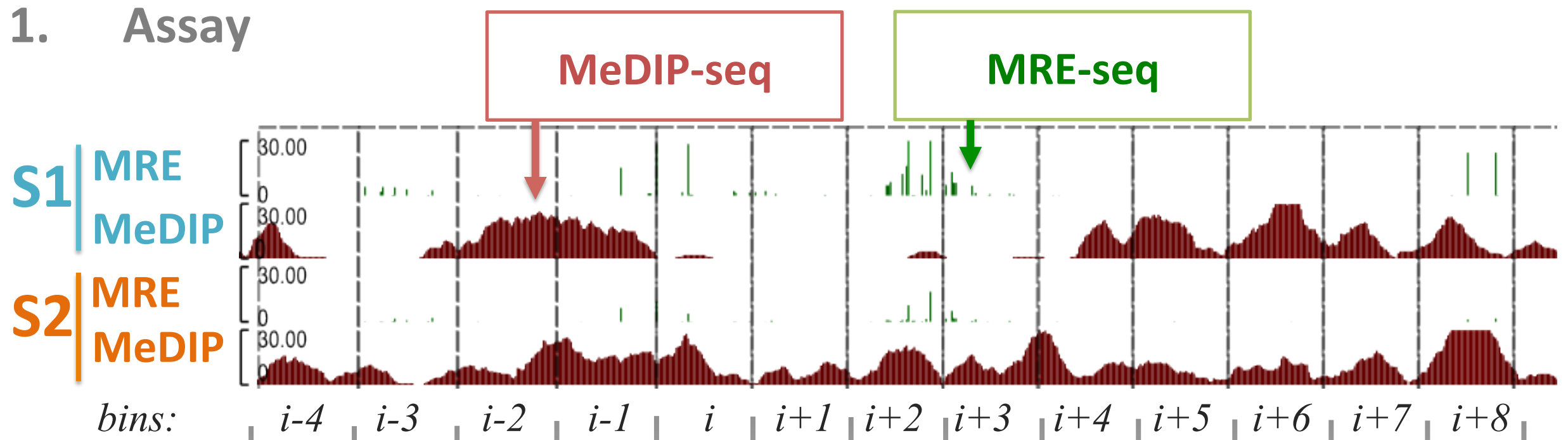


1. Assay



2. Model methylation level

$$\text{MeDIP}[\text{S1}, i], \text{MRE}[\text{S1}, i] \sim f(\mu_{\text{S1}, i}, \text{CpG sites}, \text{MRE sites})$$

$$\text{MeDIP}[\text{S2}, i], \text{MRE}[\text{S2}, i] \sim f(\mu_{\text{S2}, i}, \text{CpG sites}, \text{MRE sites})$$

μ : methylation level

3. Select DMRs

$$H_0: \mu_{\text{S1}, i} = \mu_{\text{S2}, i} \text{ vs. } H_{alt}: \mu_{\text{S1}, i} \neq \mu_{\text{S2}, i}$$

Test statistic:

$$t_i = c_1(\text{MeDIP}[\text{S1}, i] \cdot \text{MRE}[\text{S2}, i]) - c_2(\text{MeDIP}[\text{S2}, i] \cdot \text{MRE}[\text{S1}, i])$$

c_1, c_2 : normalizing factors

P-value:

$$p_i = P(|T_i| > |t_i| \mid \text{MeDIP}[\text{S1}, i] + \text{MRE}[\text{S1}, i] + \text{MeDIP}[\text{S2}, i] + \text{MRE}[\text{S2}, i] = n_i)$$

T_i : test variable

n_i : total reads

$-\log_{10}(\text{P-value})$

