

**SUPPLEMENTARY FILE 1: PSEUDO-CODE FOR THE  
A-CLUSTERING AND  $d_{bp}$ -MERGE ALGORITHMS**

**Algorithm 1** (*A-clustering*) Given ordered methylation measures, by chromosomal location, at  $m$  sites for  $n$  subjects, an  $m$ -vector of chromosomal locations  $L$ , corresponding  $m$ -vector of cluster assignments, distance measure (e.g. Spearman correlation), distance measure threshold  $\bar{D}$ , base pair distance  $\bar{d}_{bp}$  and *type* (*single*, *average* or *complete*)

- (1) Set the cluster indicator  $ind\_current\_cluster \leftarrow 1$ .
  - The matching set  $current\_cluster$  contains all the indices of sites belonging to cluster indicated by  $ind\_current\_cluster$ .
  - The set  $next\_cluster$  contains all the indices of sites belonging to cluster indicated by  $ind\_current\_cluster + 1$ .
- (2) Until no more clusters can be merged:
  - (a) Let  $merge$  be true if  $dist(current\_cluster, next\_cluster) \leq \bar{D}$  (depend on *type*), and if also  $\min(L(next\_cluster)) - \max(L(current\_cluster)) < \bar{d}_{bp}$ .
  - (b) Repeat while  $merge$  is True:  $current\_cluster \leftarrow current\_cluster \cup next\_cluster$  by updating cluster assignments
  - (c) If  $merge$  is False:  $ind\_current\_cluster \leftarrow (ind\_current\_cluster + 1) \% current\_number\_of\_clusters$  (modulo)
- (3) Output cluster assignments.

Note that we know that “no more clusters can be merged” after cycling through all clusters and merge none.

**Algorithm 2** ( *$d_{bp}$ -merge*) Given ordered methylation measures, by chromosomal location, at  $m$  sites for  $n$  subjects, an  $m$ -vector of chromosomal locations  $L$ , distance measure (e.g. Spearman correlation), a threshold  $\bar{D}$ , and base-pair distance  $\underline{d}_{bp}$ . Let  $cluster(site_k)$  be the cluster of site  $k$ ; initially it is the  $k$ th site alone.

- (1) Set the site indicator  $ind\_current\_site \leftarrow 1$ . The matching site is  $current\_site$
- (2) While  $ind\_current\_site < number\_of\_sites$ :
  - (a) Let  $site_1, \dots, site_k$  be all sites such that  $L(site_l) - L(current\_site) \leq \underline{d}_{bp}$  ordered by their distance from  $current\_site$ .
  - (b) Set  $merge \leftarrow$  False,  $l \leftarrow k$ .
  - (c) While  $merge$  is False and  $l > ind\_current\_site$ :
    - If  $dist(current\_site, site_l) < \bar{D}$ 
      - Set  $cluster(current\_site, \dots, site_l) \leftarrow cluster(current\_site)$ .
      - Set  $merge \leftarrow$  True.
    - Else  $l \leftarrow l - 1$

The following figure is Figure 1 from the paper, showing a difference in clustering results without/with using  $d_{bp}$ -merge initiation,

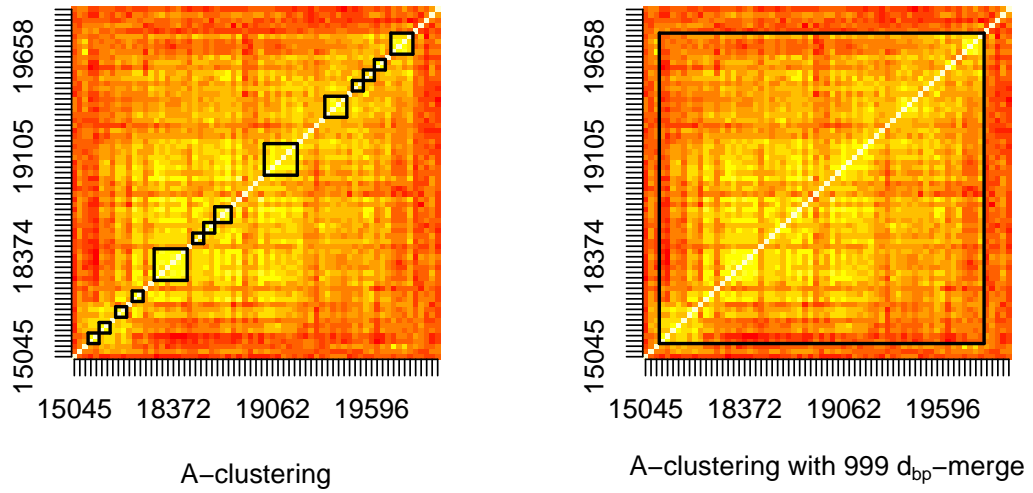


FIGURE 1. Figure 1 from the paper - in color. Left panel:  $d_{bp}$ -merge was not used. Right panel:  $d_{bp}$ -merge initiation followed by Aclust.