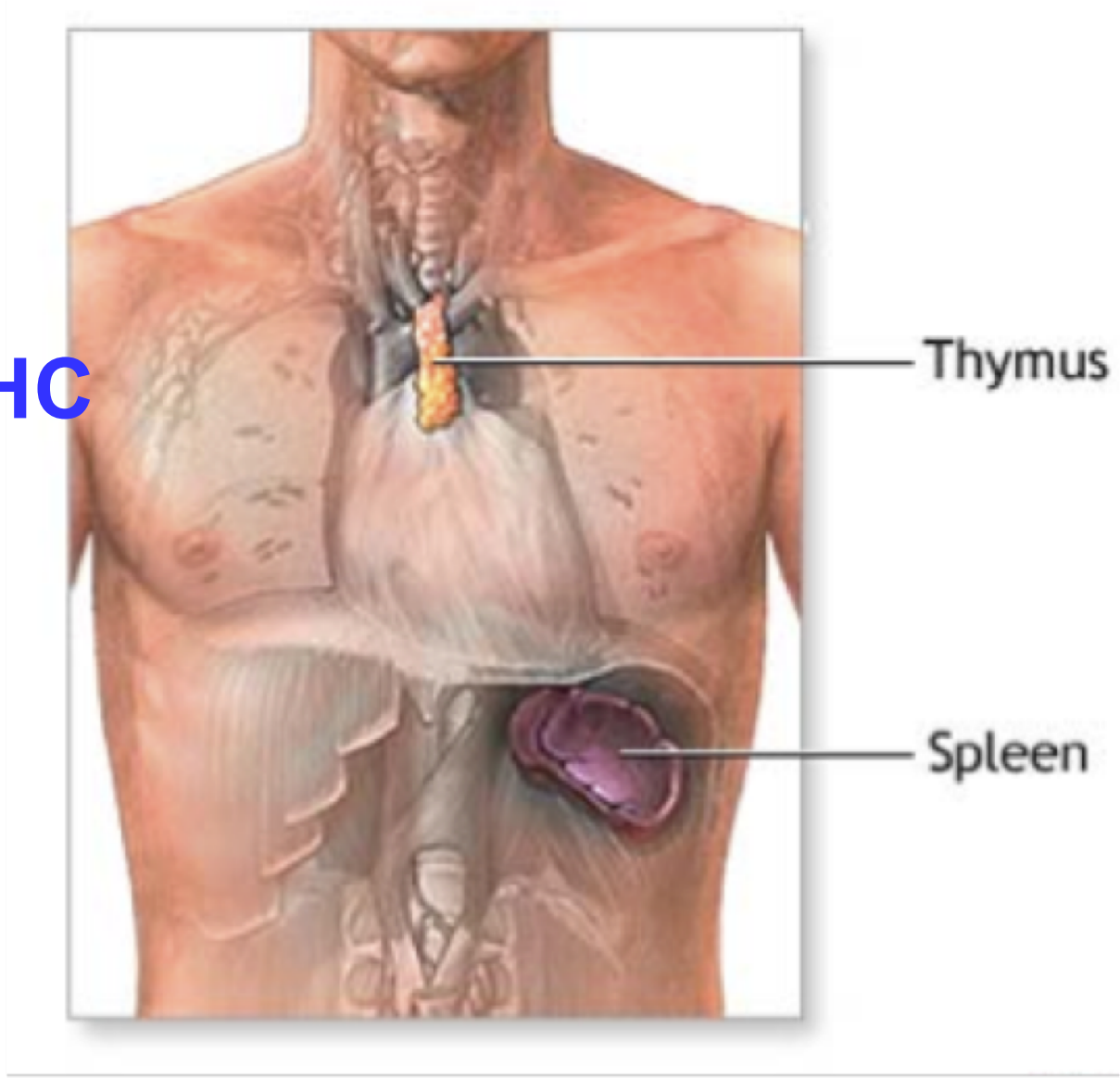
T CELL DEVELOPMENT IN THE THYMUS

Fig. 1: Baby T cells are exposed to pMHC molecules derived from endogenous ("self") proteins.



T CELL DEVELOPMENT IN THE THYMUS

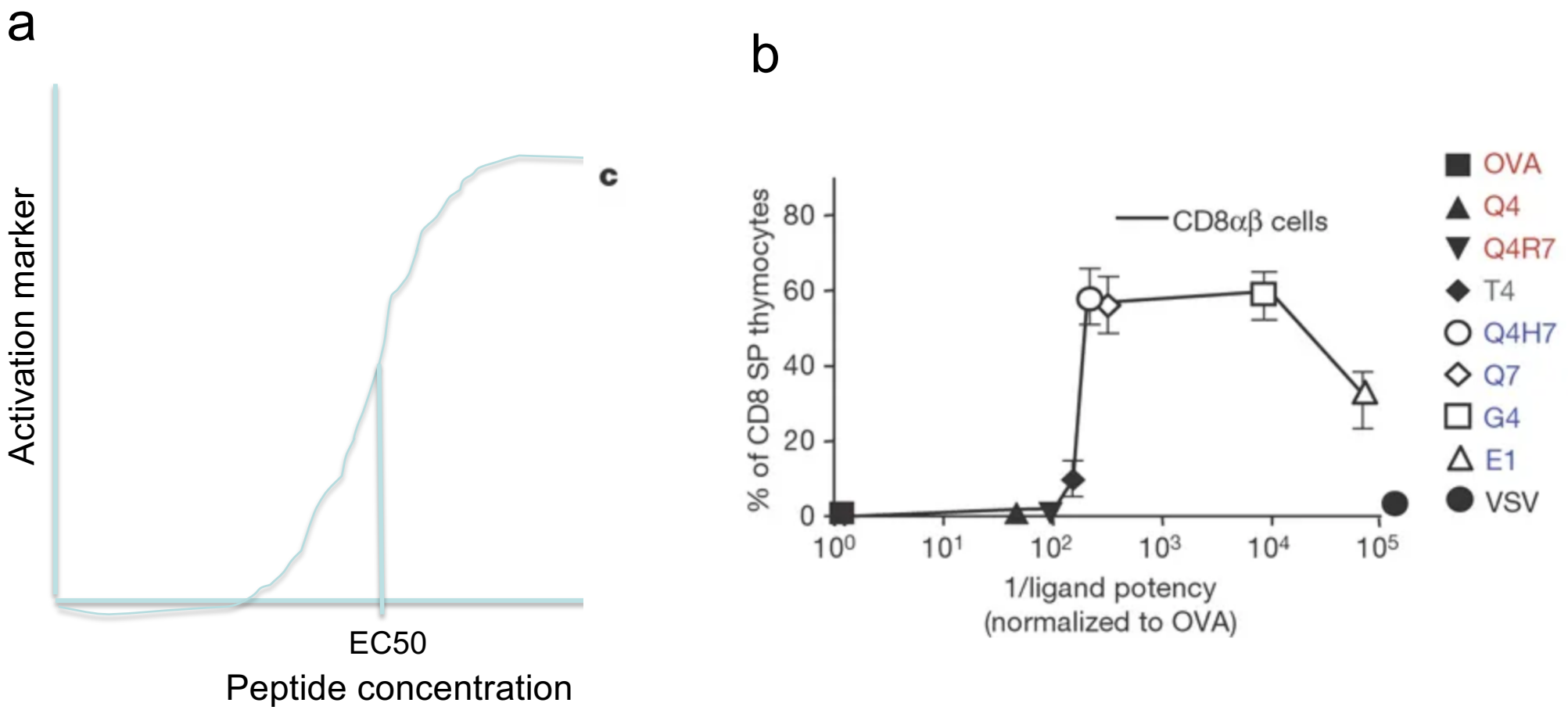


Fig 2: (a) Schematic defining EC50. (b) Binding thresholds for positive and negative selection - Fig 1 c from Daniels et al., Nature (2006).

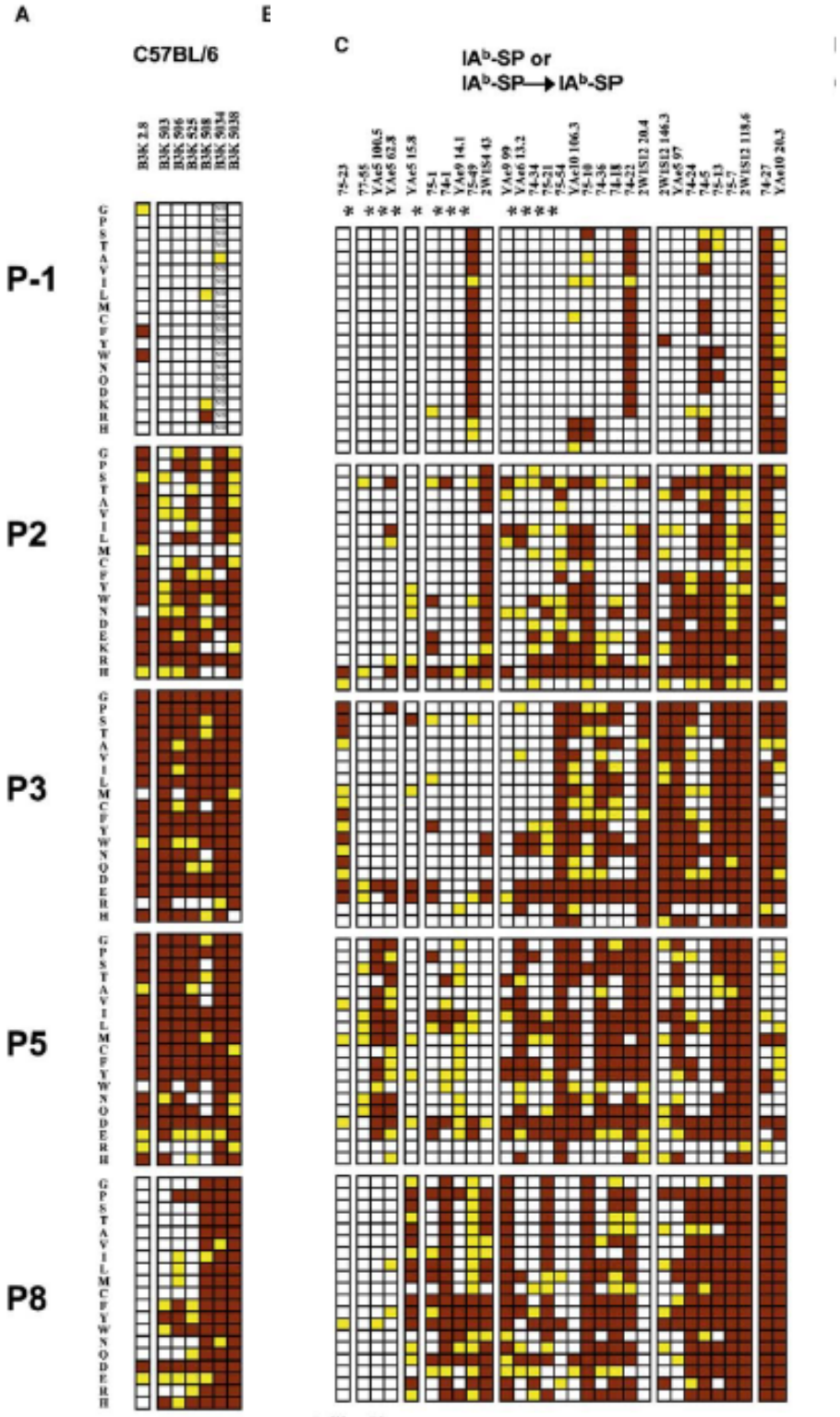


Fig. 3

< 5% of T cell Response to 3K peptide

5-50% of T cell Response to 3K peptide

> 50% of T cell response to 3K peptide

Model

Fig 4

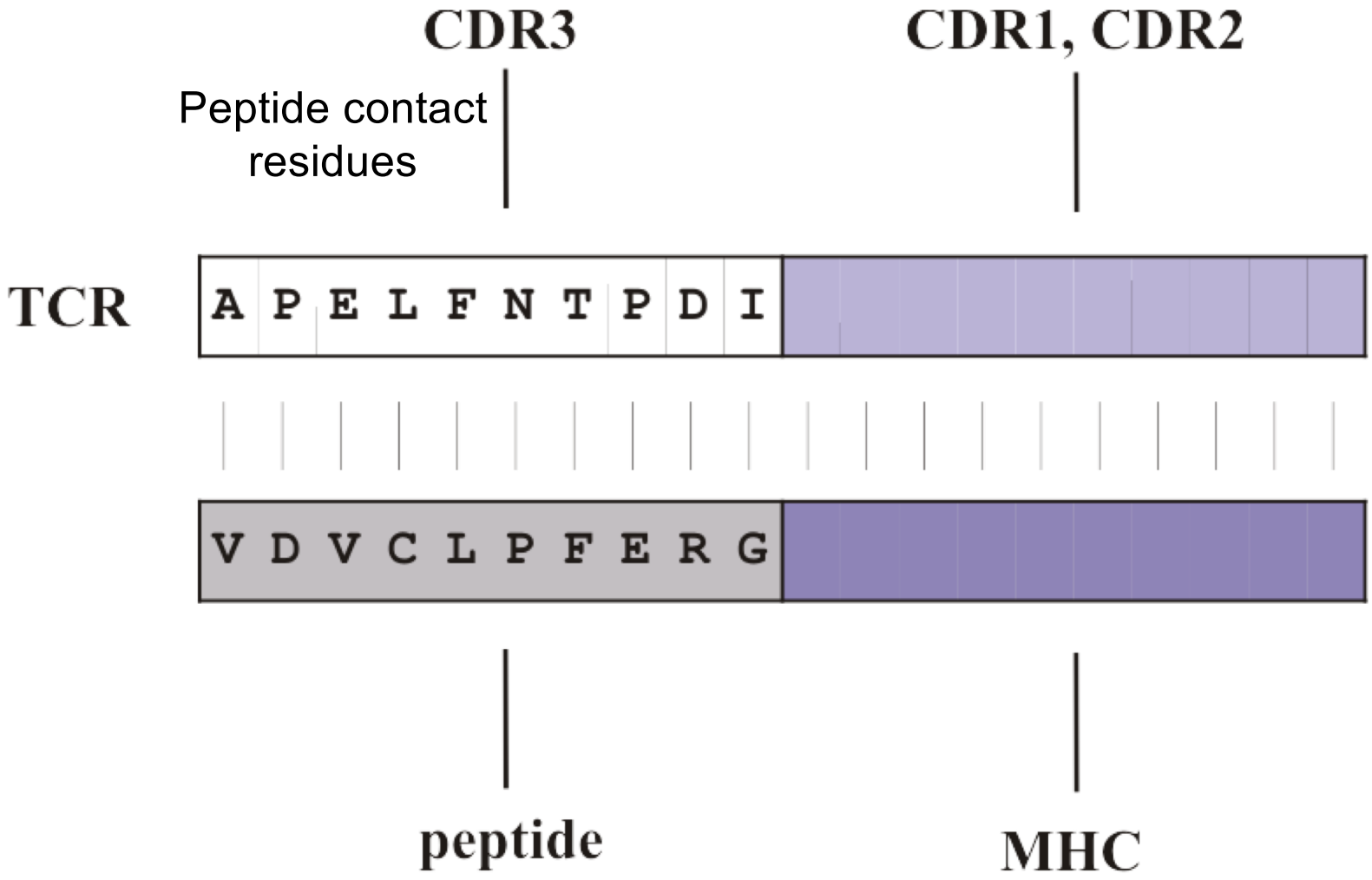

CDR3
CDR1, CDR2
Peptide contact residues
TCR
A P E L F N T P D I
V D V C L P F E R G
peptide
MHC

Fig 5 – The number of hot spots characterizing T cell recognition of pathogenic peptides is greater for T cells that develop in a thymus with a greater number of displayed self peptide-MHC molecules

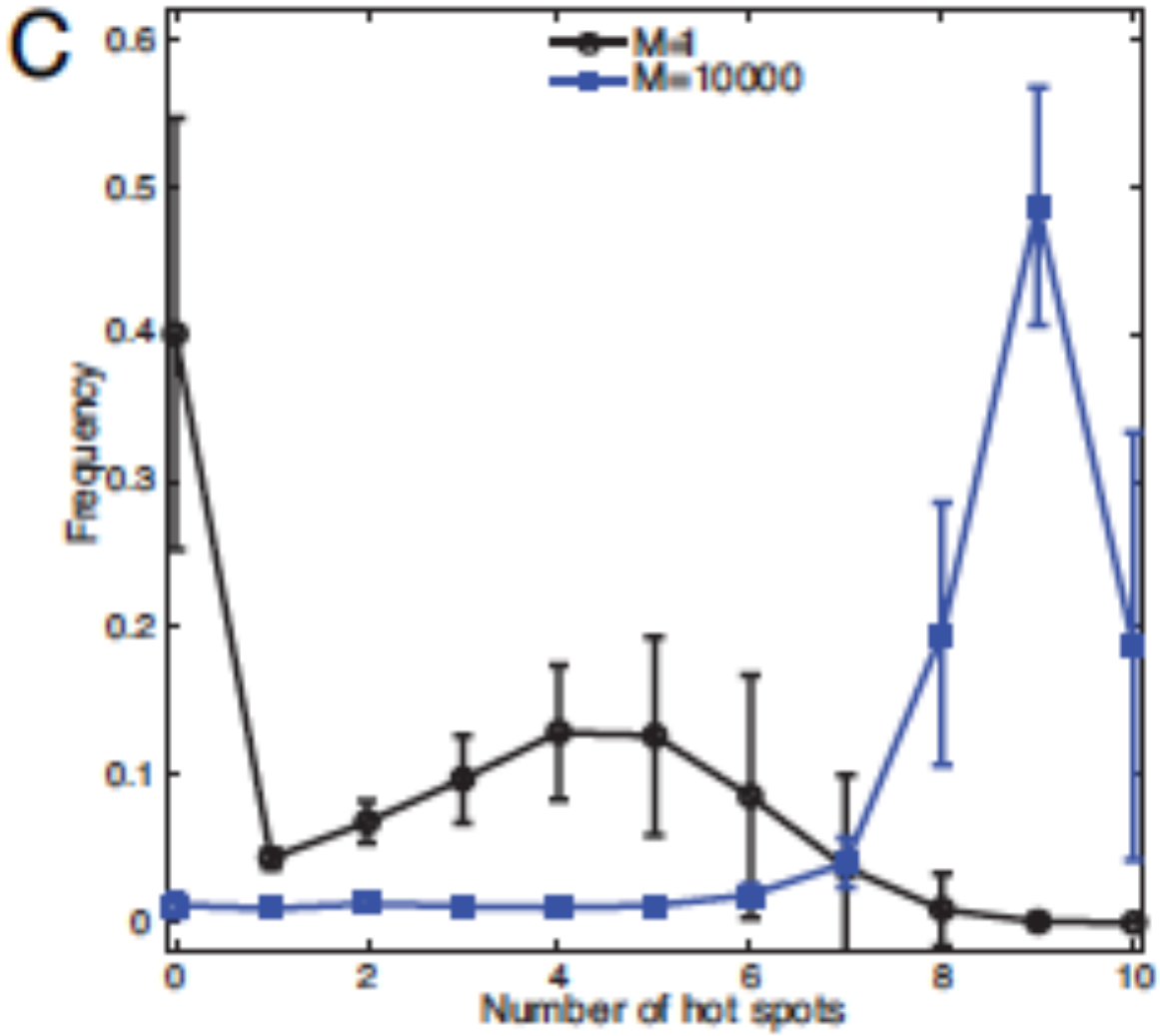


Fig. 6

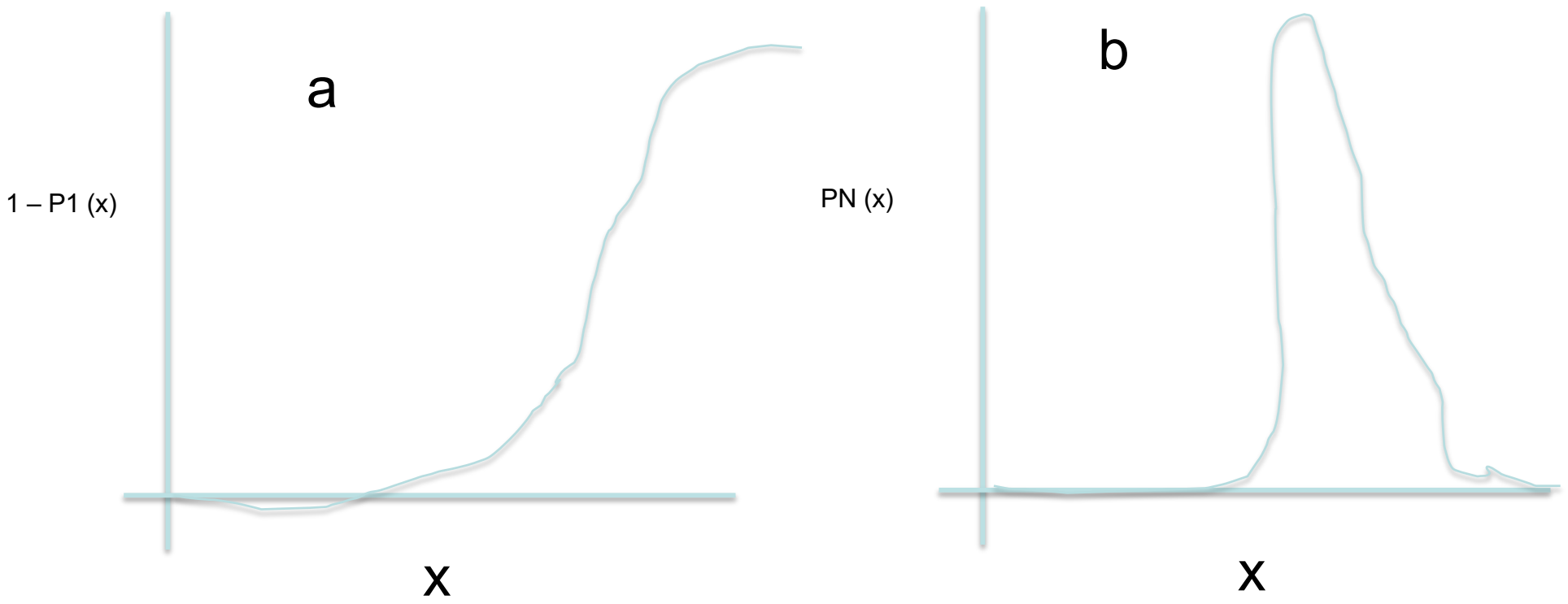


FIG 7

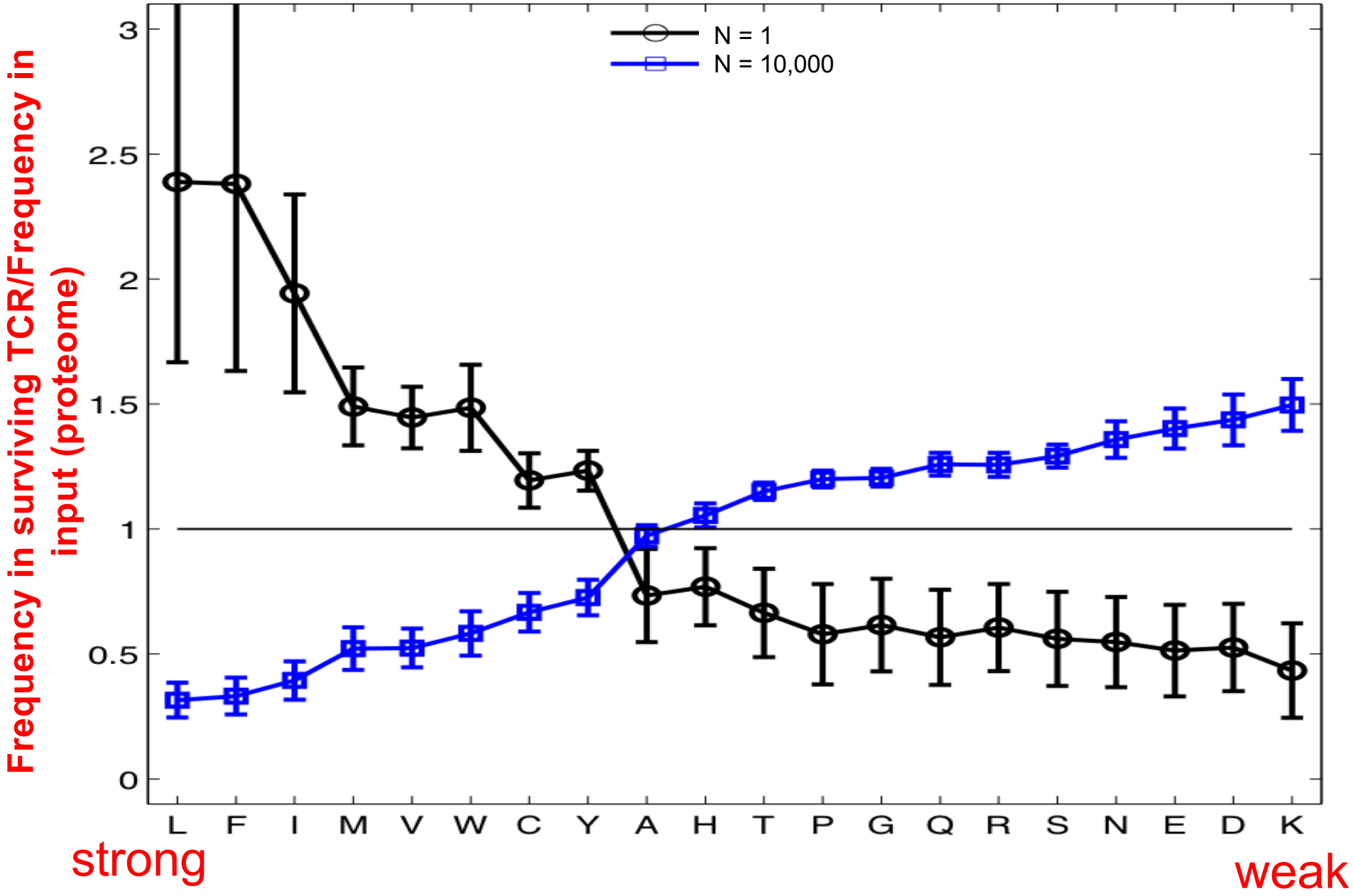
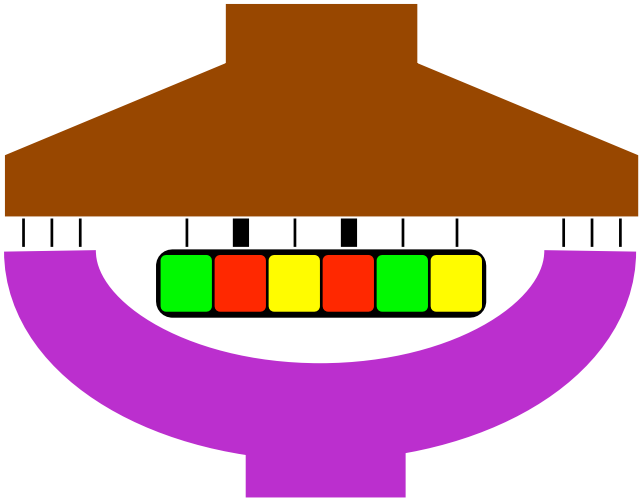

N = 1
N = 10,000
Frequency in surviving TCR/Frequency in input (proteome)
3
2.5
2
1.5
1
0.5
0
L F I M V W C Y A H T P G Q R S N E D K
strong
weak

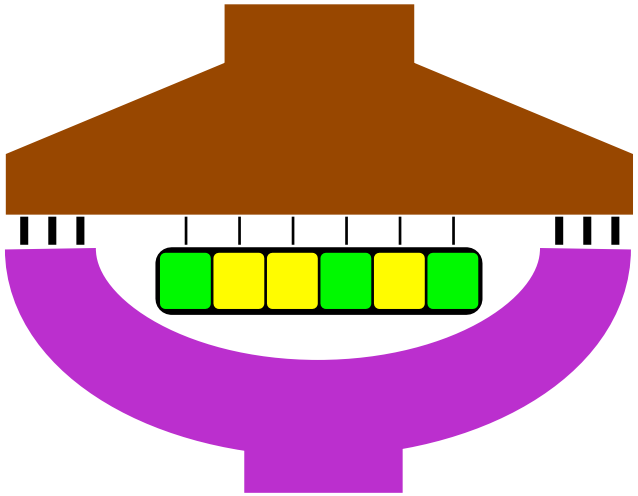
Fig 8

One peptide

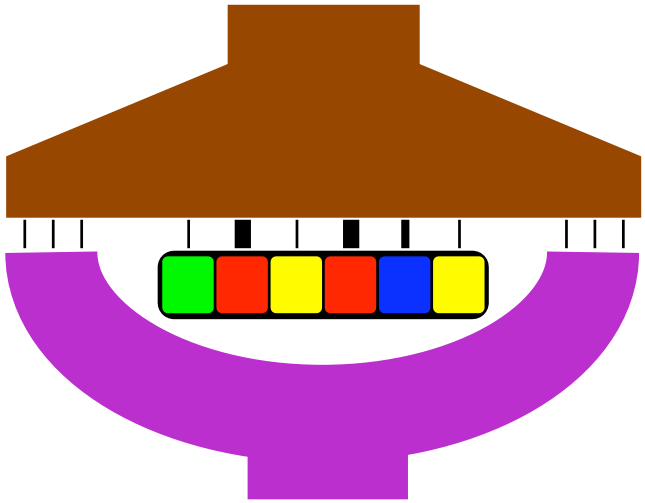


$E_N > E > E_P$

selected



Many peptides



$E > E_N$

negatively selected

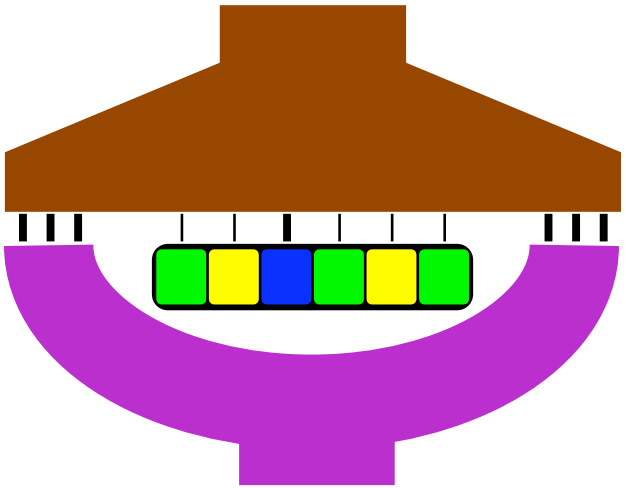
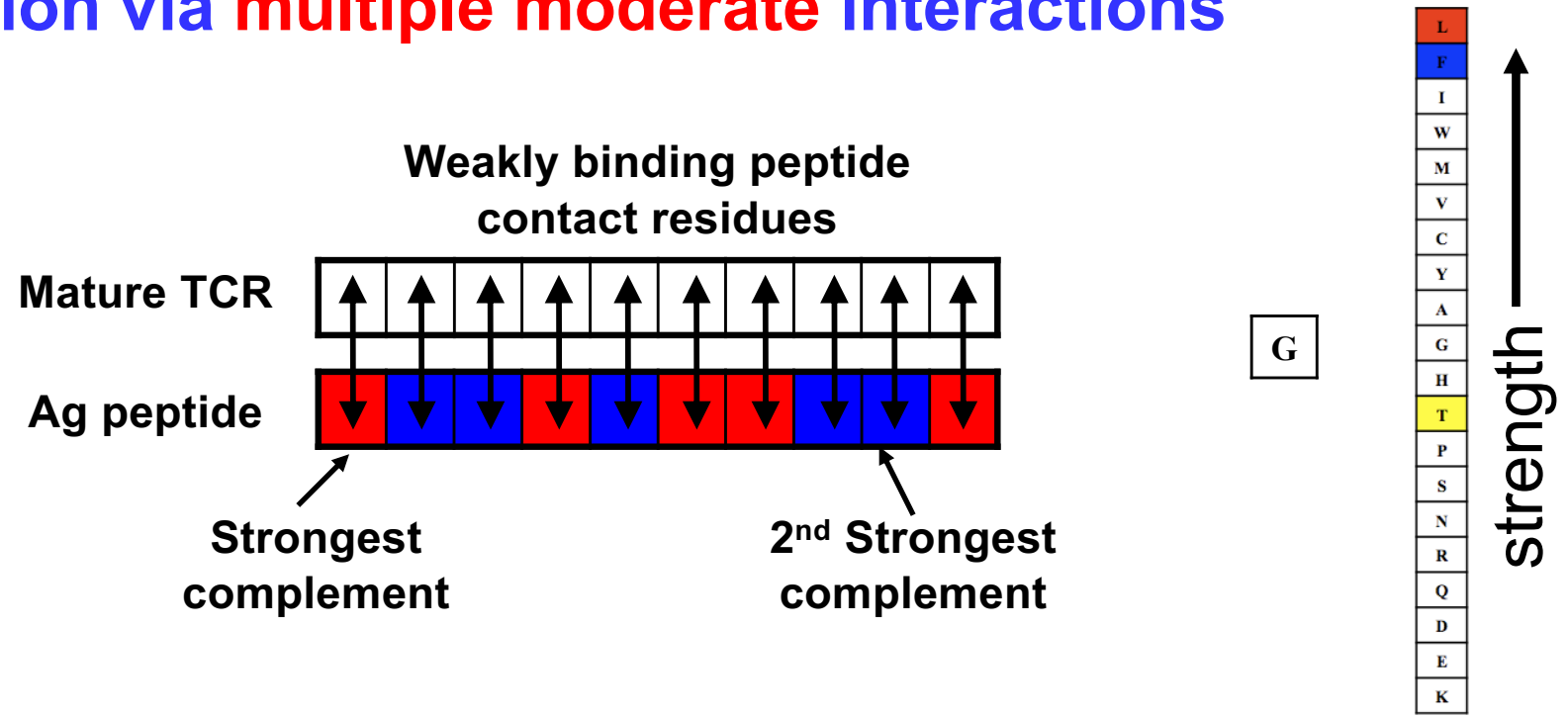


Fig 9

"Moderate" peptide contact residues on TCR must bind a sufficient number of its stronger complementary amino acids for recognition via multiple moderate interactions



Selection against one peptide – only few important contacts

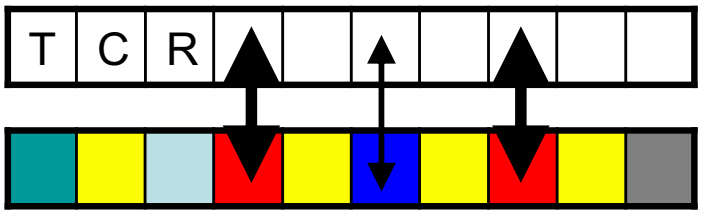


Fig. 10

Also add the CD8 figure

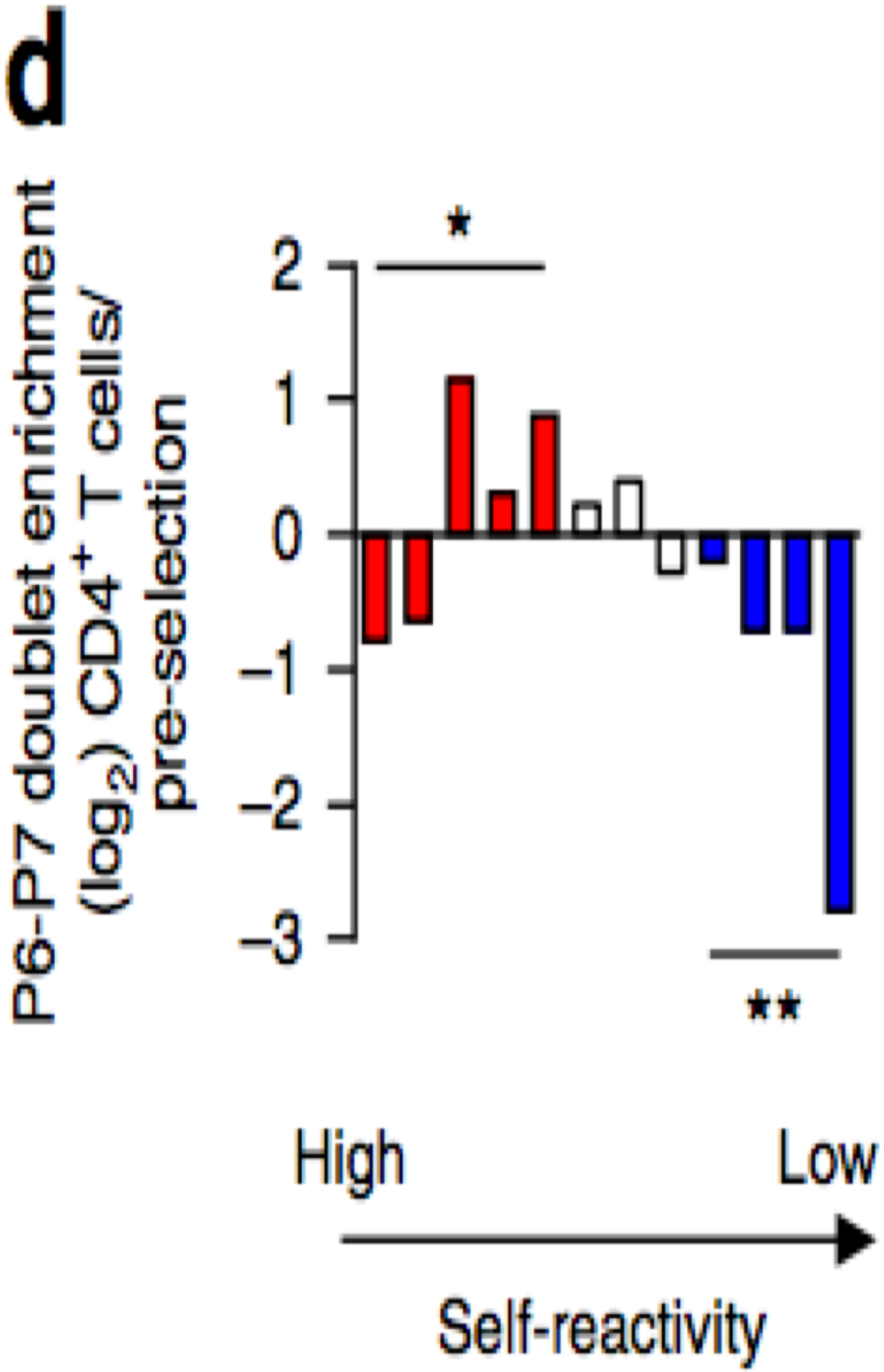


Fig 11

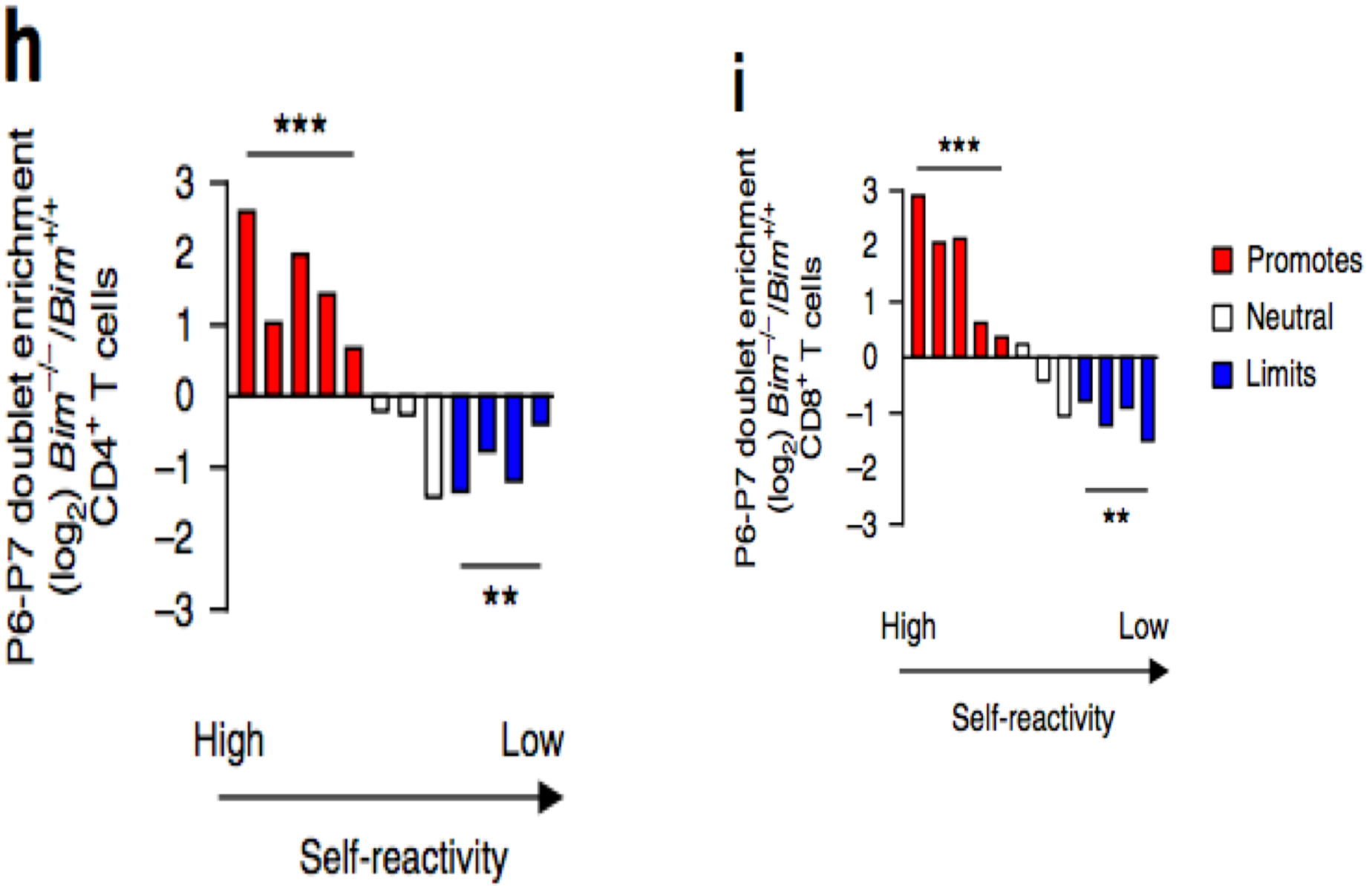

h
P6-P7 doublet enrichment
(log2) Bim−/−/Bim+/+
CD4+ T cells
***
**
3
2
1
0
−1
−2
−3
High
Low
Self-reactivity
i
P6-P7 doublet enrichment
(log2) Bim−/−/Bim+/+
CD8+ T cells
***
**
3
2
1
0
−1
−2
−3
High
Low
Self-reactivity
Promotes
Neutral
Limits

Fig 12: CD4 T cells of NOD mice show enrichment of hydrophobic residues (red) at P6 and P7 compared to B6 mice. This enrichment is not seen for CD8 T cells. Less hydrophobic residues are in blue.

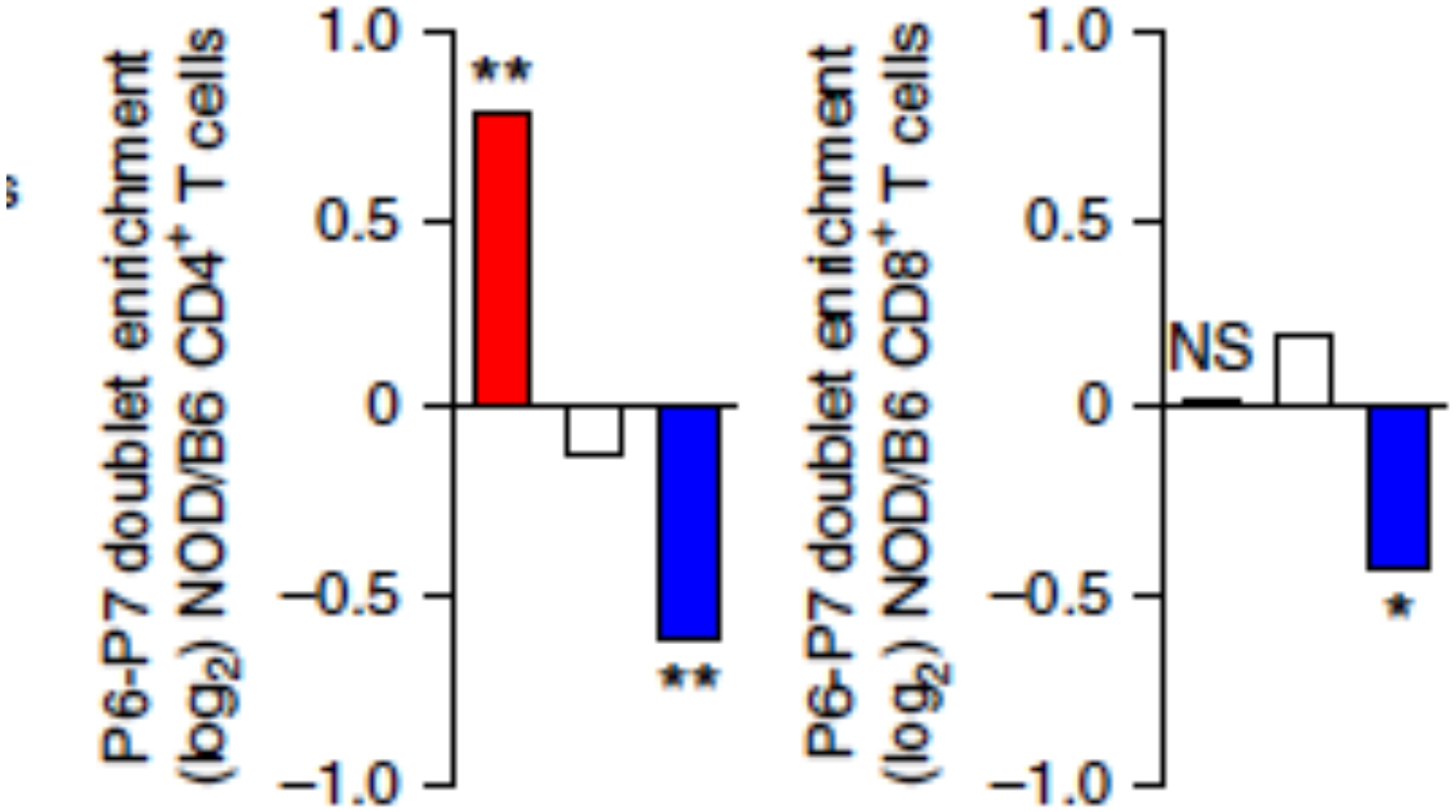


Fig 13: Compared to B6 mice, more hydrophobic residues (red) were enriched at P6 and P7 positions for mice that had the key NOD MHC, and similar levels of more hydrophobic residues as NOD mice. Less hydrophobic residues are in blue.

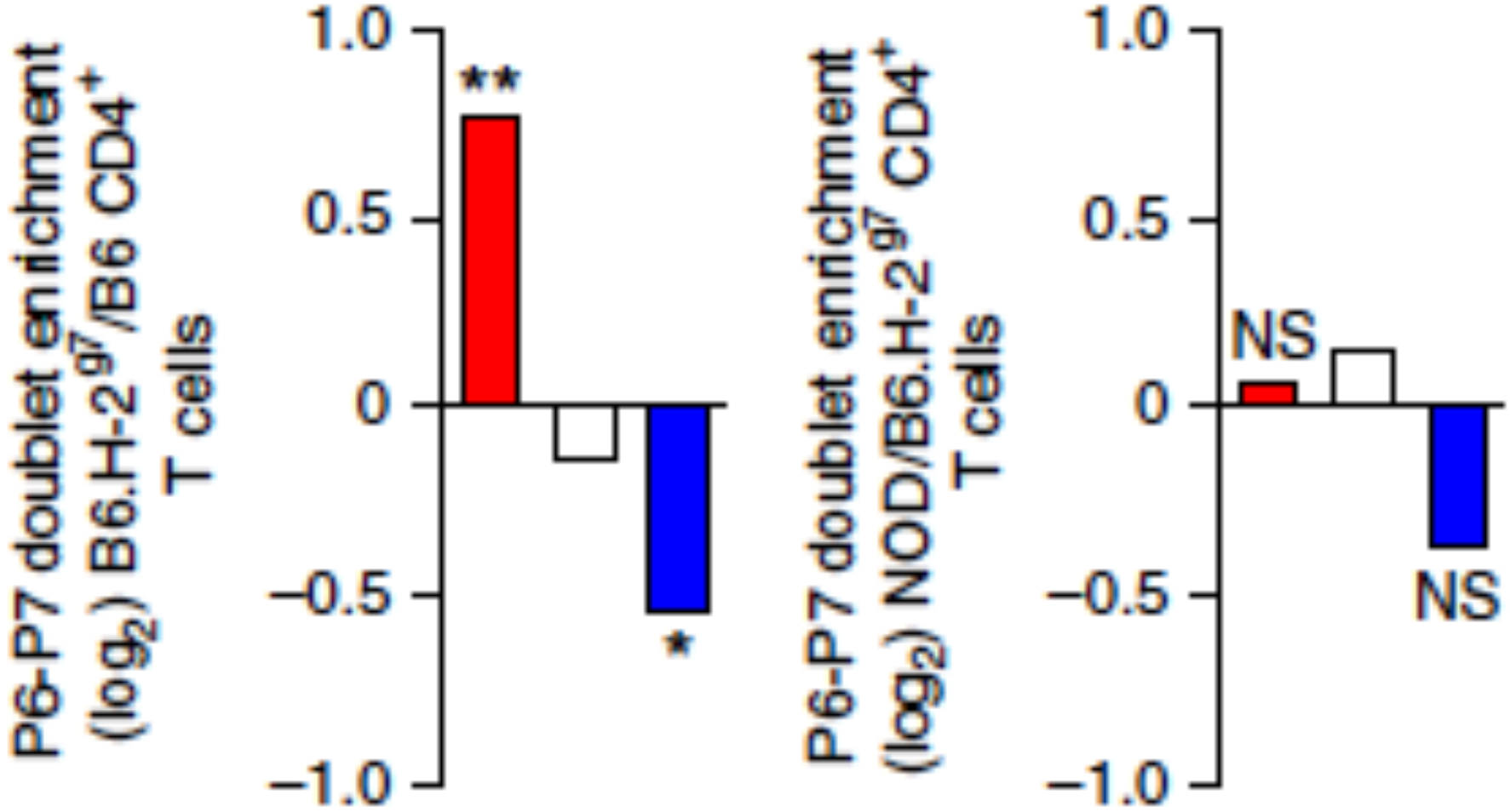


Fig 14a

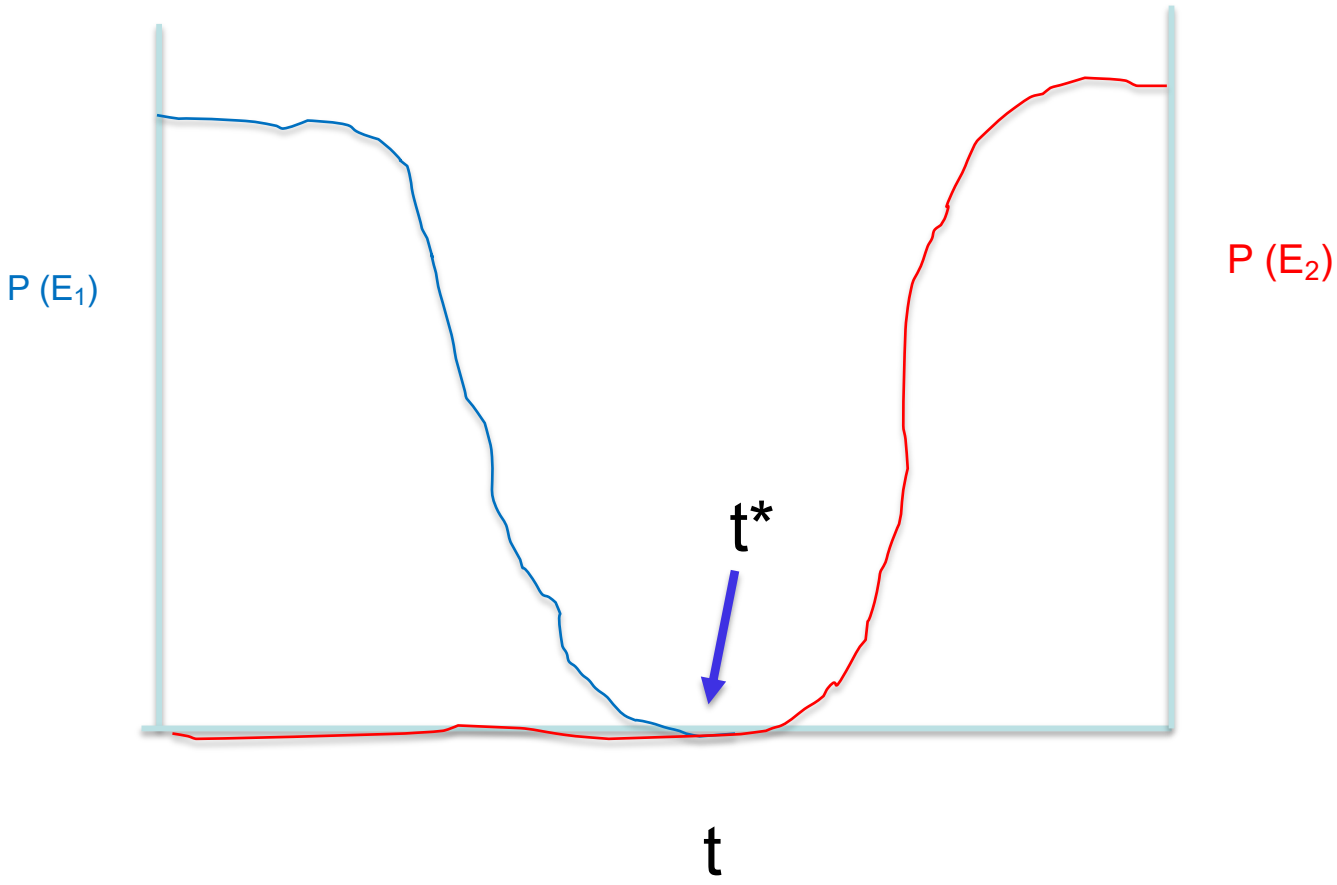


Fig 14b