

Supplementary figure 1

A

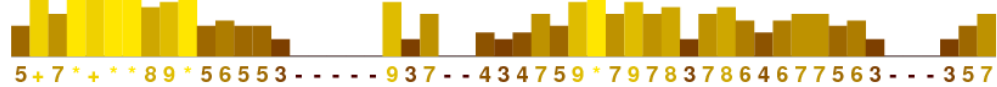
AeJHAMT/1-278 1 MNKPNLYHRANGV - - - - - QR - RDAKE I LDEHGHL L RWK - - EENED 37
 3CCF/1-242 1 KHS - - - - - FVW - - - - - QYGEDLLQLLN - - - - - PQPGE 22
 1M6E/1-359 1 MDVRQVLHMKGGAGENSYAMNSFIQRQVISITKPI TEAAITALYSGDVTVTRL 53

Conservation



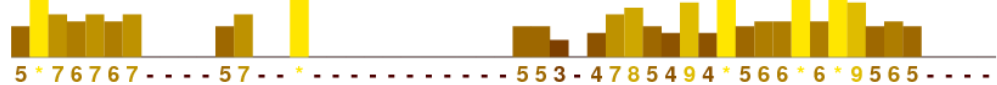
AeJHAMT/1-278 38 SLLDI GCGSGDVL I DFVI PMVPP - - KRARVLGTDVSEQMVR FARKVHSDVENL 88
 3CCF/1-242 23 F I LD L GCGT GQLTEK - - - - - I AQ - - SGAEVLGTDNAATM I EKARQNY - - - PHL 65
 1M6E/1-359 54 A I AD L G C S S G P N A L F A V T E L I K T V E E L R K K M G R E N S P E Y Q I F L N D L P G N D F N A 106

Conservation



AeJHAMT/1-278 89 F F E T L D I E G D I S S - - F - - - - - L N K W G C F D H I T S F Y C L H W V R S Q - - - - 124
 3CCF/1-242 66 H F D V A D A - - - - - R N - - F - - - - - R V D - K P L D A V F S N A M L H W V K E P - - - - 96
 1M6E/1-359 107 I F R S L P I E N D V D G V C F I N G V P G S F Y G R L F P R N T L H F I H S S Y S L M W L S Q V P I G I 159

Conservation



AeJHAMT/1-278 125 R S A F S N I Y - - - - - - - - - - - N L M A P N G D C L L G F L A R 148
 3CCF/1-242 97 E A A I A S I H - - - - - - - - - - - Q A L K S G G R F V A E F G G K 120
 1M6E/1-359 160 E S N K G N I Y M A N T C P Q S V L N A Y Y K Q F Q E D H A L F L R C R A Q E V V P G G R M V L T I L G R 212

Conservation



AeJHAMT/1-278 149 N P - - - - - I F D I Y D Q L S N S A K - - - - - W S M Y M T D V D K Y I S P Y Q Y C E N P V G E I E 189
 3CCF/1-242 121 G N - - - - - I K Y I L E A L Y N A L E - - - - - T L G I H - N P Q A L N P W Y F - - P S I G E Y V 157
 1M6E/1-359 213 R S E D R A S T E C C L I W Q L L A M A L N Q M V S E G L I E E E K M D K F N I P - Q Y T P S P T E V E A 264

Conservation



AeJHAMT/1-278 190 E I L S S V G F T K Y K I H I A D K - I Y V Y - - - - - E G I D S L K K A V Q A V - N P F 227
 3CCF/1-242 158 N I L E K Q G F D V T Y A A L F N R P T T L A - - - - - E G E F G M A N W I Q M F A S A F 197
 1M6E/1-359 265 E I L K E G S F L I D H I E A S E - - I Y W S S C T K D G D G G G S V E E E G Y N V A R C M R A V A E P L 315

Conservation



AeJHAMT/1-278 228 - S E R M P L D L Q E D F L N D Y - I A V V R R M S L S E N C C G N E N D Y K F I T P Y - - - K L V V V Y 275
 3CCF/1-242 198 - L V G L T P D Q Q V Q L I R K V - E A T L - - - - - Q D K L Y H Q E - - - S W T A D Y R R I R I V S I - 239
 1M6E/1-359 316 L L D H F G E A I I E D V F H R Y K L L I I E R M S K - - - - - E K T K F I - - - - - N V I V S L I R 356

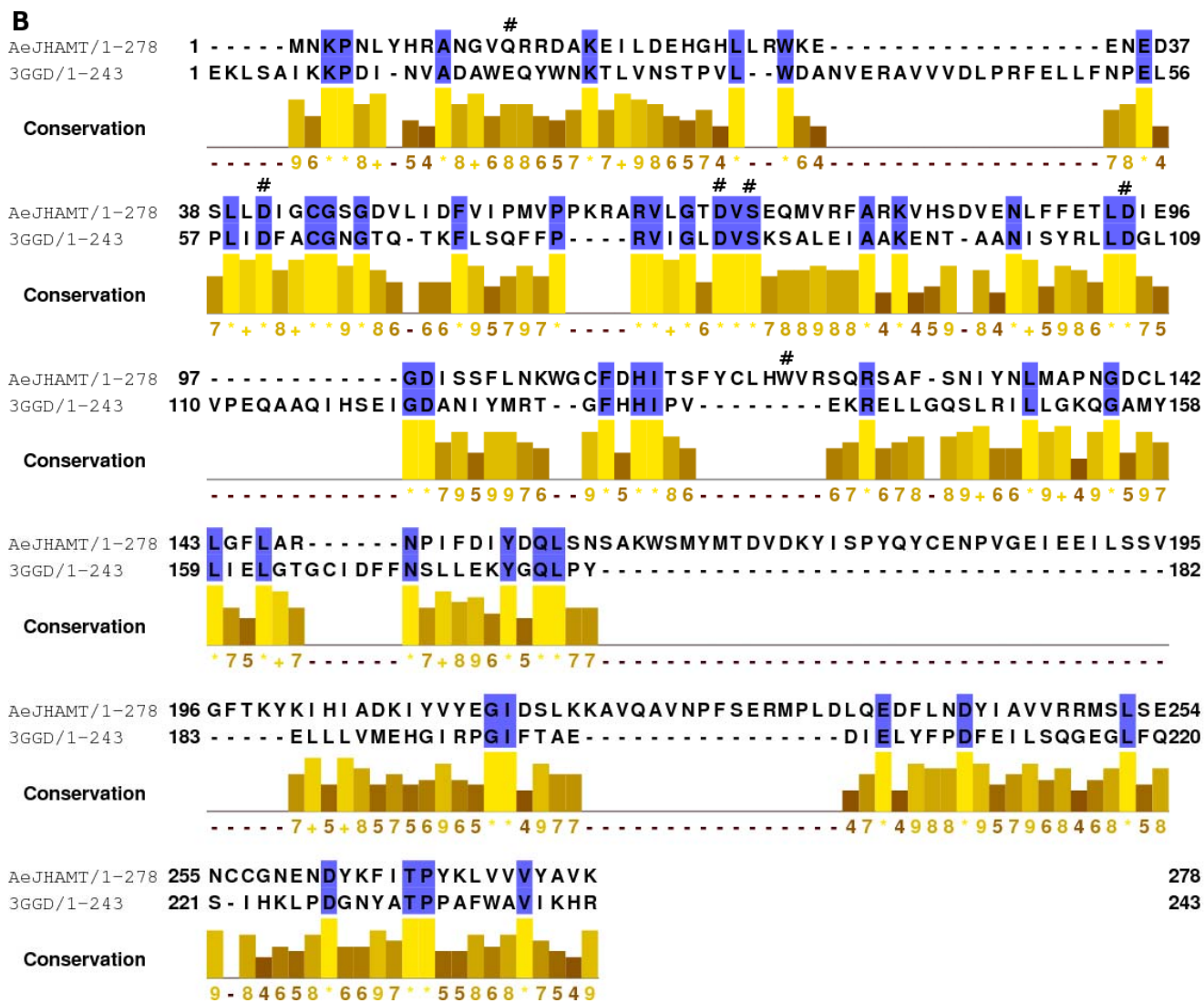
Conservation



AeJHAMT/1-278 276 A V K 278
 3CCF/1-242 240 K A Q 242
 1M6E/1-359 357 K S D 359

Conservation





(A) Sequence alignment between AeJHAMT, 3CCF and 1M6E. The alignment was performed using T-COFFEE (Poirot et al., 2003) and drawn with Jalview (Clamp et al., 2004). Residues shaded in blue are conserved (marked with * in the conservation panel). Residues shaded in light blue are semiconserved (marked with + in the conservation panel). Important residues interacting with SAM and the carboxylic acid in our docking simulations are marked with # (same residues highlighted in Figure 5). 9 to 0 values represent degree of conservation in all species. Conservation is measured as a numerical index reflecting the conservation of physicochemical properties in the alignment. Identities score the highest and the next most conserved group contain substitutions to amino acids included in the same physicochemical class as described by Livingstone, et al., 1993.

(B) Sequence alignment between AeJHAMT and 3GGD, an additional SAM-dependent methyltransferase, which was also evaluated to be used as a template. Note the absence in 3GGD of critical residues for substrate interaction such as Q14 and W120. Residues coding are the same as in A.

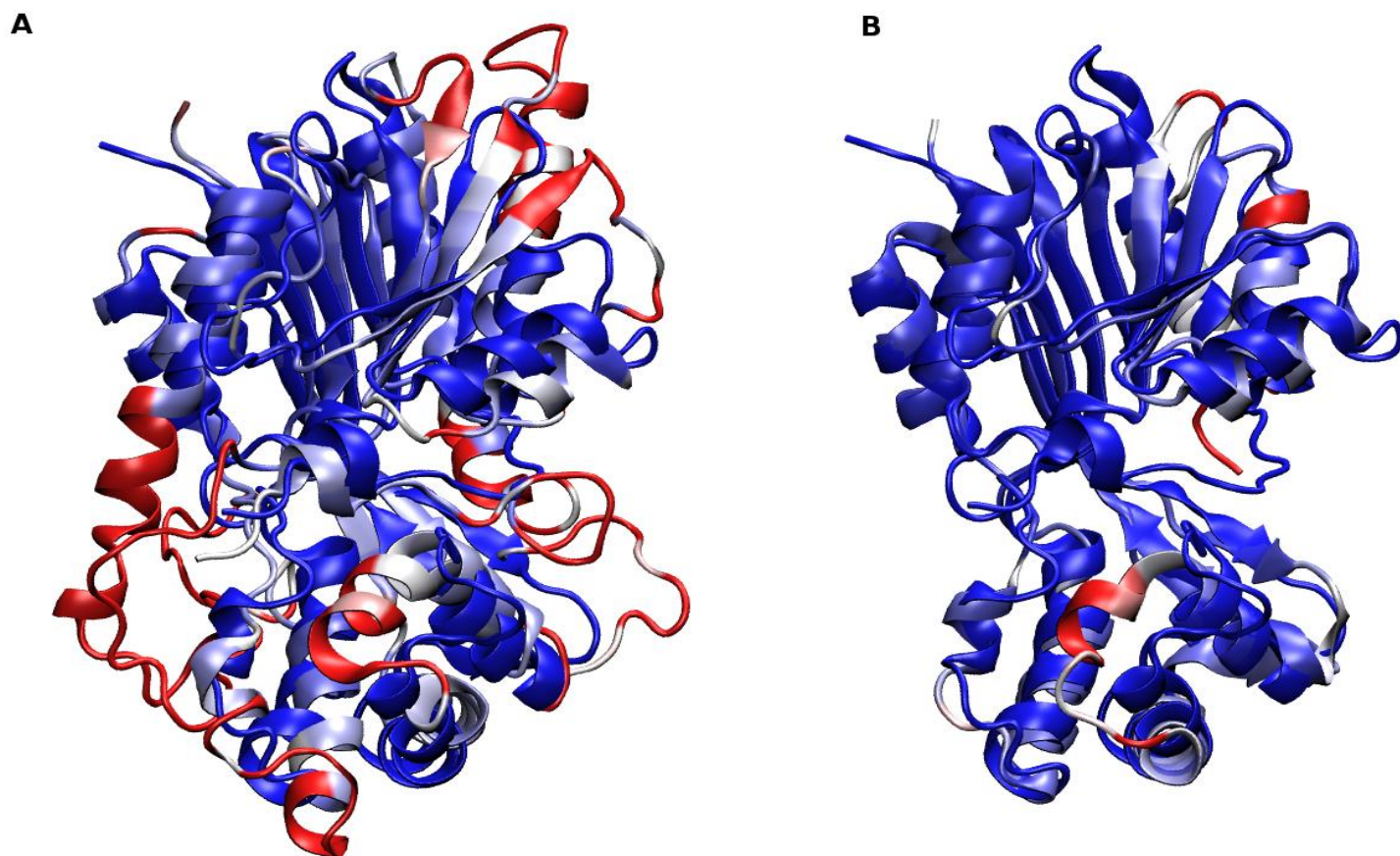
References

Clamp, M., Cuff, J., Searle, S. M., Barton, G. J. 2004. "The Jalview Java Alignment Editor". *Bioinformatics* 20, 426-7

Livingstone, C.D., Barton, G.J., 1993. Protein sequence alignments: a strategy for the hierarchical analysis of residue conservation. *Comput. Appl. Biosci.* 9, 745-756.

Poirot, O., O'Toole, E., Notredame, C. 2003. Tcoffee@igs: A web server for computing, evaluating and combining multiple sequence alignments. *Nucleic Acids Res.* 31, 3503-3506.

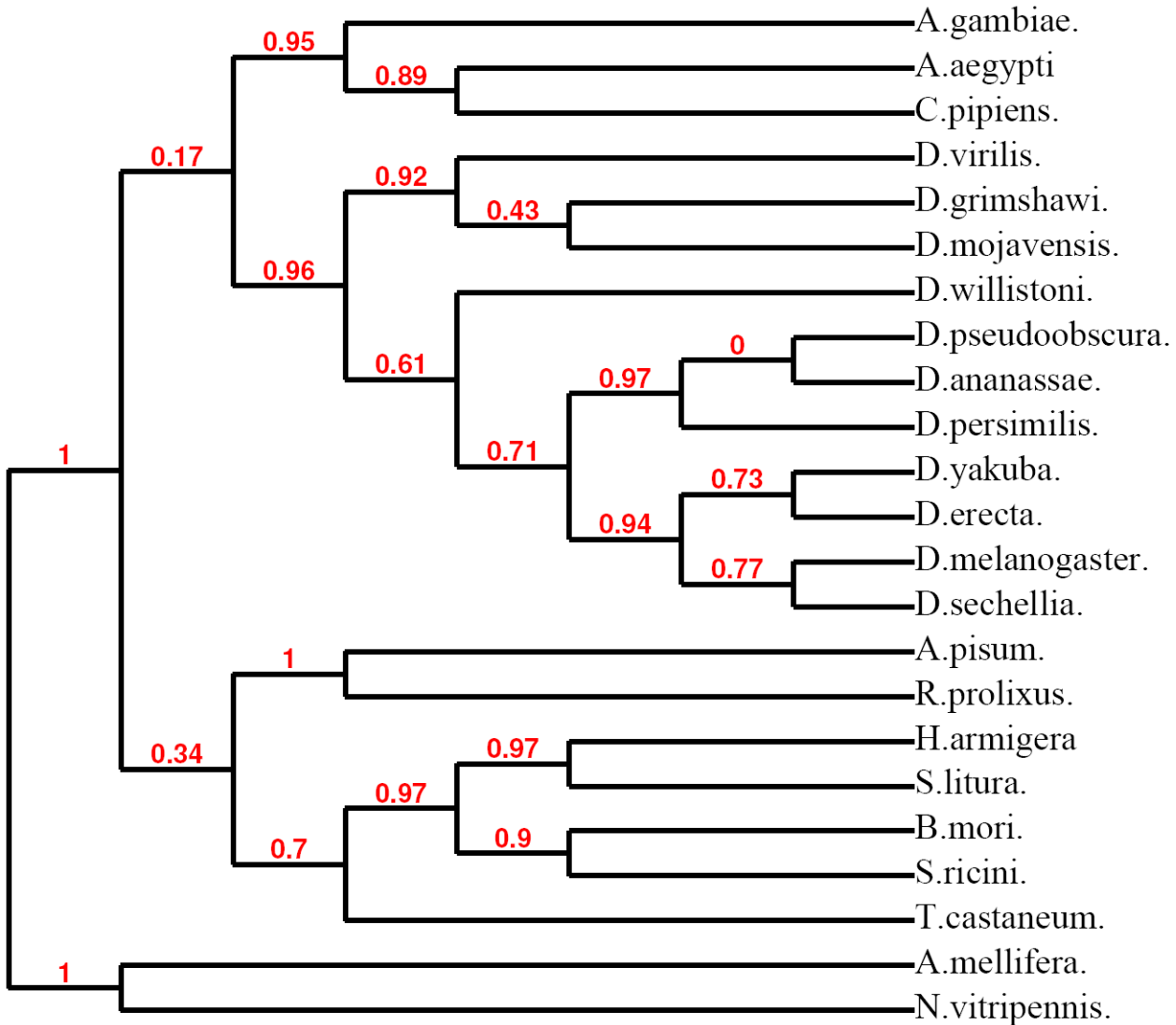
Supplementary figure 2



(A) Structural alignment between AeJHAMT and 1M6E colored showing the Root Mean Standard Deviation (RMSD) of the structurally aligned parts using AeJHAMT as a reference. Coloring goes from Blue as low RMSD to white as intermediate to red as high RMSD. (B) Same as (A) but between AeJHAMT and 3CCF. RMSD is a quantitative parameter used to estimate difference in the overall fold of proteins (Leach, 2001)

References: Leach, A. R. 2001. "Molecular Modeling, principles and applications, Second Edition", Pearson Prentice Hall, Essex, England.

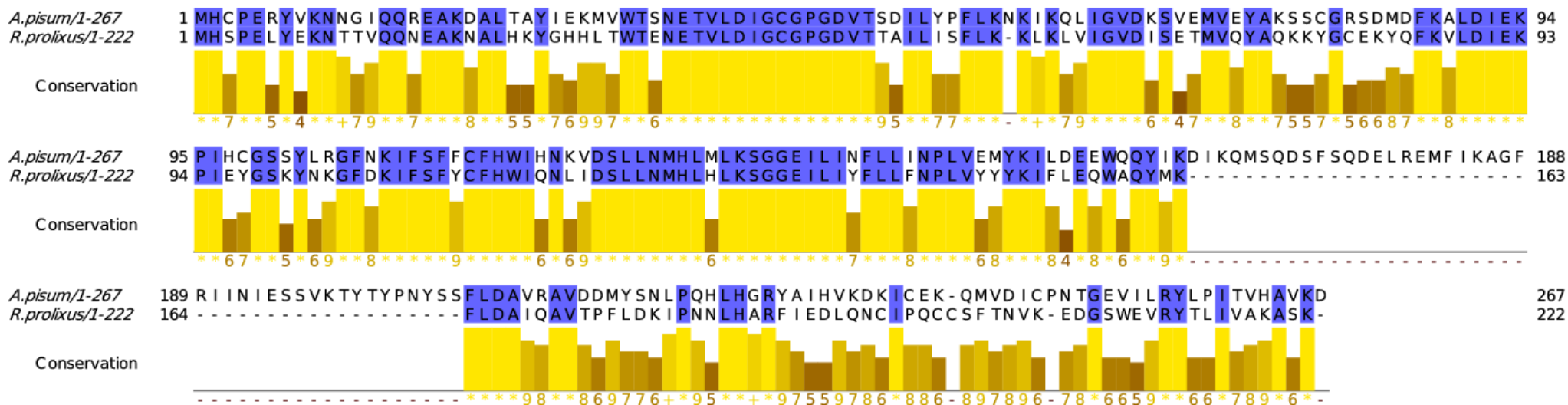
Supplementary figure 3



Phylogenetic analysis of the JHAMTs from different species of insects based on the primary amino acid sequences. Sequences are labeled with the species name. Phylogenetic analyses were done using Phylogeny.fr (Dereeper et al., 2008).

References: Dereeper A., Guignon V., Blanc G., Audic S., Buffet S., Chevenet F., Dufayard J.F., Guindon S., Lefort V., Lescot M., Claverie J.M., Gascuel O. (2008) Phylogeny.fr: robust phylogenetic analysis for the non-specialist. *Nucleic Acids Research*. 2008 Jul 1; 36 (Web Server Issue):W465-9. Epub 2008 Apr 19).

Supplementary Fig. 4



Sequence alignment between JHAMTs from *Acyrthosiphon pisum* and *Rhodnius prolixus*. The alignment was performed using TCOFEE (Poirot et al., 2003) and drawn with Jalview (Clamp et al., 2004). Residues shaded in blue are conserved (marked with * in the conservation panel). Semiconserved residues are marked with + in the conservation panel. 9 to 0 values represent degree of conservation in both species. Conservation is measured as a numerical index reflecting the conservation of physicochemical properties in the alignment. Identities score the highest and the next most conserved group contain substitutions to amino acids included in the same physicochemical class as described by Livingstone, et al., 1993. References are the same as for Supplem. Fig. 1.