Algorithm S2. (Hybrid H-bond and MSM based) Exchange State Identification Algorithm

Input:
Chemical Shift Values per residue. $CS = \{CS_1, CS_2, \ldots, CS_{33}\}$ where $CS_i \in \mathcal{R}^N$
where N is the total number of frames in the simulation.
Macro states from MSMBuilder. $MS = \{MS_1, MS_2, \ldots, MS_M\}$
where M is the total number of macrostates.
H-bond frames in minor state from Algorithm S1. $HB = \{HB_1, HB_2, \ldots, HB_H\}$
where H is the total number of relevant H-bonds found by Algorithm S1.

function SUPERSTATESEARCH(CS,MS,HB)
  $SC \leftarrow \emptyset$
  for $i \leftarrow 1 \ldots M$ **do** ▷ $M = 40$ in this study
    if $MS_i \cap HB > \delta$ **then** ▷ δ is the minimum intersection fraction $\delta = 0.002$
      $SC \leftarrow SC \cup MS_i$ ▷ SC Identifies relevant macrostates to reduce search
    end if
  end for
  for $k \leftarrow 1 \ldots \lfloor |SC|/2 \rfloor + 1$ **do**
    for $z \leftarrow 1 \ldots \binom{|SC|}{k}$ **do**
      $StatesA \leftarrow SC(z)$ ▷ $SC(x)$ is one of $\binom{|SC|}{k}$ macrostate combinations in SC
      $StatesB \leftarrow \{MS_1, MS_2, \ldots MS_{40}\} \setminus StatesA$
      $\Phi_{ex} \leftarrow \text{Estimate}\Phi_{ex}(\text{StatesA}, \text{StatesB}, \text{CS})$ ▷ See Equation (2) in main paper
      $\rho_{new} \leftarrow \rho(\mathbf{\Phi_{ex}}, \mathbf{R_{ex}})$
      if $\rho_{new} > \rho_{best}$ **then**
        $\rho_{best} \leftarrow \rho_{new}$
        $SuperA \leftarrow StatesA$
        $SuperB \leftarrow StatesB$
      end if
    end for
  end for
  return $SuperA$, $SuperB$, ρ_{best}
end function