a

```
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2yeqA  57(1):APNFSSYPFTLGVASGDPLSDSVVLWTRLAPDPLN-GGGMPKQAVPVKWEVAKDEHFRKIVRKGTEMAKPSIAHSVHVEADGLEPNKVYYYRFKTGHELSPVGKTKTLPA PGANVPQMTFAFASCQQYEHG:186(130)
Rta       32:QRRWGFDPFSLGVASGSPAADSVVLWTRL-LGPGWWDSIGE-APVPVRWEVAHDQGFSRIARRGETLALAQLGHSVHAEVAGLEPDRWYFYRFTAGHAVSPTGRTRTLPA ADALPARLRLAYASCQRWEHG:160
              * ******* * ********** *       *** **** *  *  * *   *  * **** * ****  * *** ** ** * **** *      * **** ***

[AVE_SECSTR]       CCHHHHHHhhSCCSEEEECSCSSCCCCstsScsttsCsSCCSSSSCCSHHHHHHHHHHHHHTCHHHHHHHHHSEEEECCCSTTTSTTCBTTBCSTTCsssssCHHHHHHHHHHHHHHHHHHHSCCCGGGsCccs
2yeqA       YYTAYKHMAKEKLDLVFHLGDYIYEYGPNEYVSKTGNVRTHNSAEIITLQDYRNRHAQYRSDANLKAAHAAFPWVVTWDDHEVENNYANKIPEKGQ-----SVEAFVLRRAAAYQAYYEHMPLRISSLPN--:310(254)
Rta         YYGAYRHMREEQLDLVMFLGDYIYEYPN-AT-A--AVRDFPTLGWVHTLQEYRERHALHRGDVHLQAMHAACPWLVSWDDHEVQNDYAAGQAGDGRPLGLNASSDFAARRAAAYQAYYEHMPLRASALGGAL:288
            ** ** ** * ****  ****  ******    ***  ** *** * *  * *** ** * ***** * **     *           *  ***************** * *

[AVE_SECSTR]       sscccttssCCCCEEEEETTTEEEEEECCSSSSCCCCttsSSsccccssssssCCHHHHCTTCCSSCHHHHHHHHHHHHHHHCCSSEEEEECSSCCSCCCCSSCSSSCCttTTSGGGHHHHHHHHHHHHHHHHHhTCCCEE
2yeqA       -----GPDMQLYRHFTYGNLASFNVLDTRQYRDDQANNDGN-------KPPSDESRNPNRTLLGKEQEQWLFNNLGSSTAHWNVLAQQIFFAKWNFGTSASPIYSMDSWDGYPAQRERVINFIKSKNLNNVV:431(375)
Rta         AGVAGAADVRLYGRWRFGRLADLLLLDTRQYRDRQVCGPDFKPSGQVHPSACPAWEDPGRSLLGAAQEQWLDTAFAQAGSGWTVVGQQTLFGRRDNHPGAGEQFWNDGWDGYGAARRRVTGSLQRHQVVNPV:420
                  *  **    * **   ********* *    * ***  ***** *      *  ***** ***   * * ** *      *      ****** * * **             * *

[AVE_SECSTR]       EEECSSSSEEEEEEESSTTcssSCEEEEEEEcCCSSTTCSCcSccCsthhhcsshCTTEEEEEcscEEEEEEEEEcsseEEEEEEEESCSSSSCCCCEEEEEEEEECSSTTCcEEceeccccttccsbcsccthhh
2yeqA       VLTGDVHASWASNLHVDFEKTSSKIFGAEFVGTSITSGGNGADKRADTDQILKENPHIQFFN-DYRGYVRCTVTPHQWKADYRVMPFVTEPGAAISTRASFVYQKDQTGLRKVSSTTIQGGVKQSDEVEEDR:562(506)
Rta         FLGGDVHENWVGHVKADYARQGSASLGVEFCGTSITSRAGGAEQVA-Q--RLAENPHYVFADGWRRGYSVCEFTPQRLTTTLRVLDDATREDARIETQARFTVQAGRPRLERA------------------:530
                 * ***   *       *      * ** ******  **   *      * **** *   *** * **      **     *  * * * *   *                    * *

[AVE_SECSTR]       hhhhhhhhhhhhhhhtc
2yeqA       FFSHNKAHEKQMIKKR:(522)
Rta         ----------------
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b

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[AVE_SECSTR] cccccccccccCsscCSCCCCCCCssccccccssssssscscsssttcbCcTTeeeeeeeeTTcbssCsttcccccttscccchhhhhtbCCSSEEEEeeEecscsssscsscssssseEEeeEEEECCCCHHHHSssc
4alfA  55(8):----------SRLLGFDSIPAATTD--------------T--ISLPKGYKSSVLISWGQP--LHKNGPAFDPSGNGTAAAQEVQFGDNNDGMSLFEFP--------GEKNRALMAINNEYTNYRYLYPHG:148(101)
Rta-1    52:------STPAARLRPGFEPVPIGAGD--------------R--LIVPKGYVASALAPWGEPVGLPGNLPVWRPDAGNTADEQAAQMGMHHDGLHYFPLD--------GSRRGLLVMNHEYVDDGLLHADG:151
Rta-2    51:------GTGPLLGFRSVAVSTED--------------R--VTVPQGYVAQALAAWGEPVGLPGRLPPFRPDASNTAAEQEAQLGMHHDGMHFFALE--------GGRGGLLAMNHEYTDDGLLHPDG:147
Sme      77:--------EGEASPFDFKEIEAGVDE--------------T--HHVAEGYDADILLRWGDK--VFADSPEFDP-LKQTADAQSRQFGYNNDYVGFIPLE--------GNPDHGLLVNHEYTNAEIMFPNF:172
Rta-3    68:ADVAAADVQSKALTLNFQPVPKSKAD--------------A--VLVPRGYTATPIYATGDP--LAATVPEYLNDGTDT--DFEHRAGDQHDGMEYFGLNATGTARDPNGSKRGLLVMNHEALVDQFLHANG:178
Rta-4    32:---------APAFGPGFGPLTPTLPLNTADLAVPGVFDFRDRPLISLPPGFRYWAISCTGQM--MSD---------------GTLVPGDHDGMACYRGP---------SGTTLLVRNHELNNREIKFGNA:126
               .  ..* ...     .          .        .    .: *:. . .   .   :    :. . .: .. .  :  .*:.  .  .        .. ..*:..*:.*....  .....

[AVE_SECSTR] tccssssctscsssscscscsscsscsccCsHHHHHHHHHHSEEEeeEEeeettteeeeecttcttceeeettseeeeesttttcgggccsscssscceeeCCCSEEEEEECTTSCEEEEECSggggCbcsssssc
4alfA       ---------G------MP--------QSAEDVRKALACEGVSVIEVQRKN-GQWQFVQGSRYNRRIHGNSPLRISGPAAGHELMKTSADKHGKKVLGTFQNCANGKTPWGTYLTCEENFTDCFGSSNA-QQ:254(207)
Rta-1       ---------L------KT--------WTLEKVRKSQAAHGIAVIEVEQAAGGEWRMVRPSRFARRITANTPFNLGGPAAGHPLMRTAADPQGRTVLGTFNNCAAGITPWGTYLSGEENFRNYFAAGS----:255
Rta-2       ---------F------RT--------WNAEKVRKSQAAHGVSVIEVRQQPDGGWQVVRPSRWARRITARTPMAFGGPAAGHALLRTAADPAGLRPLGTLNNCGSGRTPWGTYLTCEENFAFYFRGPD----:251
Sme         -ARVEKVTED-----GKEEDKVVLGEYTKELVDIEMAAHGGTVIEIRKVD-GKWQPVLDGKYNRRITATTEMQLSGPAAGHERVKTPSDPTGRKVFGTINNCAGGVTAWGTYMMAEENFNGYFGGELAEDH:296
Rta-3       ---------VTAATATAG-------RPVAEVDKEIAAHGVSVAEVQRRG-QSFAYDRGSRYNRRVTPLTPMQIHGPARGDGLMVTRYSPDGTTCRGTINNCGTGYTPWGTFLTGEENWAGYFTRSGG-DD:290
Rta-4       R--------G------VD--------VDPGFKYDTYANGGTSTLVLGED---GGLL-------RHYA--S-L-----------------------GTNNNCAGGPTPWGSWLSCEETTAVPNA-------:192
               . ::.  *..*..::.         ..      .   .*:.. .    ::::. .. : ... :  ..** :*. * *:**:::..*:*:. . .:

[AVE_SECSTR] ccccssscccchhhhhhtccsssscssscccctttsstcttgggbtttccssscccctggggggSsEEEECttcttsCCCEEGGGCCSCEEEEEEEEecttseseEEEEEEECSeeeCEEEEEEEeeeccsscgcss
4alfA       Q--------FDPAQKRYGVSAAS-REINWHPF---D--PRFDMAK--------NPNELNRHGWVVEIDPFDPQ-STPVKRTALGRFKHENAALAETDDGR-AVVYMGDDERGEFIYKFVSRDKINHRNA---:359(312)
Rta-1       S--------LDAHQRRWGLTAT--AFFRWAEH---D--PRFDAVG--------NPNEPNRFGWVVEVDPMDPA-STPVKRTALGRAAHEGAWVAVTRDGR-AVVYSGEDARNEYIYKFVSRDIRPAGN---:359
Rta-2       R--------PGGHEARWGIGPTG-GWFRWHEH---D--ERFDARR--------HPNEPNRFGWVVEIDPFDPA-STPVKRTALGRAAHEGATVAVTRDGR-AVVYSGEDARFEYLYKFVSRDIRPGGR---:356
Sme         P--------EFKQMKRLGTP-GG--QYEWSKF---Y--DRFDVSK--------EPNEANRFGWVVEVDPLNPT-SVPKKRTAIGRFKHEGCESIVNRDGR-VLYSGDDERYDYVYKFVTKGTYNPDDR---:399
Rta-3       AARGGPMAKSVVSLRRSGRNAGSASRHRWETAGTDDKYARWNISQVGAGPAEDYRNELNTRGYIVEIDPYDKN-VAIRKRTALGRFAHESAAFGLRAPGQPLAVVYMGDDSQGEYMYKFVSKMPWNPADAEPA:421
Rta-4       -------------------------G--------LT------------TYQKRVGVFEVPALASGFTQAIPITGMGRFSHEAAAVDPA---T-GIVYLTEDTSDSLFYRYVPYQR---------:259
               .  :  .  .   .:    .   .        .   .*    .:: ::.*.::*..::   .  ..:*::**..*:*.::::.:.. ...:.:*.::. .. *::*....

[AVE_SECSTR] ttccssscggggttGGGSEEEEEEEEcssscccssscccccssscescEEEEEECTTSttcsttsttcCcshHHHHHTHHHHHHHHHTCCCeeCEEEEEEectttccCEEEEECCbttttcsssssssscccbttbc
4alfA       --------KANRDILDHGTLYVARFDAGD--------GNPDHPKGQGQWIELTHGKNGIDAS-SG--FADQAEVLIHARLAASVVGATRMDRPEWIVVSPKDG-QVYCTLTNNAKRGE-D----GQPVGGPNP:467(420)
Rta-1       ---GLTAAQANRELLDHGTLYVARFDAD---------------GVGQWLPLVHGQGPLTAA-NG--FADQGEIVIKSRQASDLLGATKMDRPEWLAIDPVN--GTVYCTLTNNADRGKEG----MPGPDAANP:465
Rta-2       -------RGNAGLLDHGTLYAARFGAD----------------GSGRWLPLVHGQGPLTAA-NG--FADQGEIVLVKTRQASDRLGATRMDRPEWIAVAADG--WVYCTLTNNSARGSVG----QPPADAANP:456
Sme         --------AANMDLFDEGTLYVAKFDED------------GTVVTWMPLVHGEGPLTAE-NG--FASQADVLIDTRLAADALGATKMDRPEDVQPNPKTG-KVYVMLTNNTKRKE-------DEIDAANP:497
Rta-3       NRI-----TTGDKYLDEGKLYVAKFAGD------------GTGEWIELSMANPAVAGYAAYAFANQADVVVNARLAADAVGATRMDRPEWCAVHPVTG-EVYYTLTNNANRKV-SPTGSQQPVDPANP:530
Rta-4       -----------GVLLAGGRLQALRLRDFASANTGIEFLDKLNQPMAVEWVDIPNPD--P------V--DNLFVNSTRAQGQAAGAARFVRGEGAWWG--NG-QIYFCCTSG-GN---------------:348
               ..  .:::.*.*:::.::.      :  . *  .:...  ....   .  :.:...:..**:*::.**:.. .  . :*...*:*:.. :. . ..::

[AVE_SECSTR] cscccccssscccccsbsSCEEEEEEeecsttgggcttcseeeEEEEEEECCctttsttsgsccscttcctttCCcCEEEEEECtTtccEEEEECssccccttssggggttccSCEEEEEEctttCcssccccccccsss
4alfA       RE------------KNVYGQILRWRT----DRDDHASKTFAWDLFVVAGNPSVHAGTPKGG-SSNITPQNMFNSPDGLGFDKA-GRLWILTD--GDSS--NAGDFAGMGNNQMLCADPATG-----------:566(519)
Rta-1       RA-----------NNAHGHIIRWREGGEDG-GDFDAARFRWDHLVLAGDPAQP----RAG-AKGNIRGDLFACPDGLAFDAR-GMLWIQTD--AHATQMYKGEFASIGNNQMLACDVATG-----------:565
Rta-2       RA-----------GNAMGHILRWQE----A-GDFDGLRFRWNHFVLAGDPANP----RAE-ARGNVRGDAFACPDGLWADAR-GVLWIQTDMSAAVM--GRGEFARLGHNAMLAADPRTG-----------:552
Sme         RA-----------KNAFGHIVEISE----TDGDFASTKSRWDVLLKCGDPSVAE-V-GASFSTATTRNGWFGMPDNCAIDAE-GRLWVSTD--GNNE--KDTG-RTDGVWAVETEGEGRG-----------:594
Rta-3       RSYNDAATEAPASARNVNGHIIRLRE----DGGRGAATRFAWDIYLFGAEADADP-A-RVN-LSGLNDDQDFSSPDGLWFSPKTGLCFIQTD--DG--------AYTDETNCMMLIGRPGRVGDGQPVTLNYT:646
Rta-4       ------------IGAGQVWAYDP----ARD------TLALVVESTD---------------R--GVLEAPDNITLGPD-GRLYMYED--GG-----------NGNNIVGVNS-DG-----------:409
               .:.          :. .   *.:  ....     ...:.  .  .   :  .....    ..         :  **.. ... *:..... .        .  .. ..  .. ..:

[AVE_SECSTR] cccsccccccccscsbcccccccCeEEEEECcttTCEEEEEEECttSScEEEEEESTTsssssssssscccssttttccccttssssssctttccttCcsctttttttttccCceeeeeeeesssccccttsccccccccccc
4alfA       ------------------EIRRFMVGPI-GCEVTGISFSPDQKTLFVGIQHPGENG-------G-------S--------TFPEHLPNG-----------KPRSSVMAITREDGGIVGA---------:633(586)
Rta-1       ------------------EVRRFLTGPT-NSEVTGMTMTPDGRTMFINIQHPGETP-------S------D-RSDPAEPAKFSNWPDY-------RPGGRPRSSTVVIRKVDGGIVGT---------:643
Rta-2       ------------------EVRRFLVGPP-GCEVTGATMAPDGRTMFVNIQHPGENP-------S------ERGG----TGRSTWPDH-------RPGGRPRSATVVIRRLDGGLIGT---------:626
Sme         ------------------TSKLFFRVPV-GAEMCGPSFNPTSDTFFLAVQHPGDAGLATYEKPA-T-------RWPDFRDDM-------PVRPAVVAVTRQGGGKIG---------:667
Rta-3       RADGTTAEVTTHVGAKPTAATLARFLVGPV-DCEITGVTETPDGKAIFVNVQHPGESI-------SKADVNDPA-------KYTSQWPSNAGYGLGK----RPRSATLVITRDDGALIGGNGPALRNRS:756
Rta-4       ------------------ELFRVAENVVNGSEFCGGCFSHNGRFMFVNIQSPGLTL------------V------IE-GPWRKG---------Q-R----------------:458
               .  .:::...:.  ..*...*  .. :.....*...*:**.          .              .            *.............. ..  .:
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Figure S1. Sequence conservation within PhoD and PhoX families. (a) Pairwise sequence alignment of *B. subtilis* and *R. tataouinensis* PhoD family proteins. (b) Multiple sequence alignment of *P. fluorescens*, *S. meliloti* and *R. tataouinensis* PhoX family proteins. The average (or consensus) secondary structure is indicated above each position of the alignment (in black uppercase when completely conserved, grey lowercase otherwise): helices (G: 3_{10} helix; H: α-helix), strands (B: residue in isolated β-bridge; E: extended strand) or loops (S: bend; T: hydrogen bonded turn; C: random coil). The level of sequence conservation is represented below each position: 100% (asterisk), at least 75% (colon) or at least 50% (period) of identical amino acids. Sequences were ordered according to their pairwise similarity. The conserved active site residues are highlighted; their positions are those identified in the template 3D structures (*Bsu* PhoD: PDB chain 2yeqA; *Pfl* PhoX: PDB chain 4alfA). Sequence boundaries are given (corresponding PDB numbering between parentheses). The Ig-like domain and the catalytic domain of the PhoD proteins are separated by a space character in the alignment. The sequence of the PhoX protein of *Sinorhizobium meliloti* (Sme) corresponds to the Uniprot accession M4MZI0.