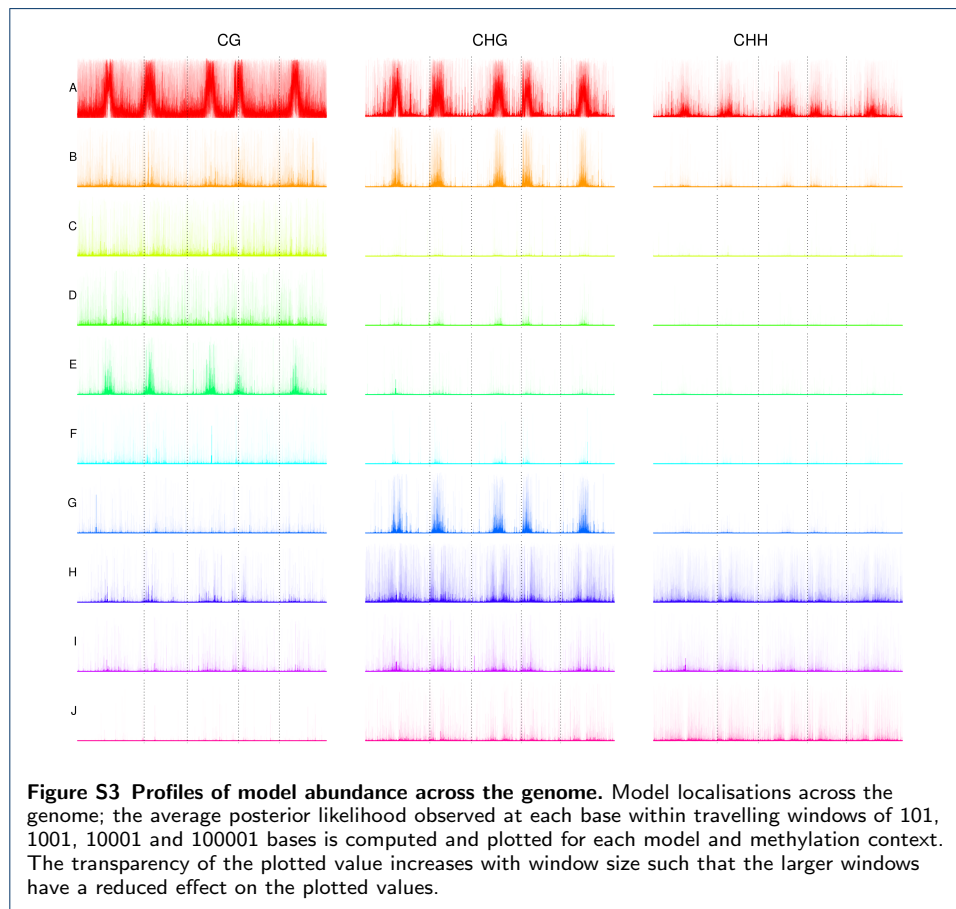
```
Rscript simulate_WGBS.R 100000 0.851721358101034 0.0158503393648432
+0.2 0.2 14.064221221 14.064221221 XXX 2 YYY 0.5
+0.0267845702643185,0.00339225464276114 plant_simulation binomial
+0.237414948538599,1e-15 0.0577772070946612,0.34
```

Version 0.4.4 of methylSig, 1.14 of methylKit, 1.10.0 of BSmooth and 3.4.2 of MethPipe were used to analyse these data using default settings for all libraries. Versions 2.9.5 of segmentSeq and 2.8.0 of baySeq were used to implement the approach described here.

## References

- Stroud, H., Greenberg, M.C., Feng, S., Bernatavichute, Y., Jacobsen, S.: Comprehensive Analysis of Silencing Mutants Reveals Complex Regulation of the Arabidopsis Methylome. *Cell* **152**(1), 352–364 (2013). doi:10.1016/j.cell.2012.10.054





**Table S1** Numbers of loci associated with models of differential methylation.

Model ID	Model definition	Estimated number of loci	Number of identified loci (FDR < 0.05)
A	{WT,dcl2/3/4,dcl2/4,dcl3,dcl2,dcl4}	CpG: 67365 CHG: 53313 CHH: 138593	CpG: 17607 CHG: 9310 CHH: 30058
B	{WT,dcl2/3/4,dcl2/4,dcl3,dcl4}>{dcl2}	CpG: 10769 CHG: 5459 CHH: 4686	CpG: 3587 CHG: 996 CHH: 137
C	{WT}>{dcl2/3/4,dcl2/4,dcl3,dcl2,dcl4}	CpG: 8624 CHG: 692 CHH: 2290	CpG: 119 CHG: 2 CHH: 4
D	{WT,dcl2/3/4,dcl2/4,dcl2,dcl4}>{dcl3}	CpG: 6989 CHG: 644 CHH: 1383	CpG: 1499 CHG: 27 CHH: 3
E	{WT,dcl2/3/4,dcl2/4,dcl3,dcl2}>{dcl4}	CpG: 6906 CHG: 631 CHH: 1306	CpG: 877 CHG: 41 CHH: 9
F	{dcl3}>{WT,dcl2/3/4,dcl2/4,dcl2,dcl4}	CpG: 6131 CHG: 866 CHH: 1527	CpG: 73 CHG: 1 CHH: 1
G	{WT,dcl2/3/4,dcl2/4,dcl4}>{dcl3,dcl2}	CpG: 5167 CHG: 654 CHH: 1672	CpG: 74 CHG: 24 CHH: 3
H	{dcl2/3/4,dcl2/4,dcl3,dcl2,dcl4}>{WT}	CpG: 3665 CHG: 797 CHH: 614	CpG: 1890 CHG: 43 CHH: 20
I	{WT,dcl2/3/4,dcl2/4,dcl3}>{dcl2,dcl4}	CpG: 2532 CHG: 738 CHH: 855	CpG: 281 CHG: 28 CHH: 1
J	{WT,dcl2/3/4,dcl2/4}>{dcl3,dcl2,dcl4}	CpG: 2365 CHG: 331 CHH: 307	CpG: 175 CHG: 1 CHH: 1
K	{WT,dcl2/4,dcl2,dcl4}>{dcl2/3/4,dcl3}	CpG: 2208 CHG: 8384 CHH: 13657	CpG: 62 CHG: 2314 CHH: 542
L	{WT,dcl2/3/4,dcl2/4,dcl2}>{dcl3,dcl4}	CpG: 1564 CHG: 229 CHH: 462	CpG: 79 CHG: 7 CHH: 1
M	{WT,dcl2/3/4,dcl2/4,dcl3}>{dcl4}>{dcl2}	CpG: 968 CHG: 9 CHH: 15	CpG: 218 CHG: 1 CHH: 1
N	{WT,dcl2/4,dcl3,dcl2}>{dcl2/3/4}>{dcl4}	CpG: 596 CHG: 7 CHH: 21	CpG: 92 CHG: 1 CHH: 1
O	{WT,dcl2/3/4,dcl3,dcl2}>{dcl2/4}>{dcl4}	CpG: 435 CHG: 2 CHH: 5	CpG: 62 CHG: 1 CHH: 1
P	{WT,dcl3,dcl2,dcl4}>{dcl2/4}>{dcl2/3/4}	CpG: 306 CHG: 12 CHH: 42	CpG: 74 CHG: 1 CHH: 1
Q	{WT,dcl3,dcl2,dcl4}>{dcl2/3/4}>{dcl2/4}	CpG: 301 CHG: 5 CHH: 14	CpG: 75 CHG: 1 CHH: 1
R	{dcl2/4}>{WT,dcl2/3/4,dcl3,dcl2,dcl4}	CpG: 2623 CHG: 3351 CHH: 4726	CpG: 7 CHG: 153 CHH: 1
S	{WT,dcl2/4,dcl3,dcl2,dcl4}>{dcl2/3/4}	CpG: 2298 CHG: 3220 CHH: 6387	CpG: 47 CHG: 360 CHH: 255
T	{dcl2/3/4,dcl2/4,dcl3,dcl4}>{WT,dcl2}	CpG: 1661 CHG: 2745 CHH: 1219	CpG: 16 CHG: 337 CHH: 3
U	{WT,dcl2/4,dcl2,dcl4}>{dcl3}>{dcl2/3/4}	CpG: 207 CHG: 1746 CHH: 5435	CpG: 10 CHG: 308 CHH: 307
V	{WT,dcl2/4,dcl4}>{dcl2/3/4,dcl3,dcl2}	CpG: 1719 CHG: 1315 CHH: 2831	CpG: 12 CHG: 63 CHH: 37
W	{dcl2/3/4,dcl2/4,dcl3}>{WT,dcl2,dcl4}	CpG: 2189 CHG: 1260 CHH: 606	CpG: 35 CHG: 54 CHH: 1
X	{WT,dcl2/3/4,dcl3,dcl2,dcl4}>{dcl2/4}	CpG: 1237 CHG: 757 CHH: 1886	CpG: 51 CHG: 79 CHH: 3