1. Consider an optimized RF model (M) built on the set of autosomal chromosomes $\{k|i \notin k\}$ binned at some resolution r

2. **for** *each chr i* **do**

    3. Construct the base-level resolution predictor space $A_{n\times p}$ where n is the length of chr i and p is the number of predictors

    4. Assign threshold $\{t|0 \leq t \leq 1\}$ and $\{\epsilon|\epsilon > 0\}$

    5. **if** $|t| > 1$ *or* $|\epsilon| > 1$ **then**

        6. Assign grid (g) of combinations of t and ϵ

        7. **for** *each combination l in g* **do**

            8. Evaluate M on $A_{n\times p}$ to get the probability of each genomic coordinate as being a domain boundary π_n

            9. Subset $\{\pi_n|\pi_n \geq t_l\}$

            10. Construct the pairwise distance matrix D between genomic coordinates where $\pi_n \geq t_l$

            11. Apply DBSCAN on D with $MinPts = 3$ and $\epsilon = \epsilon_l$

            12. **for** *each cluster k identified by DBSCAN* **do**

                13. Assign w_k as the number of coordinates that span each cluster of bases in k (PTBR)

                14. Perform PAM on the sub-distance matrix D_k to extract the cluster medoid b_k (PTBP)

                15. **for** *each predictor p* **do**

                    16. Calculate the normalized enrichment (NE) over all predictors

$$NE = \frac{1}{p}\left[\Sigma_{s=1}^{p}\left[\frac{1}{b}\Sigma_{k=1}^{b} e_{ks}\right]\right]$$

                    where $e_{ks} = \mathbf{I}\{r_s \in (b_k - f, b_k + f)\}$ is the number of elemental regions r of predictor p that overlap with each flanked boundary

                    17. Determine where NE converges as optimal $\{t, \epsilon\}$ combination

                    18. Repeat steps 12-18 on A_{nxp} with optimal $\{t, \epsilon\}$

                end

            end

        end

    else

        19. Perform steps 12-18 on A_{nxp} such that $t = t_0$ and $\epsilon = \epsilon_0$

    end

end

Algorithm 1: Psuedocode for *preciseTAD* implementation.