

# **Enhancing the prediction of protein pairings between interacting families using orthology information**

## ***Supplementary Material***

Jose M. G. Izarzugaza, David Juan, Carles Pons, Florencio Pazos\*, Alfonso Valencia

\*Corresponding author  
pazos@cnb.uam.es  
Tlf. +34.915854669  
Fax. +34.915854506

**Table S1.** List of the 14 experimentally described links between members of the sensor kinase and response regulator families of the Ntr-like two component system. The seven links between KEGG orthologous (KO) groups implicitly produced by these 14 links are shown below. All the members of these linked KOs are assumed to interact.

| Organism | Protein_1 | KOG_1  | Protein_2 | KOG_2  |
|----------|-----------|--------|-----------|--------|
| Eco      | B3869     | K07708 | B3868     | K07712 |
| Eco      | B4003     | K07709 | B4004     | K07713 |
| Eco      | B2219     | K07710 | B2220     | K07714 |
| Eco      | B2556     | K07711 | B2554     | K07715 |
| Sty      | STY3875   | K07708 | STY3876   | K07712 |
| Sty      | STY2634   | K08475 | STY2633   | K08476 |
| Sty      | STY3712   | K07709 | STY3711   | K07713 |
| Hpy      | HP0244    | K07710 | HP0703    | K02481 |
| Hpj      | JHP0229   | K02482 | JHP0643   | K02481 |
| Ctr      | CT467     | K07710 | CT468     | K02481 |
| Cpn      | CPN0584   | K07710 | CPN0586   | K02481 |
| Bbu      | BB0764    | K02482 | BB0763    | K02481 |
| Aae      | Aq_1115   | K02482 | Aq_1117   | K02481 |
| Aae      | Aq_231    | K02482 | Aq_230    | K02481 |
|          |           |        |           |        |

1. - K02481 - K02482
2. - K08476 - K08475
3. - K02481 - K07710
4. - K07715 - K07711
5. - K07714 - K07710
6. - K07713 - K07709
7. - K07712 - K07708

**Figure S1.** Boxplots showing the relationship between the accuracy and different characteristics of the pairs of domains for trees based on *Kimura* and *Scoredist* distances. See main text for details.

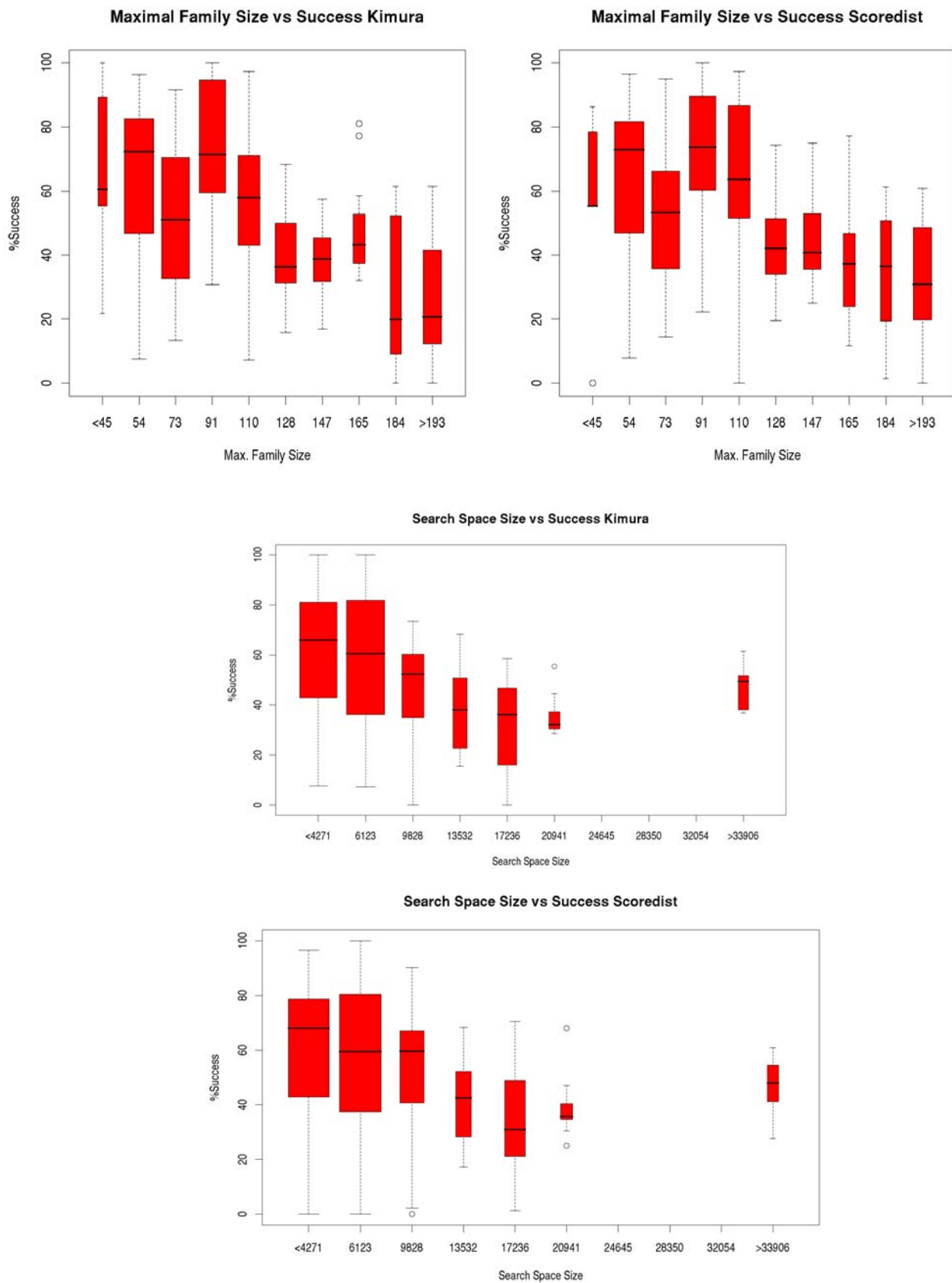


Figure S1 (cont.)

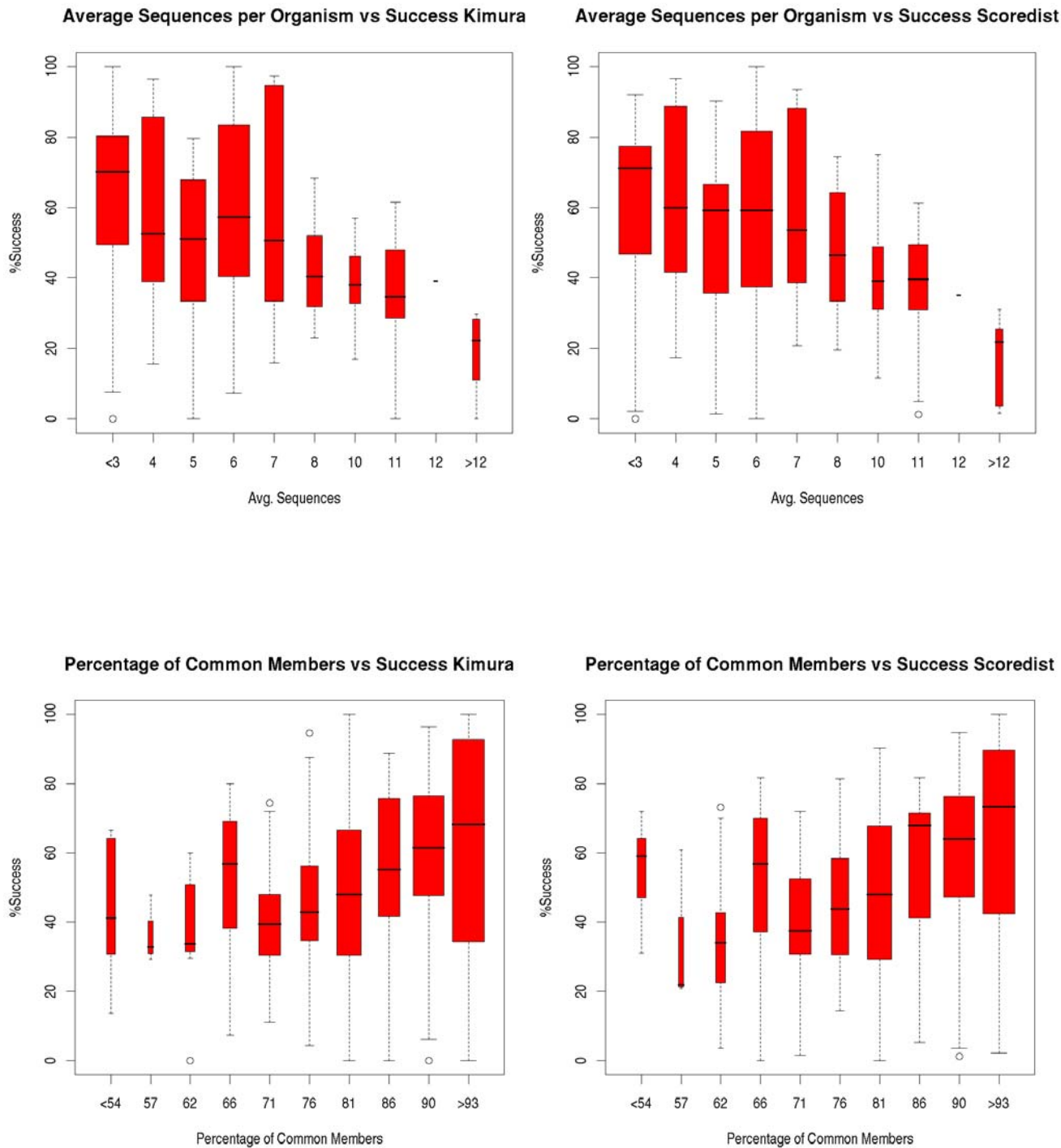
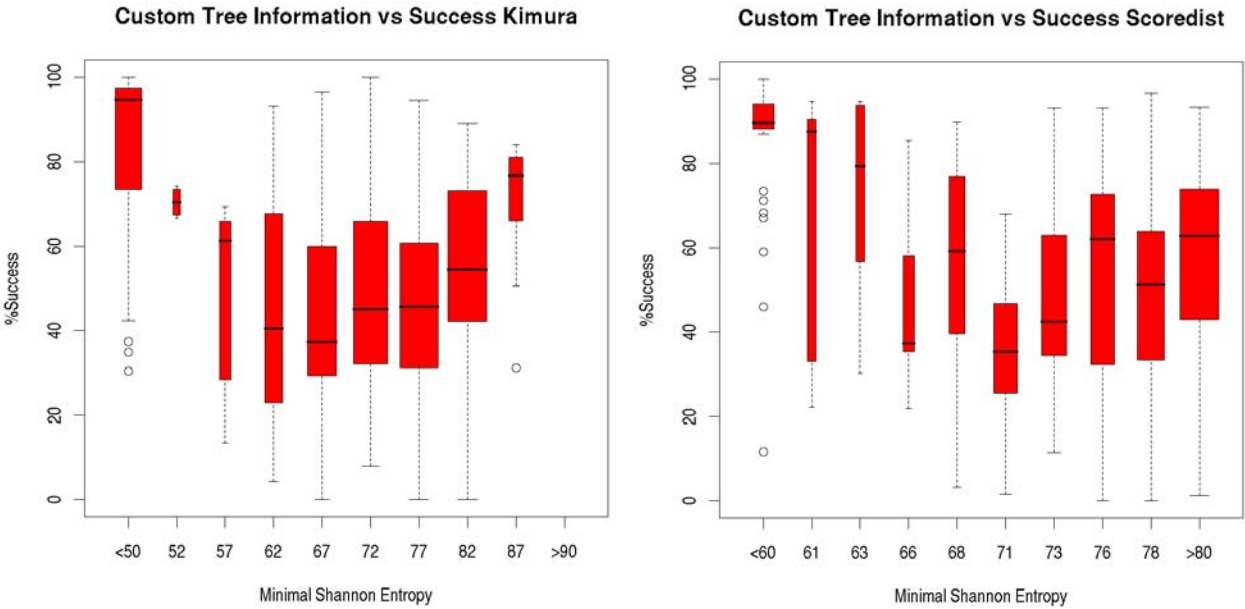


Figure S1 (cont.)



**Table S2.** Predicted pairings between the sensor kinase and response regulator families of the Ntr-like two component system corresponding to the best mapping found by TAG-TSEMA. The “reliability” and “disgregation” scores for each pairing are shown (see Izarzugaza *et al.* (2006). Nucleic Acids Res., 34:W315-319). The last column indicates whether that particular pairing is correct (“OK”), clearly wrong (“x”) or wrong possibly due to a wrong KO assignment (“bad KO (?)”). See the main text for details. A graphical representation of this mapping is shown in Figure S2.

| SENSOR           | KO     | RESPONSE         | KO     | RELIABILITY | DISGREGATION | HIT?       |
|------------------|--------|------------------|--------|-------------|--------------|------------|
| tcx:Tcr_0905     | K07708 | tcx:Tcr_0906     | K07712 | 98.4        | 96.8         | OK         |
| rpc:RPC_2577     | K07708 | rpc:RPC_2578     | K07712 | 100         | 100          | OK         |
| ypa:YPA_1084     | K07709 | ypa:YPA_1085     | K07713 | 74.8        | 50.6         | OK         |
| noc:Noc_0783     | K07711 | noc:Noc_0785     | K02481 | 73.2        | 46.4         | bad KO (?) |
| ilo:IL2436       | K07708 | ilo:IL2435       | K02481 | 100         | 100          | bad KO (?) |
| plu:plu0236      | K07708 | plu:plu0235      | K07712 | 97.4        | 94.8         | OK         |
| ecc:c3079        | K07711 | ecc:c3077        | K07715 | 73.2        | 48           | OK         |
| eci:UTI89_C4458  | K07708 | eci:UTI89_C4457  | K07712 | 97.4        | 94.8         | OK         |
| pcu:pc1365       | K07710 | pcu:pc1364       | K02481 | 100         | 100          | OK         |
| sfx:S2775        | K07711 | sfx:S2773        | K07715 | 73.2        | 48           | OK         |
| stm:STM2397      | K08475 | stm:STM2396      | K08476 | 100         | 100          | OK         |
| pst:PSPTO_0353   | K07708 | pst:PSPTO_0352   | K07712 | 100         | 100          | OK         |
| bms:BR1118       | K07708 | bms:BR1117       | K07712 | 100         | 100          | OK         |
| ret:RHE_CH01947  | K07708 | ret:RHE_CH01948  | K07712 | 100         | 100          | OK         |
| pfl:PFL_0378     | K07708 | pfl:PFL_0377     | K07712 | 100         | 100          | OK         |
| dar:Daro_3759    | K07708 | dar:Daro_3758    | K02481 | 100         | 100          | bad KO (?) |
| dvu:DVU3382      | K07709 | dvu:DVU3381      | K07713 | 50.2        | 23.6         | OK         |
| eba:ebA960       | K07711 | eba:ebA966       | K02481 | 73.2        | 46.4         | bad KO (?) |
| ppu:PP_5047      | K07708 | ppu:PP_5048      | K07712 | 100         | 100          | OK         |
| sbo:SBO_4024     | K07709 | sbo:SBO_4025     | K07713 | 74.8        | 50.6         | OK         |
| hch:HCH_06659    | K07711 | hch:HCH_06661    | K07715 | 73.2        | 48.2         | OK         |
| eli:ELI_06280    | K07708 | eli:ELI_06275    | K07712 | 100         | 100          | OK         |
| nmu:Nmul_A1159   | K07711 | nmu:Nmul_A2671   | K02481 | 100         | 100          | x          |
| ece:Z5579        | K07709 | ece:Z5580        | K07713 | 74.8        | 50.6         | OK         |
| atc:AGR_C_2663   | K07708 | atc:AGR_C_2665   | K07712 | 100         | 100          | OK         |
| gme:Gmet_2562    | K07708 | gme:Gmet_2453    | K02481 | 30          | -40          | bad KO (?) |
| hpy:HP0244       | K07710 | hpy:HP0703       | K02481 | 100         | 100          | OK         |
| ypa:YPA_3519     | K07708 | ypa:YPA_3520     | K07712 | 97.4        | 94.8         | OK         |
| cca:CCA00157     | K07710 | cca:CCA00155     | K02481 | 100         | 100          | OK         |
| dde:Dde_0110     | K07709 | dde:Dde_0109     | K07713 | 73          | 48.6         | OK         |
| abo:ABO_2260     | K07708 | abo:ABO_2259     | K07712 | 100         | 100          | OK         |
| stm:STM2564      | K07711 | stm:STM2562      | K07715 | 73.2        | 48           | OK         |
| bpa:BPP2987      | K07708 | bpa:BPP2986      | K07712 | 100         | 100          | OK         |
| bja:blr4487      | K07708 | bja:blr4488      | K07712 | 100         | 100          | OK         |
| spt:SPA0302      | K07711 | spt:SPA0304      | K07715 | 73.2        | 48           | OK         |
| ecp:ECP_2558     | K07711 | ecp:ECP_2556     | K07715 | 73.2        | 48           | OK         |
| she:Shewmr4_0258 | K07708 | she:Shewmr4_0257 | K07712 | 100         | 100          | OK         |
| rme:Rmet_2060    | K07708 | rme:Rmet_2059    | K07712 | 100         | 100          | OK         |
| rpa:RPA2592      | K07708 | rpa:RPA2593      | K07712 | 100         | 100          | OK         |
| ecs:ECs4926      | K07709 | ecs:ECs4927      | K07713 | 74.8        | 50.6         | OK         |
| cpj:CPj0584      | K07710 | cpj:CPj0586      | K02481 | 100         | 100          | OK         |

|                 |        |                 |        |      |      |            |
|-----------------|--------|-----------------|--------|------|------|------------|
| mag:amb2366     | K07708 | mag:amb2367     | K07712 | 100  | 100  | OK         |
| sec:SC2559      | K07711 | sec:SC2557      | K02481 | 73.2 | 48   | bad KO (?) |
| sfl:SF3939      | K07708 | sfl:SF3938      | K07712 | 97.4 | 94.8 | OK         |
| bmf:BAB1_1141   | K07708 | bmf:BAB1_1140   | K07712 | 100  | 100  | OK         |
| ppr:PBPR2770    | K08475 | ppr:PBPR2771    | K08476 | 100  | 100  | OK         |
| sdY:SDY_3874    | K07708 | sdY:SDY_3875    | K07712 | 97.4 | 94.8 | OK         |
| ype:YPO0023     | K07708 | ype:YPO0022     | K07712 | 97.4 | 94.8 | OK         |
| pfo:Pfl_0340    | K07708 | pfo:Pfl_0339    | K07712 | 100  | 100  | OK         |
| eba:ebA4117     | K07708 | eba:ebA4116     | K02481 | 100  | 100  | bad KO (?) |
| ecs:ECs3422     | K07711 | ecs:ECs3420     | K07715 | 73.2 | 48   | OK         |
| nwi:Nwi_1444    | K07708 | nwi:Nwi_1445    | K07712 | 100  | 100  | OK         |
| cpt:CpB0608     | K07710 | cpt:CpB0610     | K02481 | 100  | 100  | OK         |
| ypn:YPN_0250    | K07708 | ypn:YPN_0249    | K07712 | 97.4 | 94.8 | OK         |
| ece:Z3833       | K07711 | ece:Z3830       | K07715 | 73.2 | 48   | OK         |
| lip:LI1078      | K07709 | lip:LI1079      | K07713 | 74.8 | 49.6 | OK         |
| sec:SC2398      | K08475 | sec:SC2397      | K08476 | 100  | 100  | OK         |
| ecv:APECO1_4340 | K07710 | ecv:APECO1_4339 | K07714 | 100  | 100  | OK         |
| eco:b4003       | K07709 | eco:b4004       | K07713 | 74.8 | 50.6 | OK         |
| eca:ECA3257     | K07711 | eca:ECA3255     | K07715 | 97.4 | 94.8 | OK         |
| sfx:S3807       | K07708 | sfx:S3808       | K07712 | 97.4 | 94.8 | OK         |
| xac:XAC0207     | K07708 | xac:XAC0208     | K07712 | 100  | 100  | OK         |
| yps:YPTB2876    | K07711 | yps:YPTB2874    | K07715 | 73.2 | 48   | OK         |
| ecp:ECP_4080    | K07708 | ecp:ECP_4079    | K07712 | 97.4 | 94.8 | OK         |
| ecv:APECO1_3975 | K07711 | ecv:APECO1_3977 | K07715 | 73.2 | 48   | OK         |
| ecc:c4961       | K07709 | ecc:c4962       | K07713 | 74.8 | 50.6 | OK         |
| bte:BTH_I1845   | K07708 | bte:BTH_I1846   | K07712 | 100  | 100  | OK         |
| vfi:VF0096      | K07708 | vfi:VF0095      | K07712 | 100  | 100  | OK         |
| pat:PatI_1027   | K07708 | pat:PatI_1028   | K07712 | 97.4 | 94.8 | OK         |
| neu:NE0015      | K07711 | neu:NE0017      | K07715 | 64.8 | 29.6 | OK         |
| cpa:CP0164      | K07710 | cpa:CP0162      | K02481 | 100  | 100  | OK         |
| bbu:BB0764      | K02482 | bbu:BB0763      | K02481 | 100  | 100  | OK         |
| ype:YPO2916     | K07711 | ype:YPO2914     | K07715 | 97.4 | 94.8 | OK         |
| pol:Bpro_1119   | K07711 | pol:Bpro_1117   | K02481 | 100  | 100  | bad KO (?) |
| eco:b3869       | K07708 | eco:b3868       | K07712 | 97.4 | 94.8 | OK         |
| spt:SPA4010     | K07709 | spt:SPA4011     | K02481 | 74.8 | 50.6 | bad KO (?) |
| pca:Pcar_0496   | K07711 | pca:Pcar_0498   | K07715 | 100  | 100  | OK         |
| psp:PSPPH_4852  | K07708 | psp:PSPPH_4853  | K07712 | 100  | 100  | OK         |
| cvi:CV3591      | K07708 | cvi:CV3592      | K07712 | 100  | 100  | OK         |
| vpa:VP0119      | K07708 | vpa:VP0118      | K07712 | 100  | 100  | OK         |
| ppr:PBPR3494    | K07708 | ppr:PBPR3495    | K07712 | 100  | 100  | OK         |
| ypn:YPN_1222    | K07711 | ypn:YPN_1224    | K07715 | 73.2 | 48   | OK         |
| reu:Reut_A2055  | K07708 | reu:Reut_A2054  | K02481 | 100  | 100  | bad KO (?) |
| wsu:WS1590      | K02482 | wsu:WS0367      | K02481 | 100  | 100  | OK         |
| ypm:YP_0984     | K07709 | ypm:YP_0983     | K07713 | 74.8 | 50.6 | OK         |
| ypm:YP_2541     | K07711 | ypm:YP_2543     | K07715 | 73.2 | 48   | OK         |
| ssn:SSON_4176   | K07709 | ssn:SSON_4177   | K07713 | 74.8 | 50.6 | OK         |
| sec:SC4054      | K07709 | sec:SC4055      | K02481 | 74.8 | 50.6 | bad KO (?) |
| vpa:VPA0826     | K08475 | vpa:VPA0827     | K08476 | 100  | 100  | OK         |
| pae:PA5124      | K07708 | pae:PA5125      | K07712 | 100  | 100  | OK         |

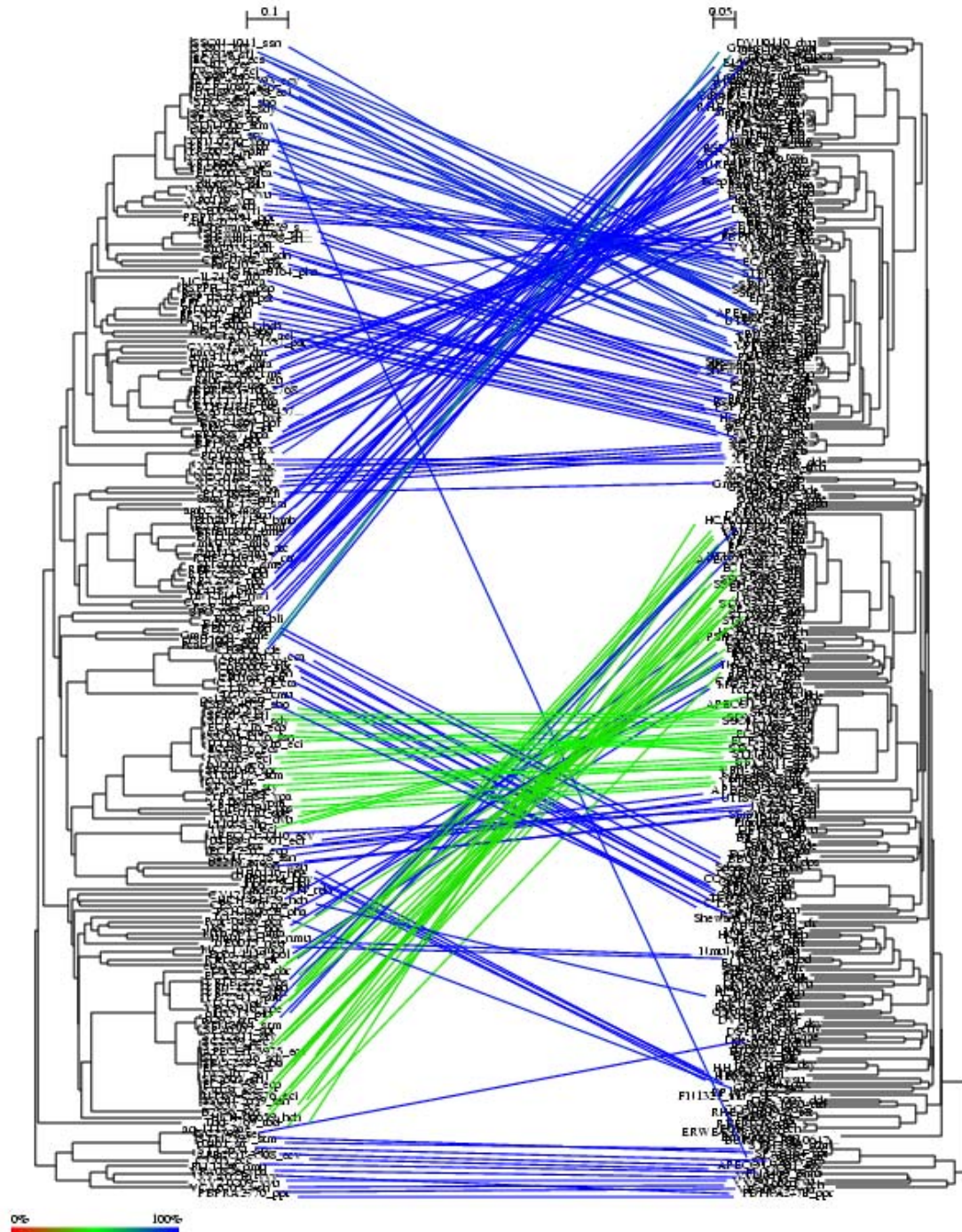
|                 |        |                 |        |      |       |            |
|-----------------|--------|-----------------|--------|------|-------|------------|
| ecp:ECP_2262    | K07710 | ecp:ECP_2263    | K07714 | 100  | 100   | OK         |
| ecc:c4818       | K07708 | ecc:c4817       | K07712 | 97.4 | 94.8  | OK         |
| nar:Saro_1927   | K07708 | nar:Saro_1928   | K07712 | 100  | 100   | OK         |
| sec:SC3898      | K07708 | sec:SC3897      | K02481 | 97.4 | 94.8  | bad KO (?) |
| sdn:Sden_3457   | K07708 | sdn:Sden_3458   | K07712 | 100  | 100   | OK         |
| tbd:Tbd_2501    | K07708 | tbd:Tbd_2500    | K07712 | 100  | 100   | OK         |
| bbr:BB2953      | K07708 | bbr:BB2952      | K07712 | 100  | 100   | OK         |
| stm:STM4173     | K07709 | stm:STM4174     | K07713 | 74.8 | 50.6  | OK         |
| pha:PSHAa0620   | K07711 | pha:PSHAa0622   | K07715 | 100  | 100   | OK         |
| ypa:YPA_2355    | K07711 | ypa:YPA_2353    | K07715 | 73.2 | 48    | OK         |
| ecj:JW3840      | K07708 | ecj:JW3839      | K07712 | 97.4 | 94.8  | OK         |
| son:SO4471      | K07708 | son:SO4472      | K07712 | 100  | 100   | OK         |
| dar:Daro_1802   | K07711 | dar:Daro_1804   | K02481 | 73   | 46    | bad KO (?) |
| ssn:SSON_2278   | K07710 | ssn:SSON_2279   | K07714 | 100  | 100   | OK         |
| sbo:SBO_2584    | K07711 | sbo:SBO_2582    | K07715 | 73.2 | 48    | OK         |
| stt:t3615       | K07708 | stt:t3616       | K07712 | 97.4 | 94.8  | OK         |
| aae:aq_231      | K02482 | aae:aq_230      | K02481 | 75.4 | 50.8  | OK         |
| rfr:Rfer_2981   | K07708 | rfr:Rfer_2982   | K07712 | 100  | 100   | OK         |
| xcb:XC_0197     | K02482 | xcb:XC_0198     | K02481 | 100  | 100   | OK         |
| ecc:c5203       | K08475 | ecc:c5204       | K08476 | 100  | 100   | OK         |
| cps:CPS_0398    | K07708 | cps:CPS_0397    | K07712 | 100  | 100   | OK         |
| spt:SPA3847     | K07708 | spt:SPA0464     | K08476 | 97.4 | 94.8  | bad KO (?) |
| bpe:BP1597      | K07708 | bpe:BP1598      | K07712 | 100  | 100   | OK         |
| tcx:Tcr_2189    | K07711 | tcx:Tcr_1444    | K02481 | 100  | 100   | x          |
| cpn:CPn0584     | K07710 | cpn:CPn0586     | K02481 | 100  | 100   | OK         |
| atu:Atu1445     | K07708 | atu:Atu1446     | K07712 | 100  | 100   | OK         |
| ssn:SSON_4041   | K07708 | ssn:SSON_4040   | K07712 | 97.4 | 94.8  | OK         |
| ecc:c2762       | K07710 | ecc:c2763       | K07714 | 100  | 100   | OK         |
| cps:CPS_4270    | K07711 | cps:CPS_4272    | K07715 | 100  | 100   | OK         |
| ypm:YP_0024     | K07708 | ypm:YP_0023     | K07712 | 97.4 | 94.8  | OK         |
| aci:ACIAD1369   | K07708 | aci:ACIAD1368   | K07712 | 100  | 100   | OK         |
| ypk:y1313       | K07711 | ypk:y1315       | K07715 | 97.4 | 97.4  | OK         |
| eco:b2219       | K07710 | eco:b2220       | K07714 | 100  | 100   | OK         |
| bmb:BruAb1_1124 | K07708 | bmb:BruAb1_1123 | K02481 | 100  | 100   | bad KO (?) |
| bme:BMEI0865    | K07708 | bme:BMEI0866    | K07712 | 100  | 100   | OK         |
| sgl:SG2231      | K07708 | sgl:SG2232      | K07712 | 97.4 | 94.8  | OK         |
| ece:Z5405       | K07708 | ece:Z5404       | K07712 | 97.4 | 94.8  | OK         |
| vch:VC2748      | K07708 | vch:VC2749      | K07712 | 100  | 100   | OK         |
| hhe:HH0140      | K02482 | hhe:HH1635      | K02481 | 100  | 100   | OK         |
| ecj:JW3967      | K07709 | ecj:JW3968      | K07713 | 74.8 | 50.6  | OK         |
| yps:YPTB0023    | K07708 | yps:YPTB0022    | K07712 | 97.4 | 94.8  | OK         |
| hch:HCH_01429   | K07711 | hch:HCH_00696   | K02481 | 94.6 | 89.2  | x          |
| sfl:SF2603      | K07711 | sfl:SF2601      | K07715 | 73.2 | 48    | OK         |
| eci:UTI89_C2501 | K07710 | eci:UTI89_C2502 | K07714 | 100  | 100   | OK         |
| rpd:RPD_2589    | K07708 | rpd:RPD_2590    | K07712 | 100  | 100   | OK         |
| pca:Pcar_1993   | K07708 | pca:Pcar_1994   | K07712 | 100  | 100   | OK         |
| rru:Rru_A1677   | K07708 | rru:Rru_A1678   | K07712 | 100  | 100   | OK         |
| yps:YPTB1204    | K07709 | yps:YPTB1205    | K07713 | 74.8 | 50.6  | OK         |
| gsu:GSU1004     | K07708 | gsu:GSU1320     | K02481 | 29.6 | -40.8 | bad KO (?) |



|                     |        |                     |        |      |      |            |
|---------------------|--------|---------------------|--------|------|------|------------|
| cfe:CF0850          | K07710 | cfe:CF0852          | K02481 | 100  | 100  | OK         |
| psb:Psyr_4821       | K07708 | psb:Psyr_4822       | K07712 | 100  | 100  | OK         |
| pha:PSHAa0164       | K07708 | pha:PSHAa0163       | K07712 | 100  | 100  | OK         |
| eca:ECA0028         | K07708 | eca:ECA0027         | K07712 | 97.4 | 94.8 | OK         |
| bga:BG0787          | K02482 | bga:BG0786          | K02481 | 100  | 100  | OK         |
| bma:BMA1741         | K07708 | bma:BMA1740         | K07712 | 100  | 100  | OK         |
| xfa:XF1849          | K07708 | xfa:XF1848          | K07712 | 100  | 100  | OK         |
| hpj:jhp0229         | K02482 | hpj:jhp0643         | K02481 | 100  | 100  | OK         |
| xcc:XCC0188         | K07708 | xcc:XCC0189         | K07712 | 100  | 100  | OK         |
| ecv:APECO1_2593     | K07708 | ecv:APECO1_2594     | K07712 | 97.4 | 94.8 | OK         |
| ctr:CT467           | K07710 | ctr:CT468           | K02481 | 100  | 100  | OK         |
| sil:SPO2088         | K02482 | sil:SPO2087         | K02481 | 100  | 100  | OK         |
| rso:RSc1260         | K07708 | rso:RSc1261         | K02481 | 100  | 100  | bad KO (?) |
| stt:t0461           | K08475 | stt:t0462           | K08476 | 100  | 100  | OK         |
| xcv:XCV0191         | K07708 | xcv:XCV0192         | K07712 | 100  | 100  | OK         |
| rpb:RPB_2883        | K07708 | rpb:RPB_2882        | K07712 | 100  | 100  | OK         |
| ssn:SSON_2639       | K07711 | ssn:SSON_2637       | K07715 | 73.2 | 48   | OK         |
| rfr:Rfer_2788       | K07711 | rfr:Rfer_2786       | K02481 | 73.2 | 46.4 | bad KO (?) |
| cmu:TC0752          | K07710 | cmu:TC0753          | K02481 | 100  | 100  | OK         |
| vvy:VVA0716         | K08475 | vvy:VVA0717         | K08476 | 100  | 100  | OK         |
| pmu:PM1459          | K08475 | pmu:PM1460          | K08476 | 100  | 100  | OK         |
| stt:t0292           | K07711 | stt:t0293           | K07715 | 73.2 | 48   | OK         |
| hch:HCH_01034       | K07708 | hch:HCH_01033       | K07712 | 99.2 | 98.4 | OK         |
| bpm:BURPS1710b_2768 | K07708 | bpm:BURPS1710b_2766 | K07712 | 100  | 100  | OK         |
| sty:STY2634         | K08475 | sty:STY2633         | K08476 | 100  | 100  | OK         |
| sdv:SDY_3723        | K07709 | sdv:SDY_3722        | K07713 | 74.8 | 50.6 | OK         |
| ecj:JW2213          | K07710 | ecj:JW2214          | K07714 | 100  | 100  | OK         |
| pol:Bpro_1809       | K07708 | pol:Bpro_1810       | K07712 | 100  | 100  | OK         |
| vch:VCA0705         | K08475 | vch:VCA0704         | K08476 | 100  | 100  | OK         |
| eco:b2556           | K07711 | eco:b2554           | K07715 | 73.2 | 48   | OK         |
| sme:SMc01042        | K07708 | sme:SMc01043        | K07712 | 100  | 100  | OK         |
| mlo:mlr0397         | K07708 | mlo:mlr0398         | K07712 | 100  | 100  | OK         |
| xft:PD1020          | K07708 | xft:PD1021          | K07712 | 100  | 100  | OK         |
| par:Psyc_1537       | K07708 | par:Psyc_1538       | K07712 | 100  | 100  | OK         |
| cvi:CV4218          | K07711 | cvi:CV4220          | K07715 | 100  | 100  | OK         |
| sty:STY2811         | K07711 | sty:STY2809         | K07715 | 73.2 | 48   | OK         |
| cta:CTA_0511        | K07710 | cta:CTA_0512        | K02481 | 100  | 100  | OK         |
| ecv:APECO1_3508     | K08475 | ecv:APECO1_3507     | K08476 | 100  | 100  | OK         |
| stt:t3458           | K07709 | stt:t3457           | K07713 | 74.8 | 50.6 | OK         |
| vvy:VV0197          | K07708 | vvy:VV0196          | K07712 | 100  | 100  | OK         |
| tbd:Tbd_2769        | K07711 | tbd:Tbd_2771        | K07715 | 68   | 36   | OK         |
| eci:UTI89_C2876     | K07711 | eci:UTI89_C2873     | K07715 | 73.2 | 71.6 | OK         |
| sty:STY3875         | K07708 | sty:STY3876         | K07712 | 97.4 | 94.8 | OK         |
| aae:aq_1115         | K02482 | aae:aq_164          | K02481 | 75.4 | 50.8 | OK         |
| sfx:S3660           | K07709 | sfx:S3659           | K07713 | 74.8 | 50.6 | OK         |
| rsp:RSP_2837        | K07708 | rsp:RSP_2838        | K02481 | 99.8 | 99.6 | bad KO (?) |
| plu:plu3313         | K07711 | plu:plu3311         | K07715 | 97.4 | 94.8 | OK         |
| vvu:VV2_0209        | K08475 | vvu:VV2_0210        | K08476 | 100  | 100  | OK         |
| sty:STY3712         | K07709 | sty:STY3711         | K07713 | 74.8 | 50.6 | OK         |

|                     |        |                     |        |      |      |            |
|---------------------|--------|---------------------|--------|------|------|------------|
| bps:BPSL2317        | K07708 | bps:BPSL2316        | K07712 | 100  | 100  | OK         |
| sfl:SF4075          | K07709 | sfl:SF4076          | K07713 | 74.8 | 50.6 | OK         |
| shm:Shewmr7_3763    | K07708 | shm:Shewmr7_3764    | K07712 | 100  | 100  | OK         |
| mca:MCA1715         | K07711 | mca:MCA1713         | K07715 | 100  | 100  | OK         |
| bur:Bcep18194_A5457 | K07708 | bur:Bcep18194_A5456 | K07712 | 100  | 100  | OK         |
| ecp:ECP_4216        | K07709 | ecp:ECP_4217        | K07713 | 74.8 | 50.6 | OK         |
| stm:STM4006         | K07708 | stm:STM4005         | K07712 | 97.4 | 94.8 | OK         |
| ecj:JW5407          | K07711 | ecj:JW2538          | K07715 | 73.2 | 48   | OK         |
| vwu:VV1_0891        | K07708 | vwu:VV1_0892        | K07712 | 100  | 100  | OK         |
| sfr:Sfri_0321       | K07708 | sfr:Sfri_0320       | K07712 | 100  | 100  | OK         |
| sal:Sala_1276       | K07708 | sal:Sala_0950       | K02481 | 97.2 | 94.4 | x          |
| sdv:SDY_2746        | K07711 | sdv:SDY_2744        | K07715 | 73.2 | 48   | OK         |
| ecs:ECs4791         | K07708 | ecs:ECs4790         | K07712 | 97.4 | 94.8 | OK         |
| sbo:SBO_3881        | K07708 | sbo:SBO_3880        | K07712 | 97.4 | 94.8 | OK         |
| xoo:XOO4484         | K07708 | xoo:XOO4483         | K02481 | 100  | 100  | bad KO (?) |
| mfa:Mfla_2449       | K07708 | mfa:Mfla_2450       | K02481 | 100  | 100  | bad KO (?) |
| shn:Shewana3_0259   | K07708 | shn:Shewana3_0258   | K07712 | 100  | 100  | OK         |

**Figure S2.** Graphical representation of the predicted pairings between the sensor kinase and response regulator families of the Ntr-like two component system corresponding to the best mapping found by TAG-TSEMA. The colour of the links corresponds to their “reliability” score according to the scale shown at the bottom (see Izarzugaza *et al.* (2006). *Nucleic Acids Res.*, 34:W315-319).



**Figure S3.** Relationship between the number of organisms, the average number of sequences per organism and the accuracy. The bottom-left panel shows the a 3D representation of the space defined by these three variables, while the other panels show different 2D projections of that space. The accuracy is also represented with a color gradient (right).

