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**Algorithm 1: PROMISE - Promiscuity Indices Estimator**

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**Input:**  $6n \leftarrow$  number of proteins in the set - each EC number has  $n$  elements  
**Input:**  $Score \leftarrow \{Score_{ij} : \forall i, j \in 6n, i \neq j\}$  CLASP score when motif from Protein  $j$  is queried in Protein  $i$   
**Input:**  $Pred \leftarrow \{Pred_{ij} : \forall i, j \in 6n, i \neq j\}$  Predicted residues in Protein  $i$  responsible for activity known for Protein  $j$   
**Input:**  $EC \leftarrow \{EC_{ij} : \forall i, j \in 6n, i \neq j\}$  Level in which the EC numbers of Protein  $i$  and Protein  $j$  differ  
**Input:**  $thr \leftarrow$  Ignore matches whose CLASP score  $Score_{ij}$  is less than this value  
**Input:**  $shellrad \leftarrow$  Radius of shell which is to be considered as the active site -  $5\text{\AA}$   
**Input:**  $Vic \leftarrow \{Vic_i : \forall i \in 6n\}$  Residues in vicinity of active site of Protein  $i$  within distance  $shellrad$   
**Output:**  $PromIdx \leftarrow \{PromIdx_i : \forall i \in 6n\}$  Promiscuity Indices  
**begin**  
  **for**  $i \leftarrow 1$  **to**  $6n$  **do**  
     $PromIdx_i = 0$ ;  $empirical = 10$  ; // initialize  
    **for**  $j \leftarrow 1$  **to**  $6n, i \neq j$  **do**  
      /\* Discard poor matches\*/  
      if( $Score_{ij} \geq thr$ ) continue ;  
      /\* Score of difference in catalytic activity - ie level in  
      which the EC numbers of the native and predicted activity differ\*/  
       $\delta_{scoreij} = empirical / EC_{ij}$  ;  
      /\* Score for the quality of the spatial and  
      electrostatic congruence of the predicted function\*/  
       $\delta_{scoreij} = \delta_{scoreij} / Score_{ij}$  ;  
      /\* check if in vicinity of the native active site \*/  
      if( $Pred_{ij} \wedge Vic_{ij} \neq \phi$  ) then  
         $PromIdx_i = PromIdx_i + \delta_{scoreij}$  ;  
      endif  
    **end**  
  **end**  
  Normalize( $PromIdx$ ); // most promiscuous protein has a promiscuity index of 1  
**end**

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