

**Additional Table 2:** Top five amino acid alphabets for each method on myoglobin and myosin rod alignments.

(A) Tetrapod Myoglobin		Rank		NMI	RMI	SCA8	M <sub>P</sub>	GCTMPCA7	AS
1	CHARGE_HIS_2	A1_4		A3_2	CHARGE_HIS_2	CHARGE_2	A4_7	CHARGE_HIS_3	
2	CHARGE_2	A1_3		A3_4	CHARGE_HIS_3	CHARGE_HIS_2	A1_10	CHARGE_2	
3	CHARGE_HIS_3	A1_7		A4_4	A1_7	CHARGE_3	A4_10	CHARGE_3	
4	A1_4	CHARGE_HIS_2		A5_10	A1_4	CHARGE_HIS_3	A5_5	CHARGE_HIS_2	
5	CHARGE_3	CHARGE_2		A4_7	A1_2	A4_4	A5_10	POLARITY_HIS_4	

  

(B) Chordate Myosin		Rank		NMI	RMI	SCA6	M <sub>P</sub>	LnLCorr99	AS	CoMap
1	CHARGE_3	CHARGE_3	A4_3		CHARGE_3	A5_9	DEF99		A1_2	ORIG
2	CHARGE_2	CHARGE_2	A4_4		CHARGE_HIS_3	A2_9	A4		A5_5	A4
3	CHARGE_HIS_3	CHARGE_HIS_3	A3_3		CHARGE_2	A5_10	A5	CHARGE_3	VOLUME	
4	CHARGE_HIS_2	CHARGE_HIS_2	A3_4		CHARGE_HIS_2	ORIG	A2	A2_5	A2	
5	A3_9	A4_4	CHARGE_2		SIZE_2	A3_9	A1	A5_9	A1	

For each method and alignment combination, the top five ranking alphabets are presented. Rankings are determined based on the p-value at  $(i, i+4)$  in the given alignment. Methods that did not achieve any significant p-values (at  $\alpha = 0.01$ ) for the given alignment are not included as those rankings are not meaningful.