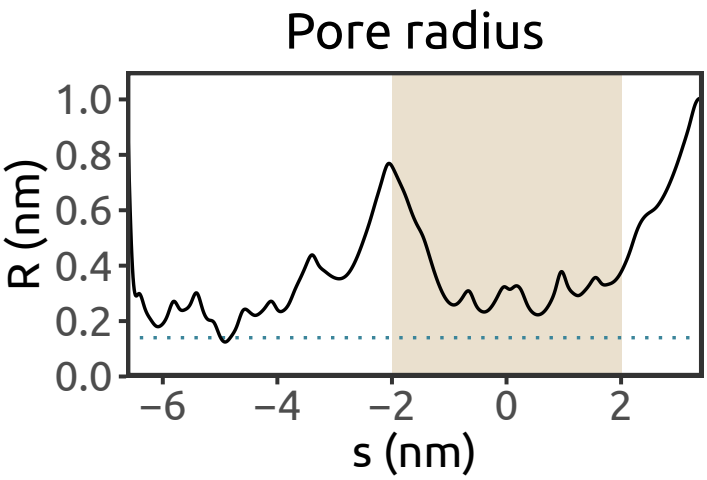
Dataset S1. Radius and hydrophobicity profiles for all ion channel structures analysed. Each channel structure is oriented with the cytoplasmic (or mitochondrial matrix) side in the negative *s*-axis direction. The approximate position of the lipid bilayer membrane, centred at $s = 0$ nm, is indicated by a beige shading. Simulation results are coloured red if the main barrier to water permeation has height > 2.6 kJ mol^{-1} and blue otherwise, with a similar colour divide for the heuristic scores, at a cut-off of 0.55.

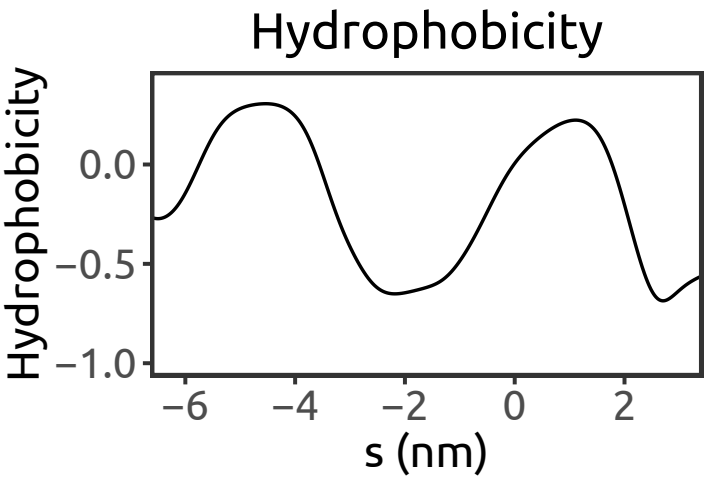
5HT3R (PDB ID: 4PIR)

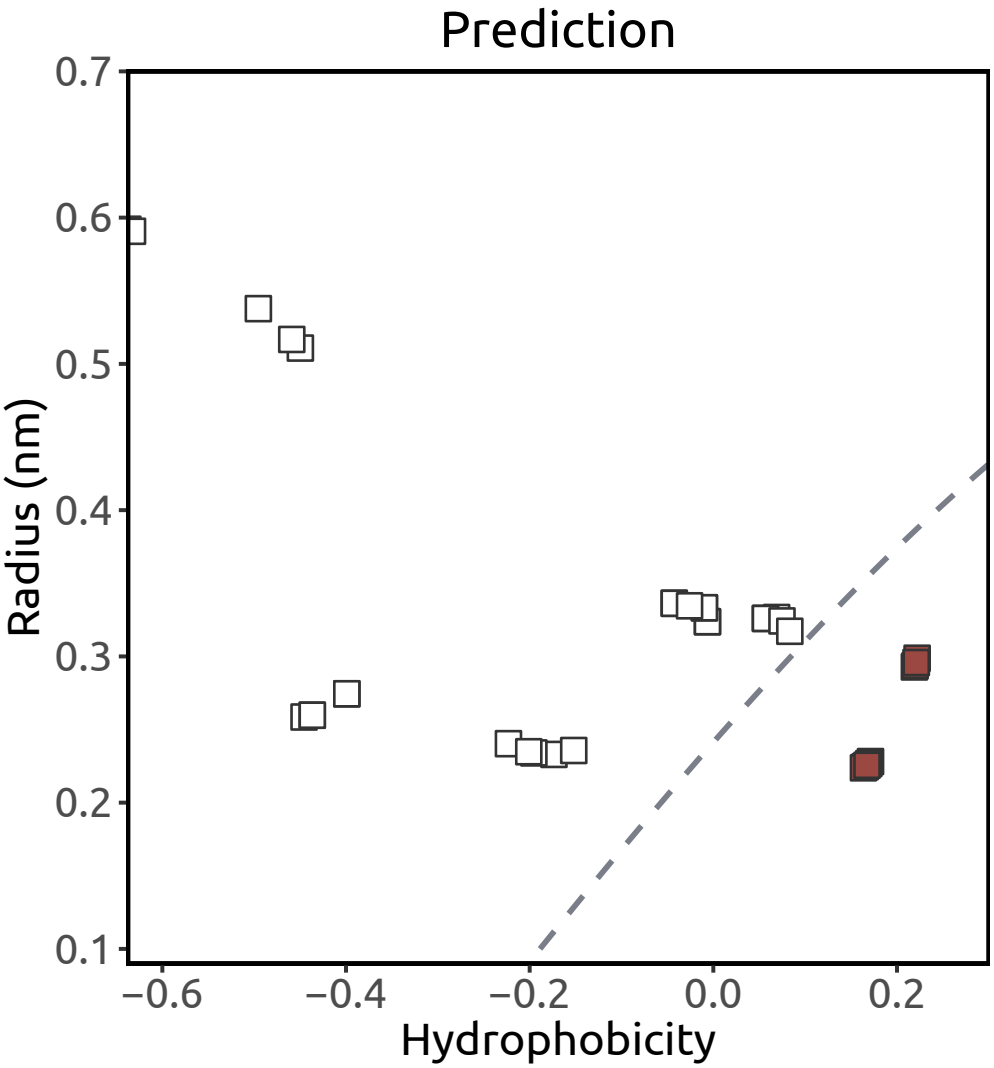
Mus musculus

X–ray (3.5 Å)

Hassaine et al., 2014







Heuristic score:

0.93 (n = 10)

Simulation result:

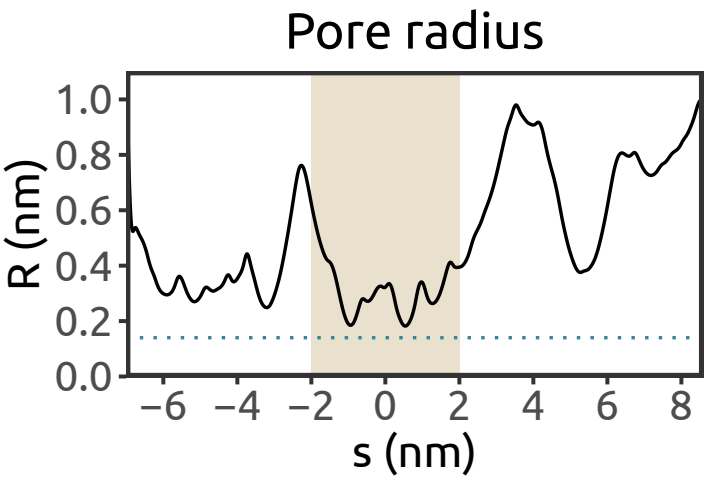
barrier to water

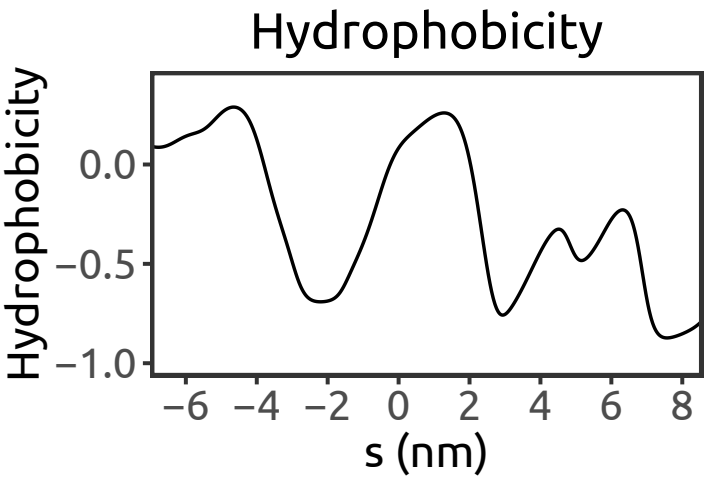
5HT3R (PDB ID: 6BE1)

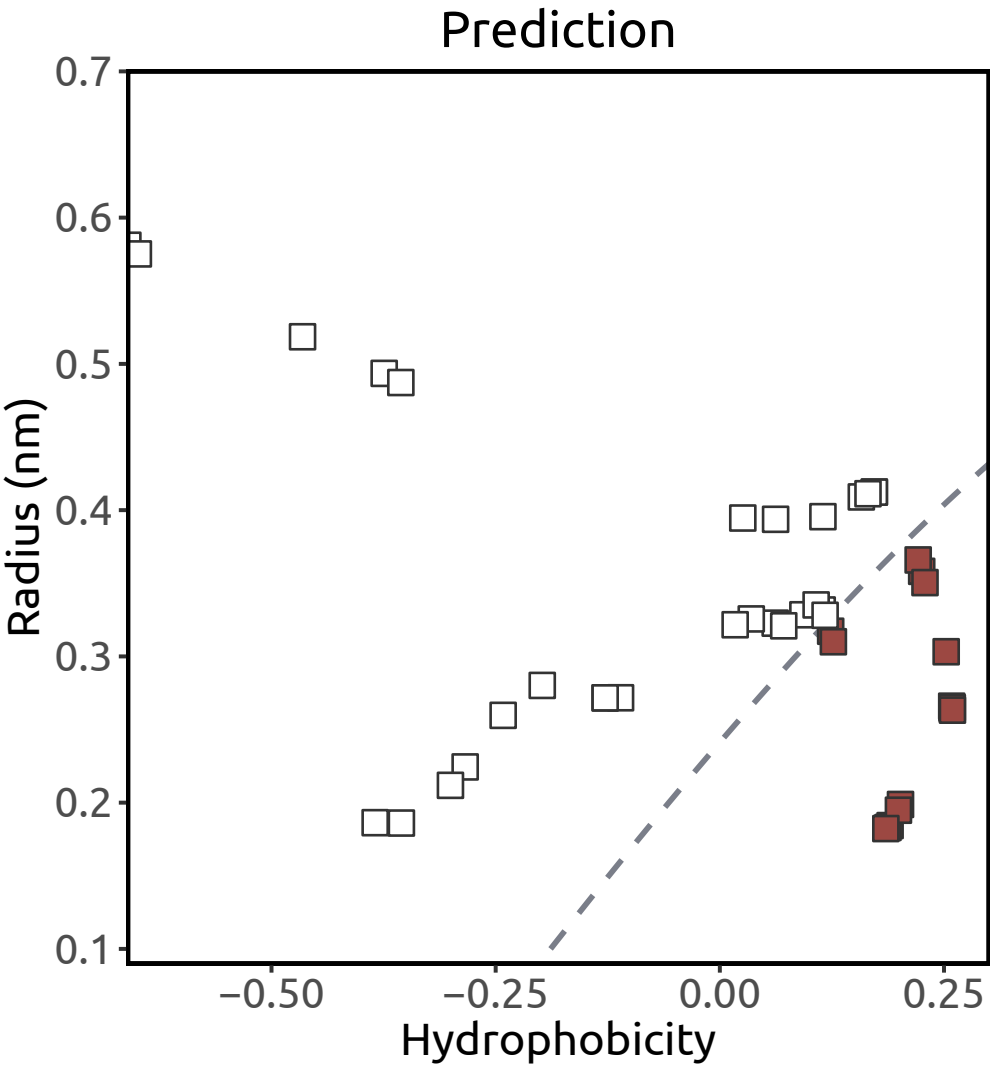
Mus musculus

cryo–EM (4.31 Å)

Basak et al., 2018







Heuristic score:

1.45 (n = 15)

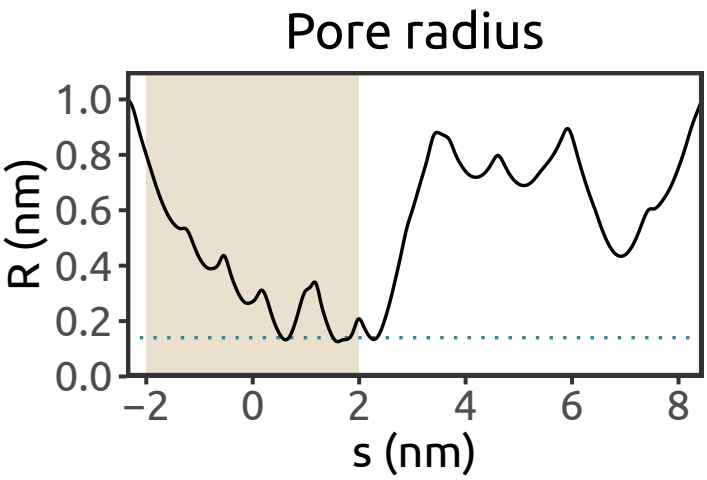
Simulation result:

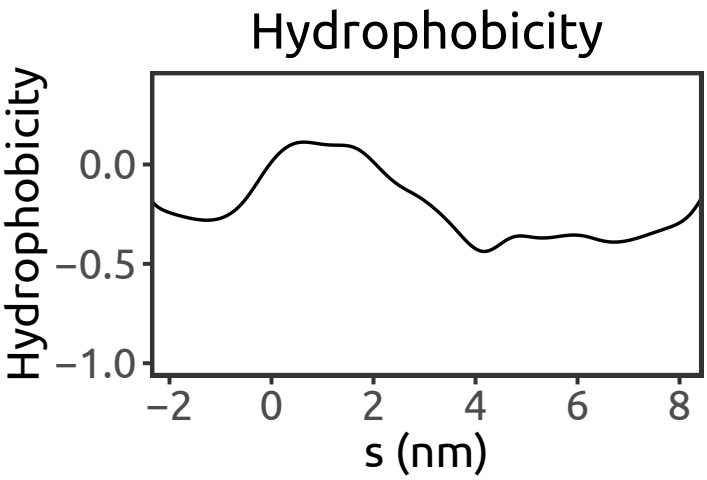
barrier to water

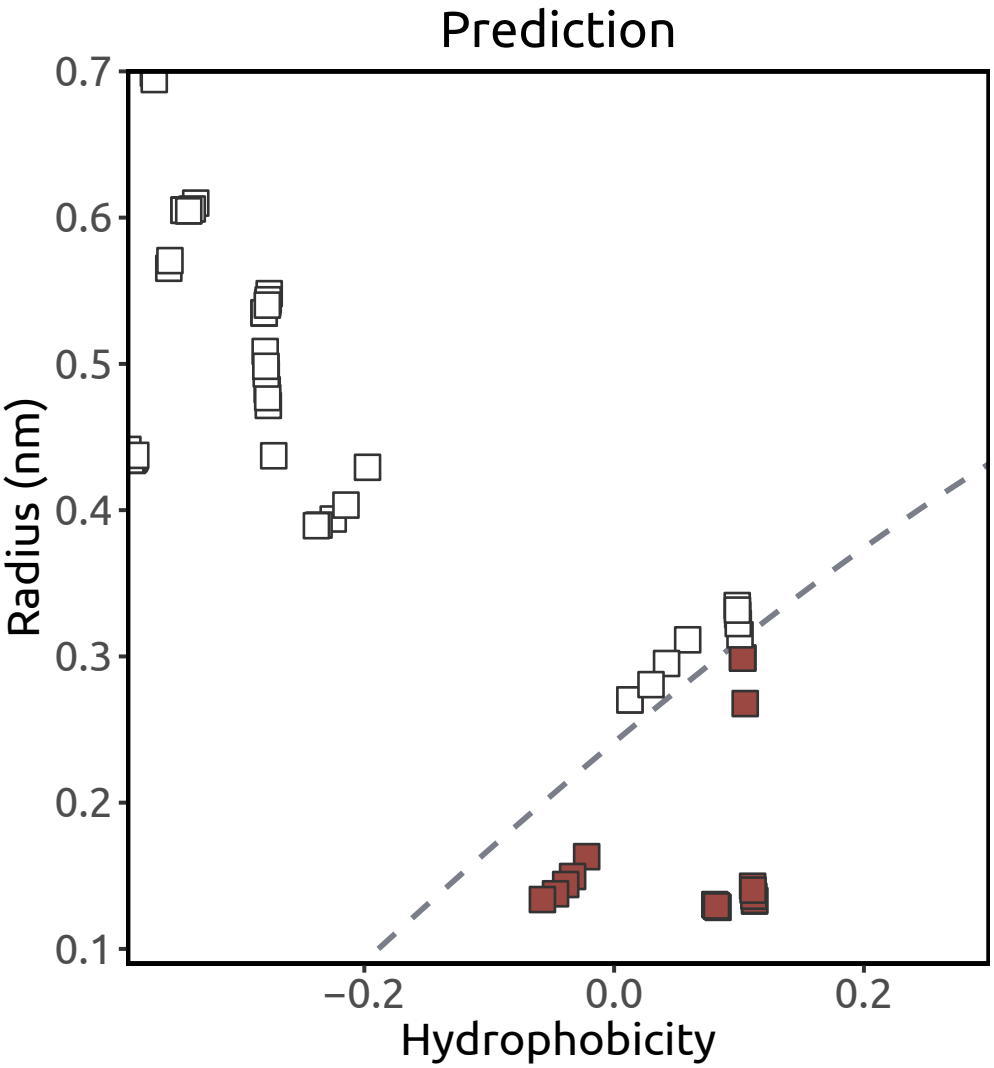
ELIC (PDB ID: 2VL0)

Erwinia chrysanthemi
X–ray (3.3 Å)

Hilf & Dutzler, 2008







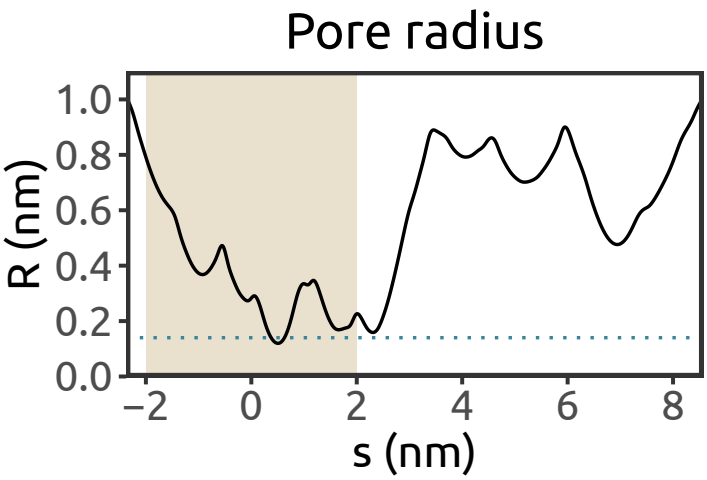
Heuristic score:
1.78 (n = 19)

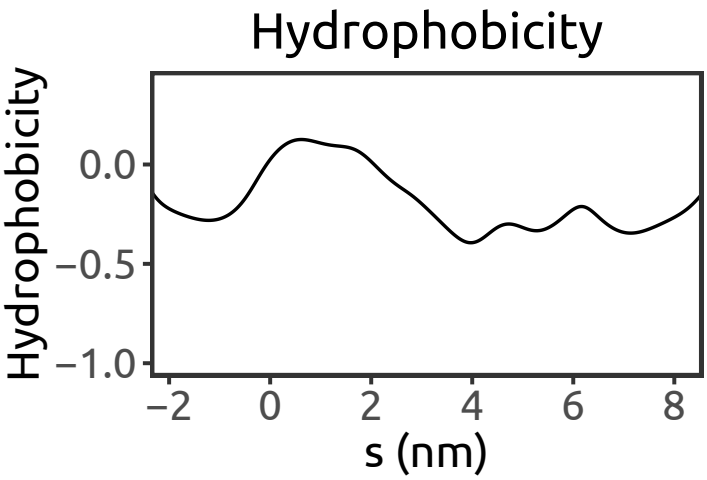
Simulation result:
barrier to water

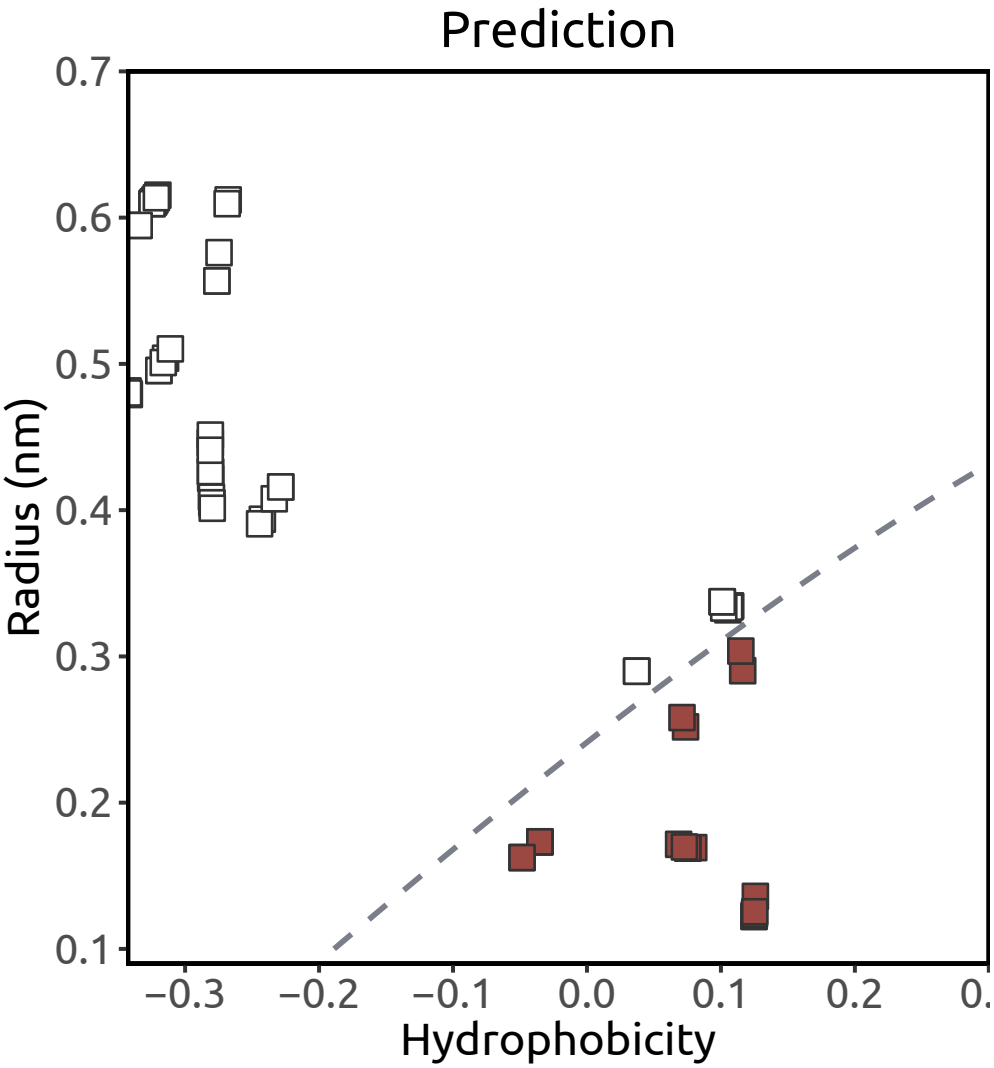
ELIC (PDB ID: 3RQW)

Erwinia chrysanthemi
X–ray (2.91 Å)

Pan et al., 2012







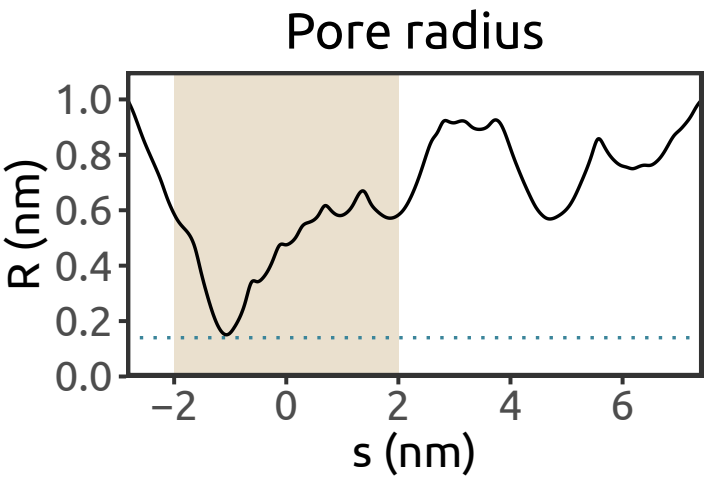
Heuristic score:
1.61 (n = 19)

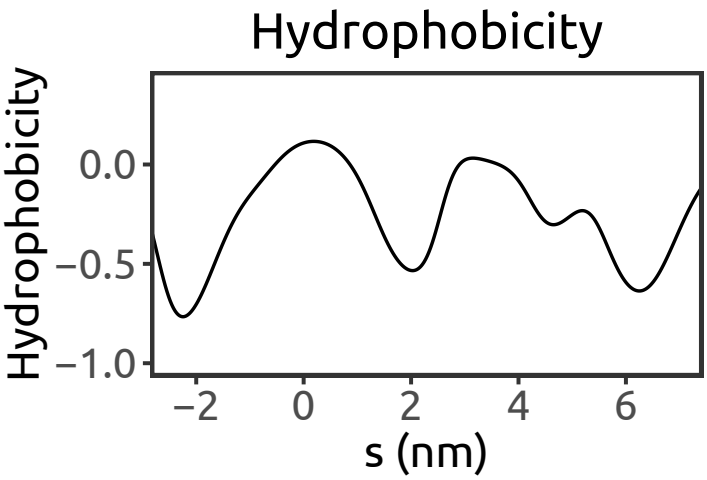
Simulation result:
barrier to water

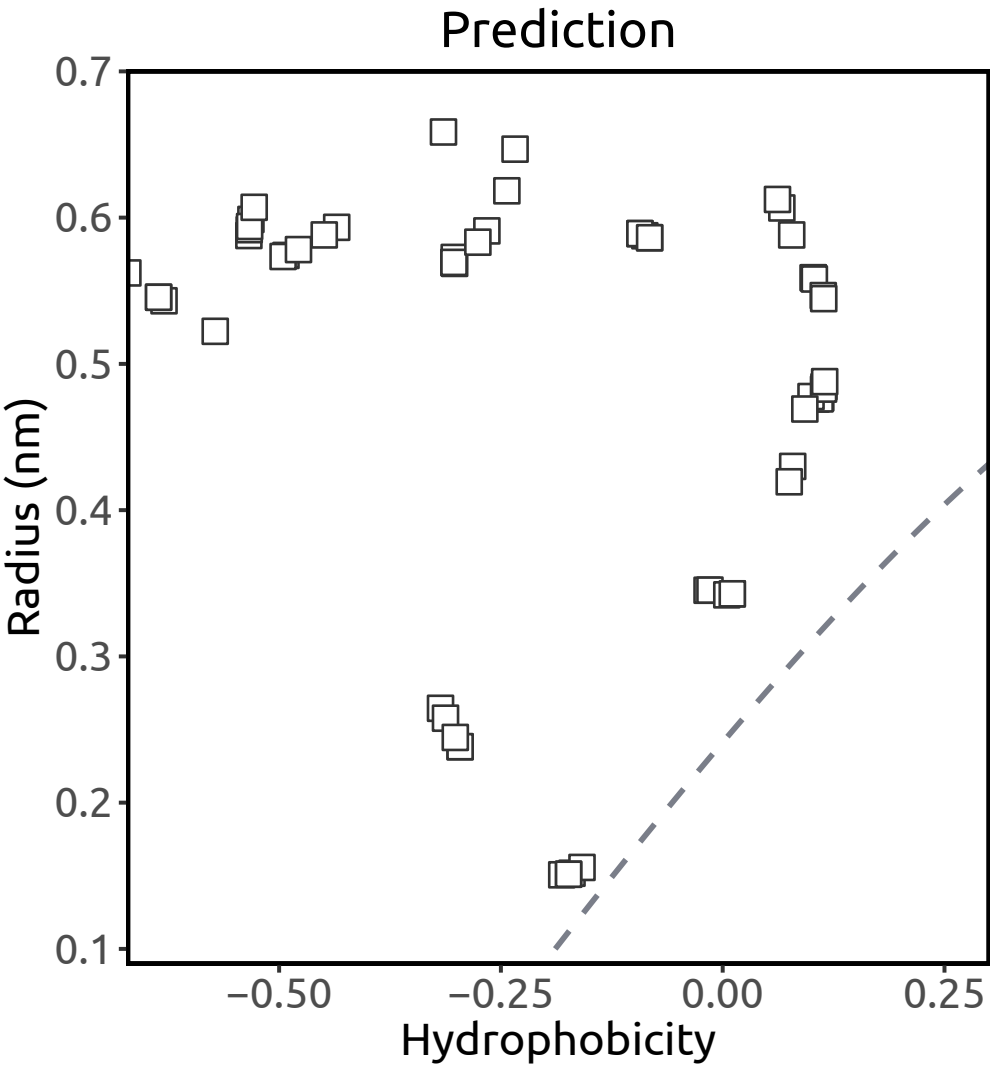
GABAAR (PDB ID: 4COF)

Homo sapiens
X–ray (2.97 Å)

Miller et al., 2014







Heuristic score:
0 (n = 0)

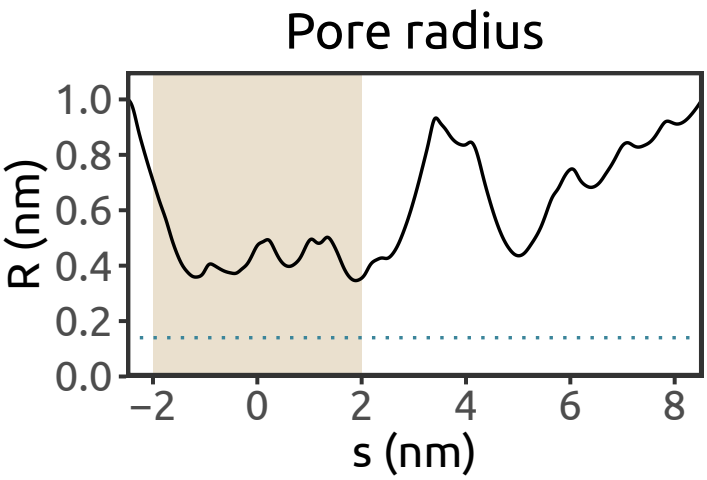
Simulation result:
hydrated channel

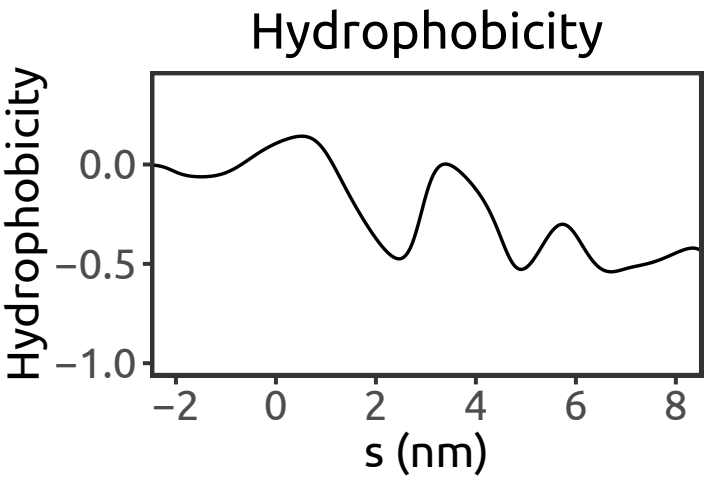
GABAAR (PDB ID: 6A96)

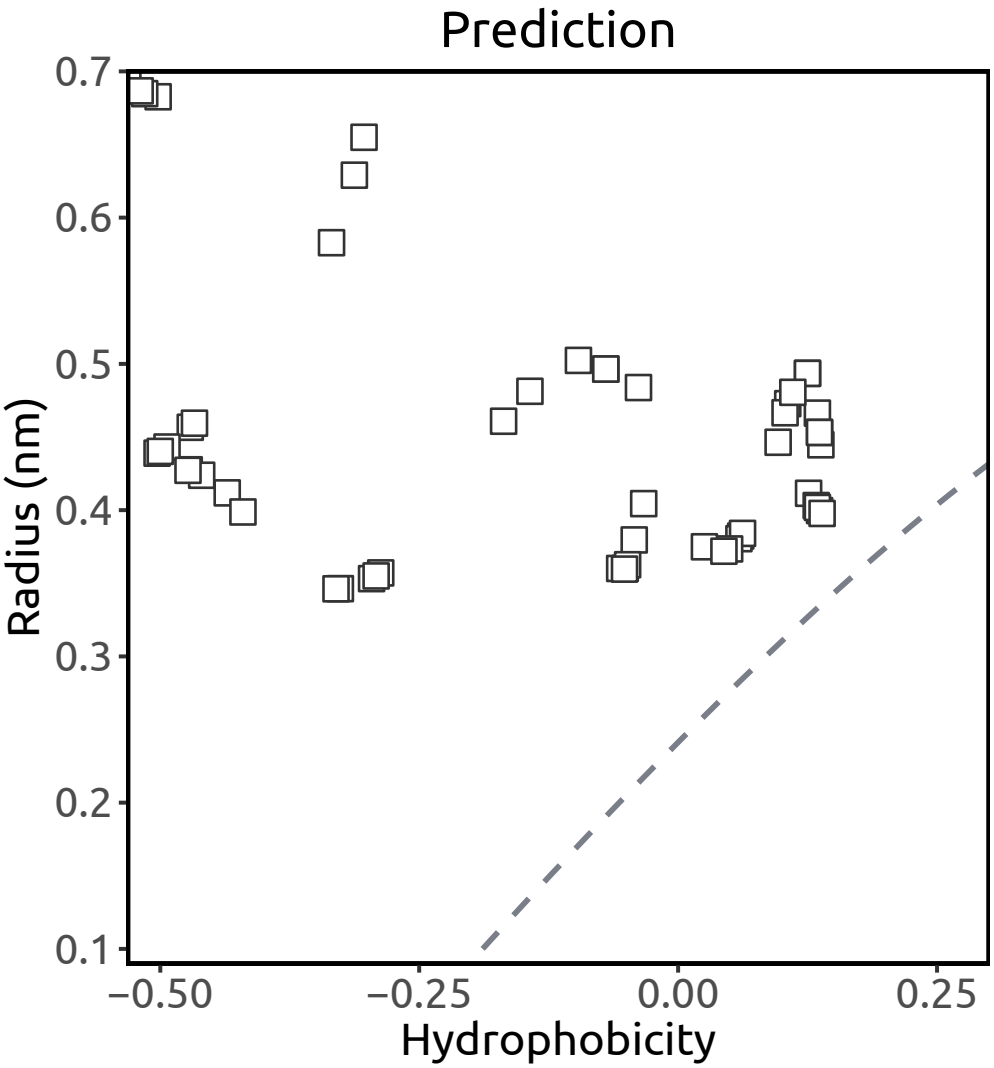
Homo sapiens

cryo–EM (3.51 Å)

Liu et al., 2018







Heuristic score:

0 (n = 0)

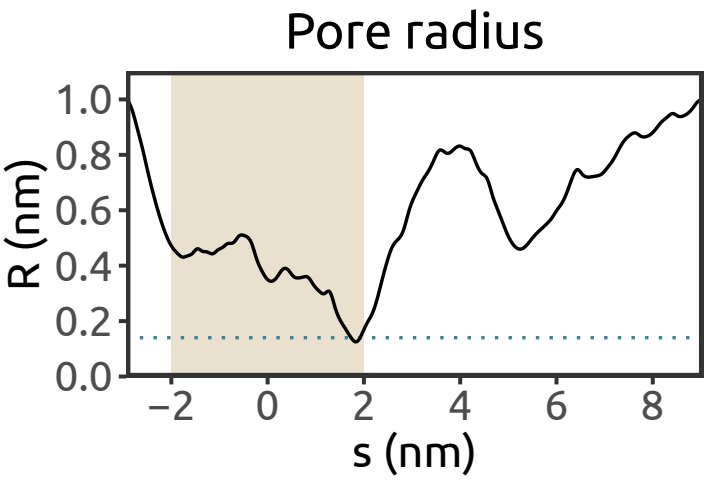
Simulation result:

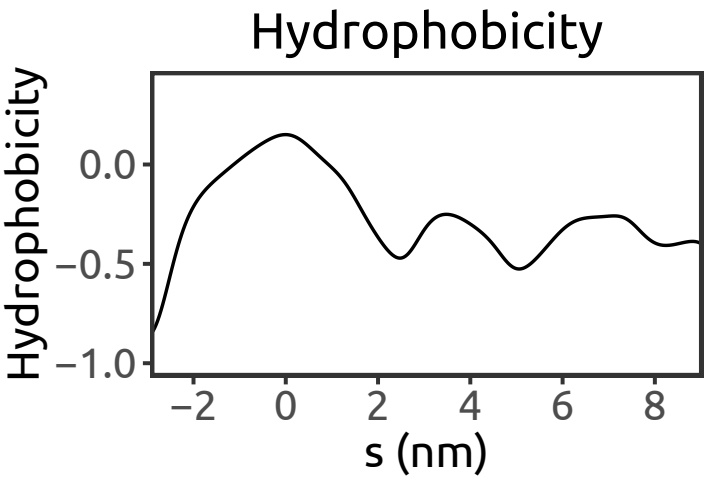
hydrated channel

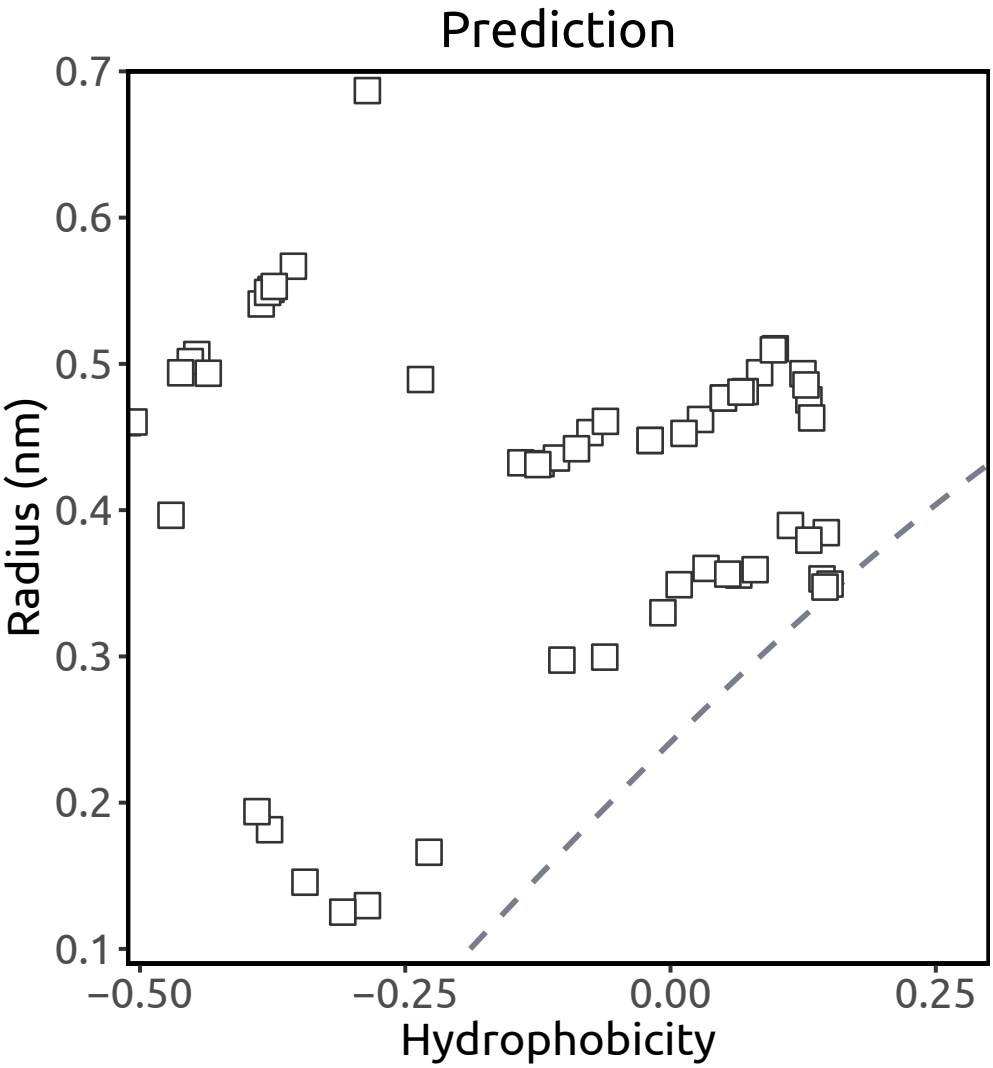
GABAAR (PDB ID: 6D6T)

Homo sapiens
cryo–EM (3.86 Å)

Zhu et al., 2018







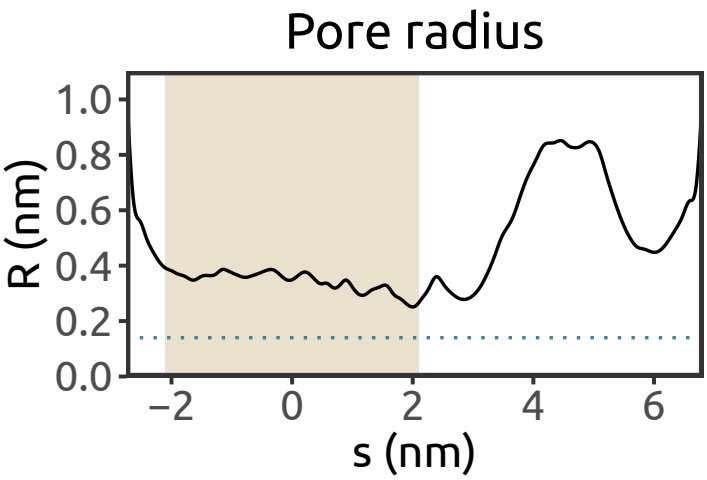
Heuristic score:
0 (n = 0)

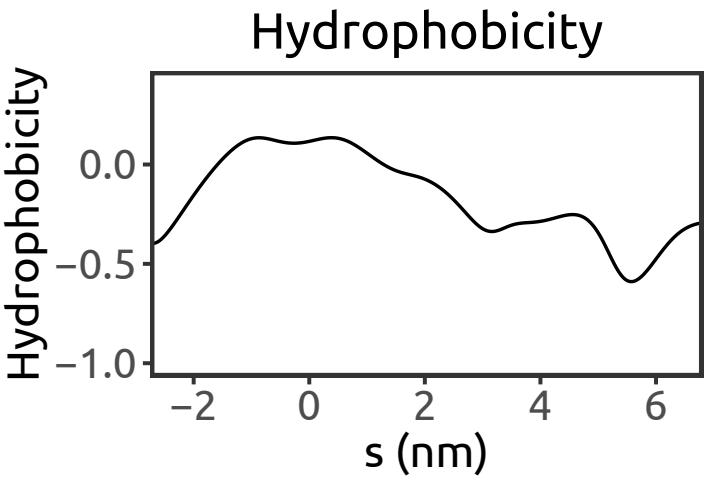
Simulation result:
hydrated channel

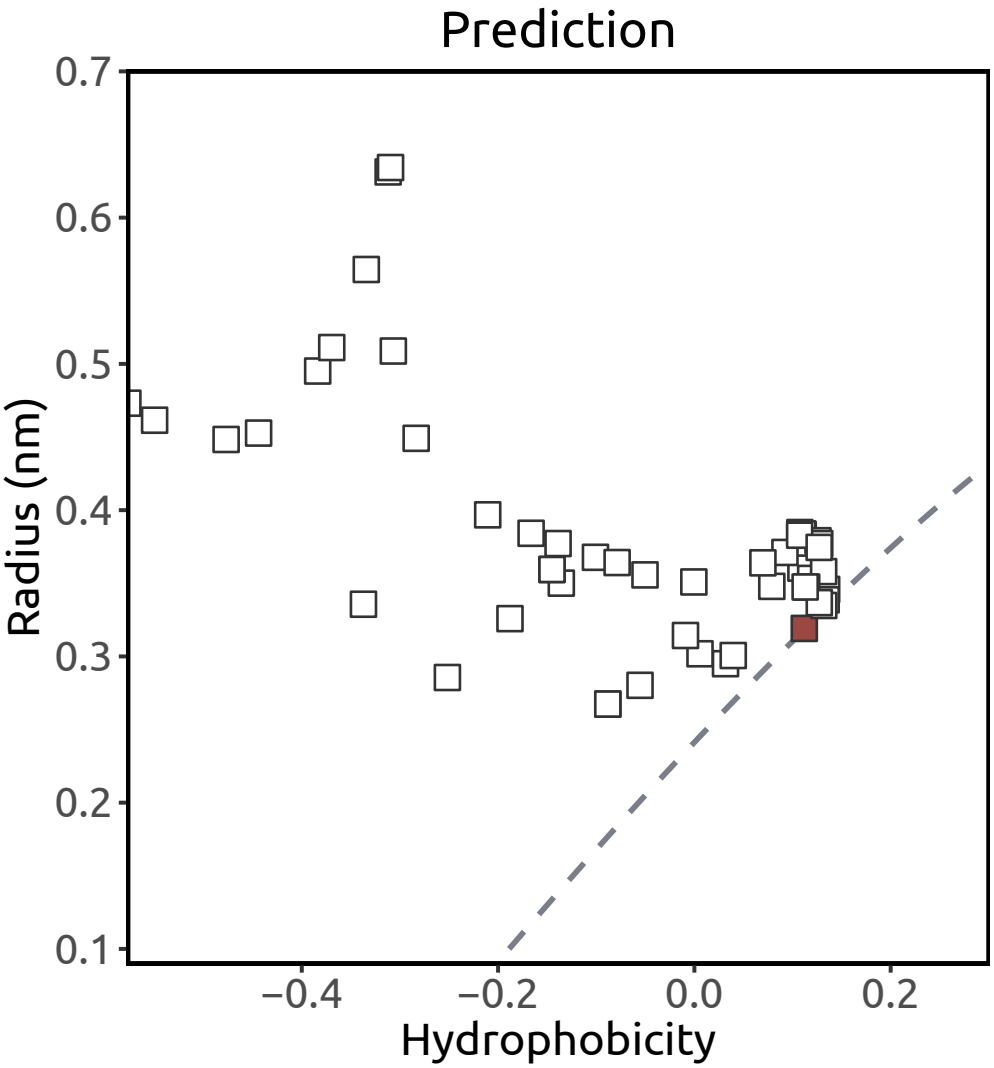
GABAAR (PDB ID: 6D6U)

Homo sapiens
cryo–EM (3.92 Å)

Zhu et al., 2018







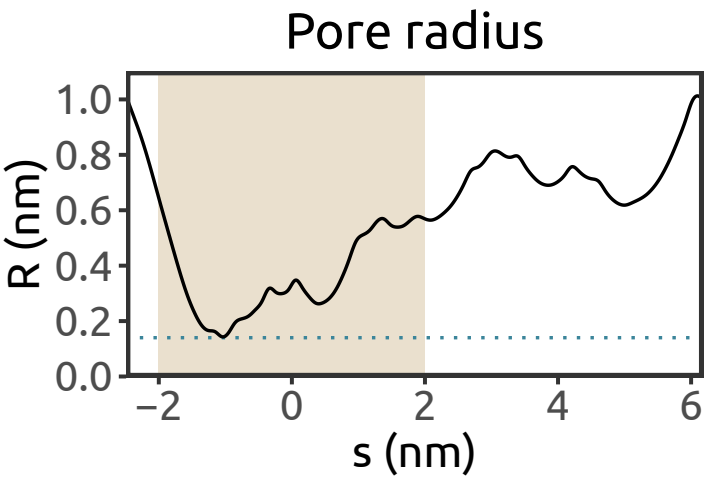
Heuristic score:
0 (n = 1)

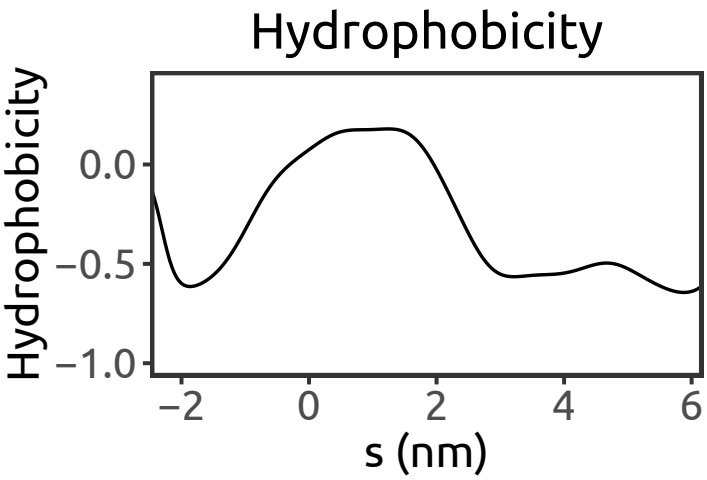
Simulation result:
barrier to water

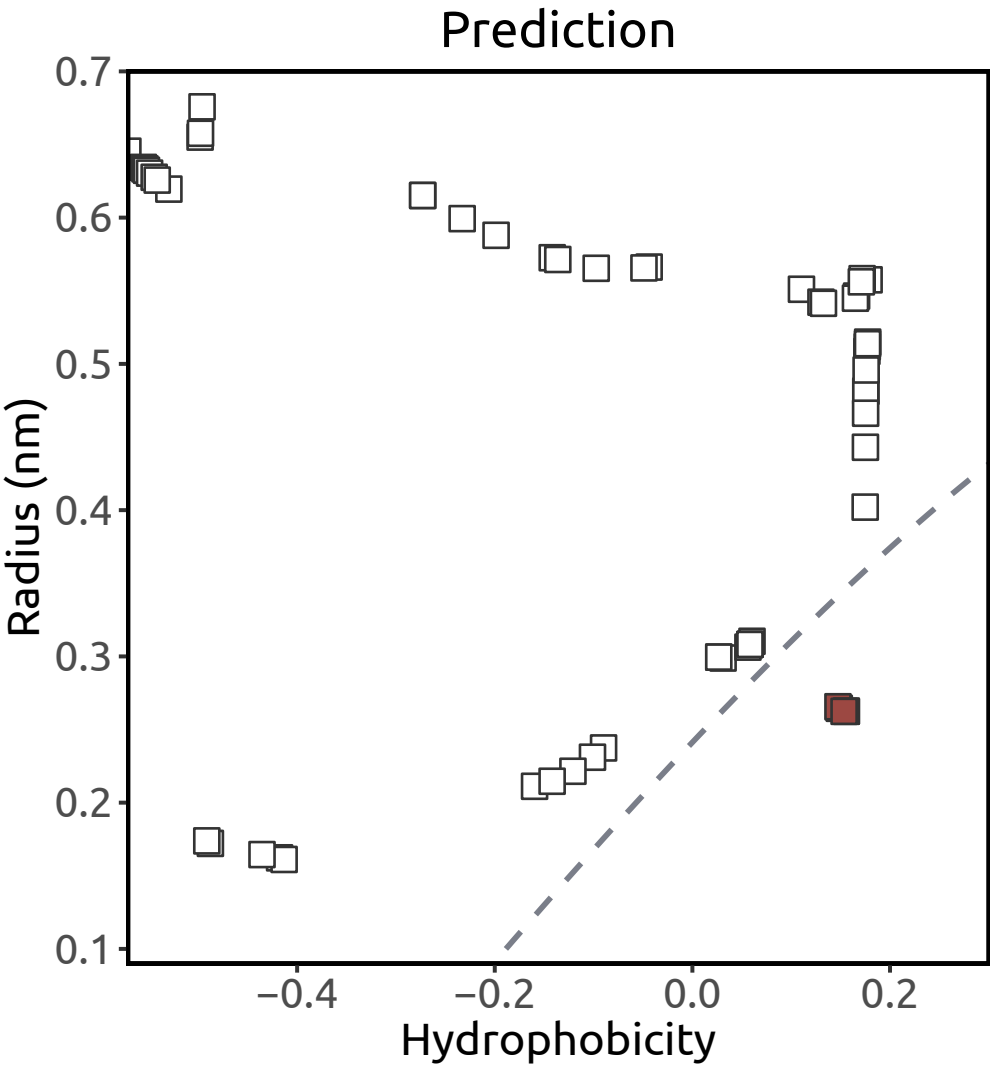
GLIC (PDB ID: 2XQ7)

Gloeobacter violaceus
X–ray (3.4 Å)

Hilf et al., 2010







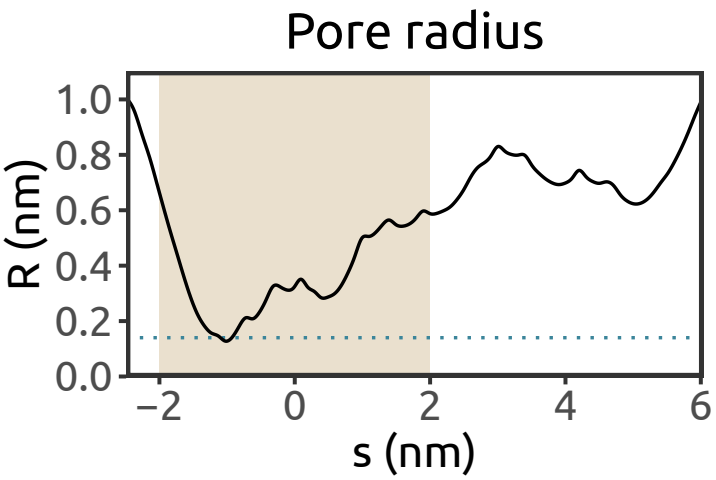
Heuristic score:
0.34 (n = 5)

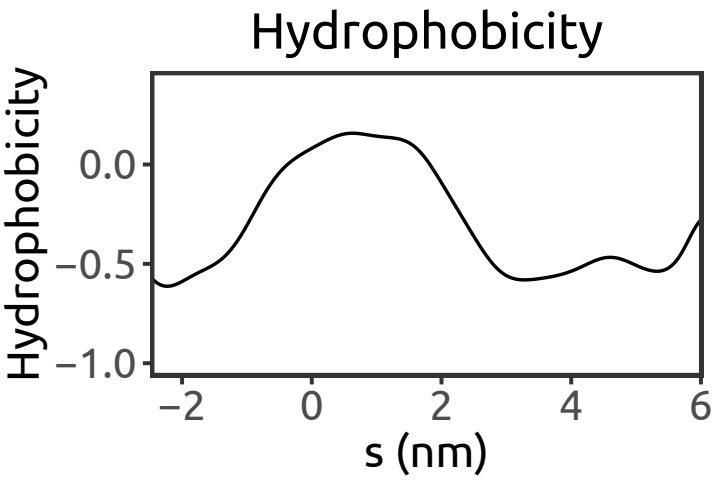
Simulation result:
hydrated channel

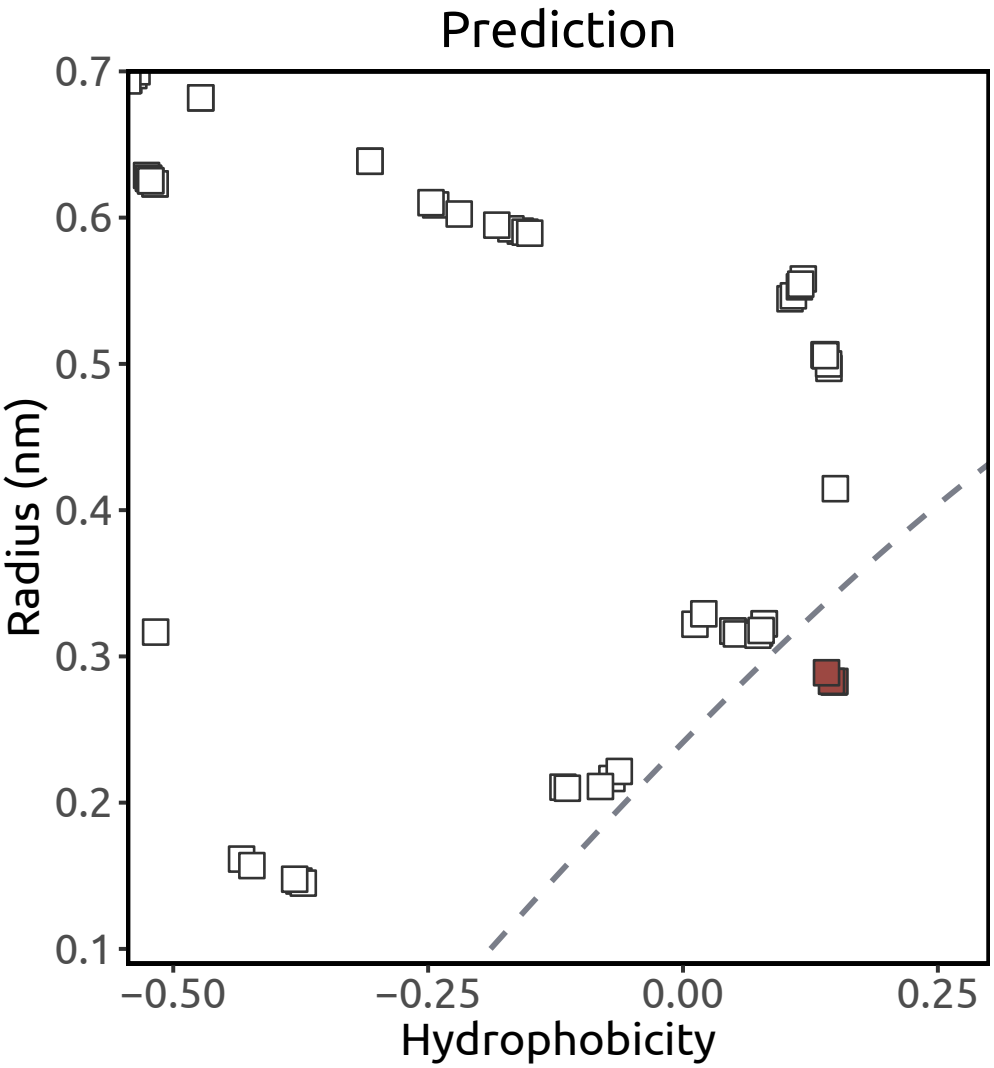
GLIC (PDB ID: 3EHZ)

Gloeobacter violaceus
X–ray (3.1 Å)

Hilf & Dutzler, 2009







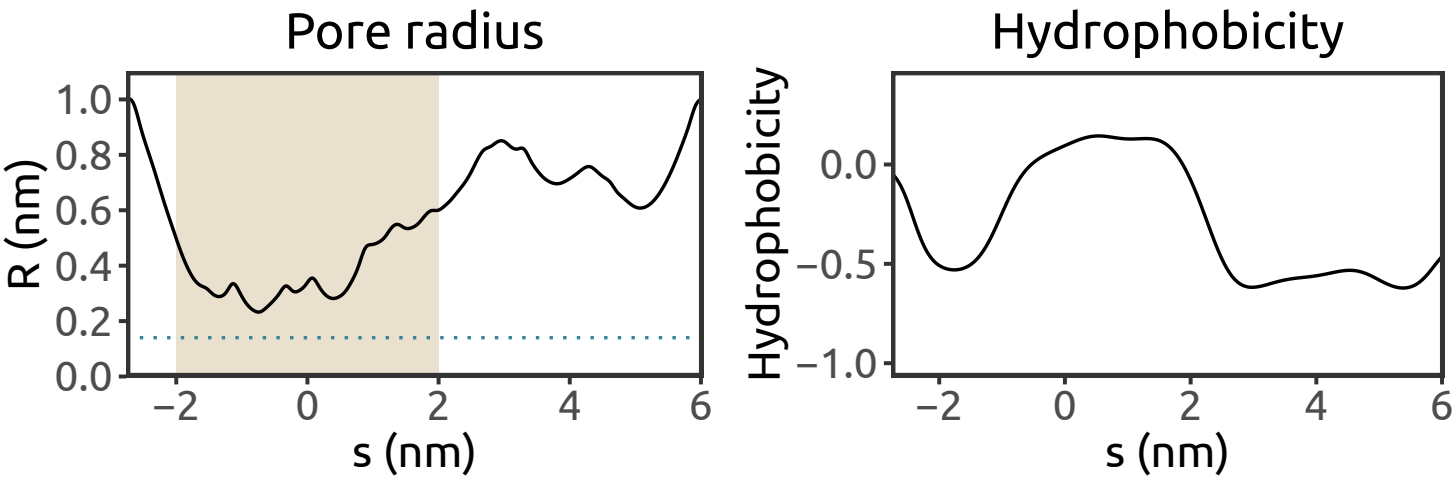
Heuristic score:
0.24 (n = 5)

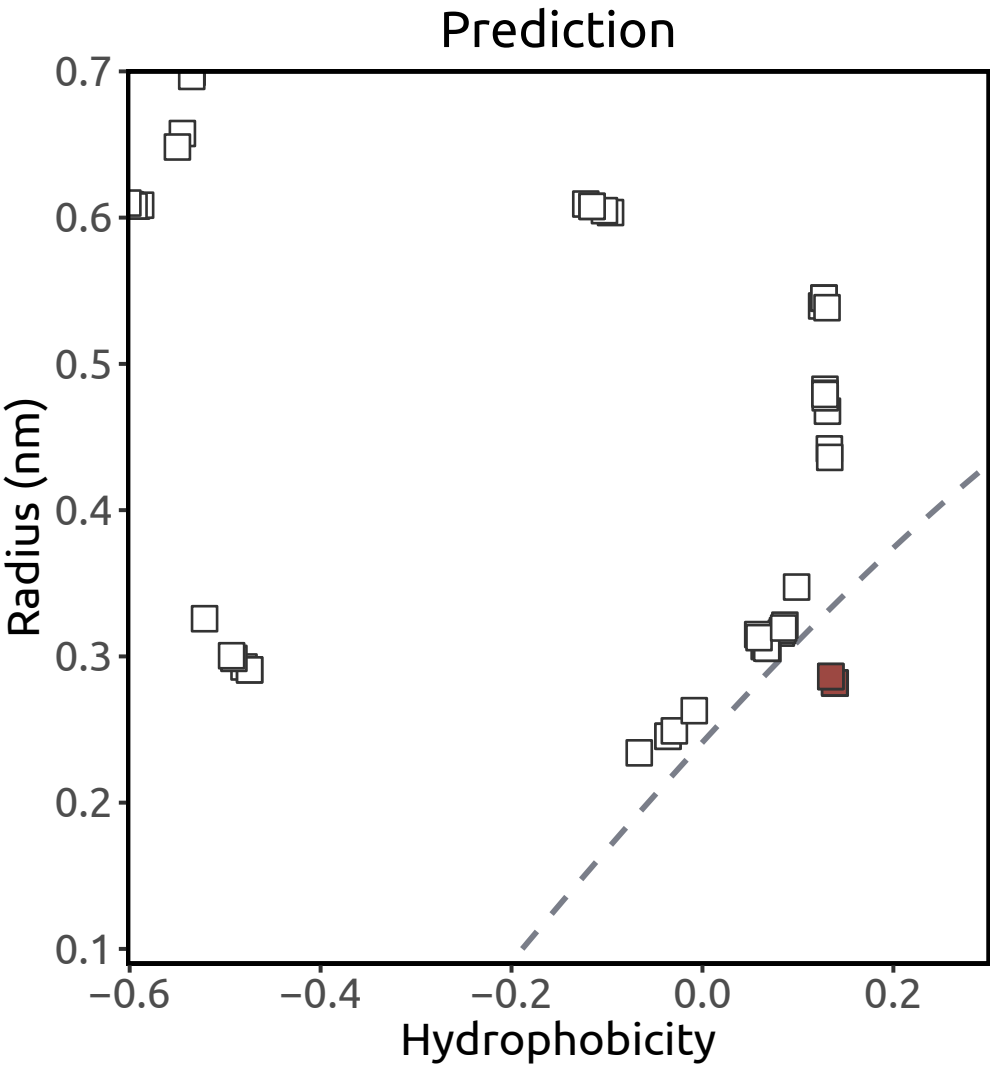
Simulation result:
hydrated channel

GLIC (PDB ID: 4F8H)

Gloeobacter violaceus
X–ray (2.99 Å)

Pan et al., 2012





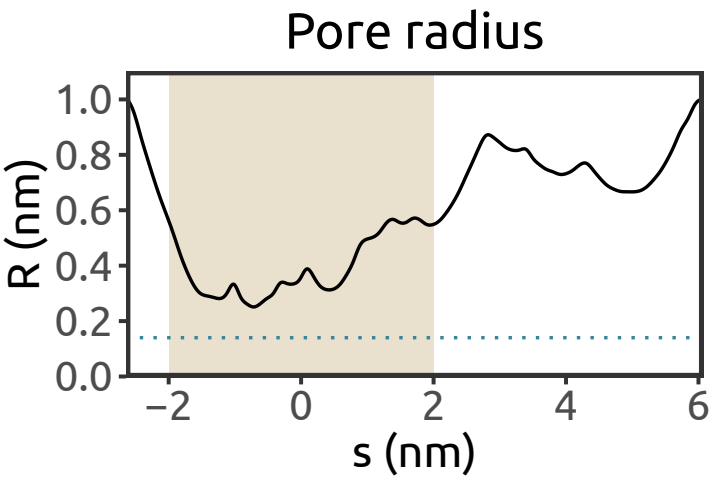
Heuristic score:
0.21 (n = 5)

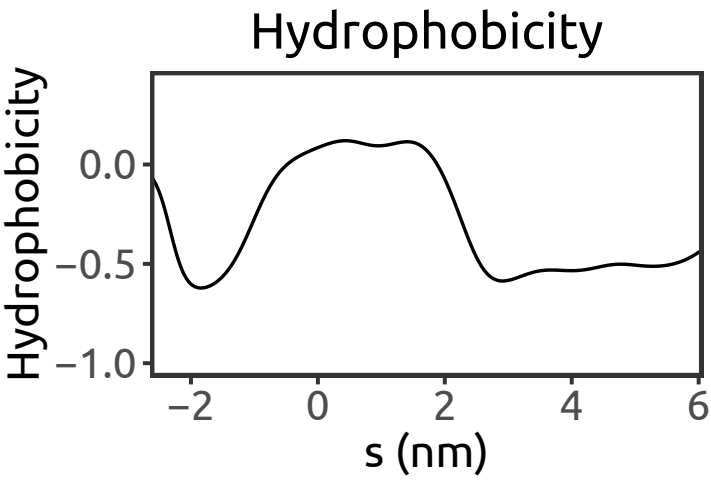
Simulation result:
hydrated channel

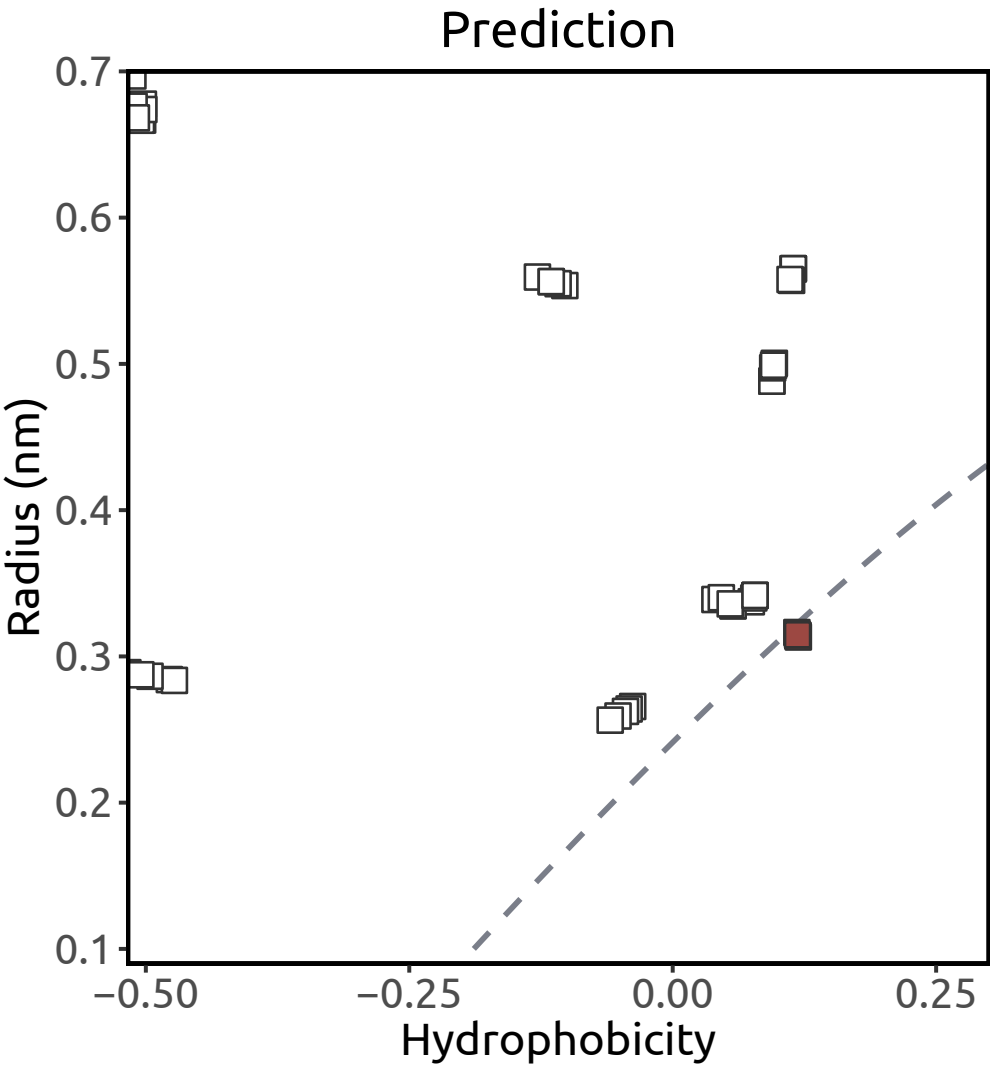
GLIC (PDB ID: 4HFI)

Gloeobacter violaceus
X–ray (2.4 Å)

Sanguet et al., 2013







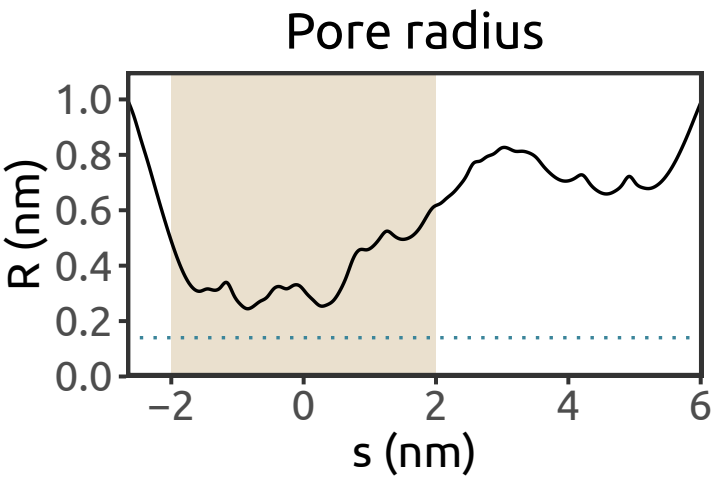
Heuristic score:
0.04 (n = 5)

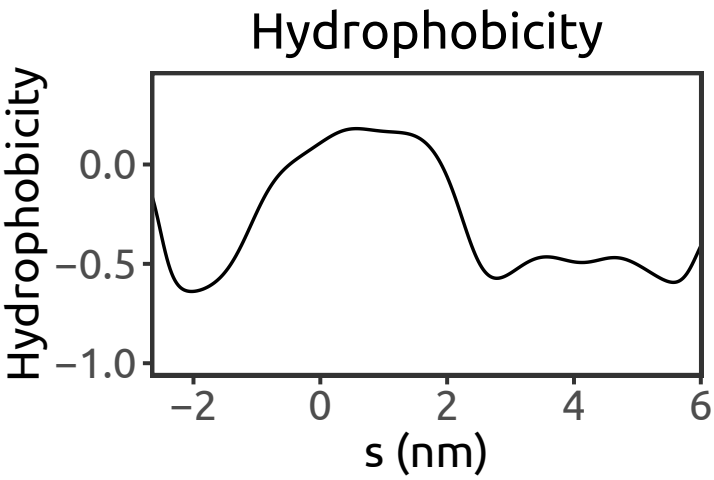
Simulation result:
hydrated channel

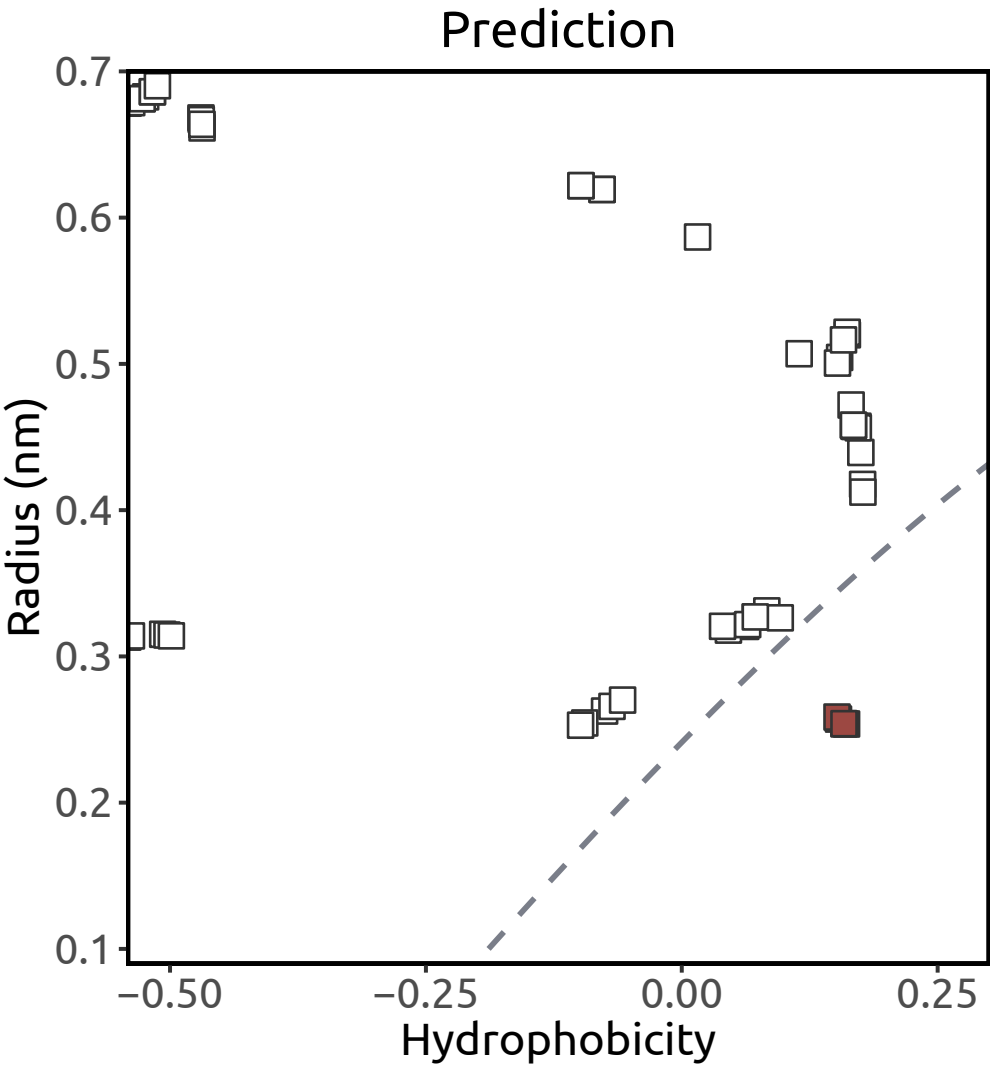
GLIC (PDB ID: 4NPP)

Gloeobacter violaceus
X–ray (3.35 Å)

Sanguet et al., 2014







Heuristic score:
0.39 (n = 5)

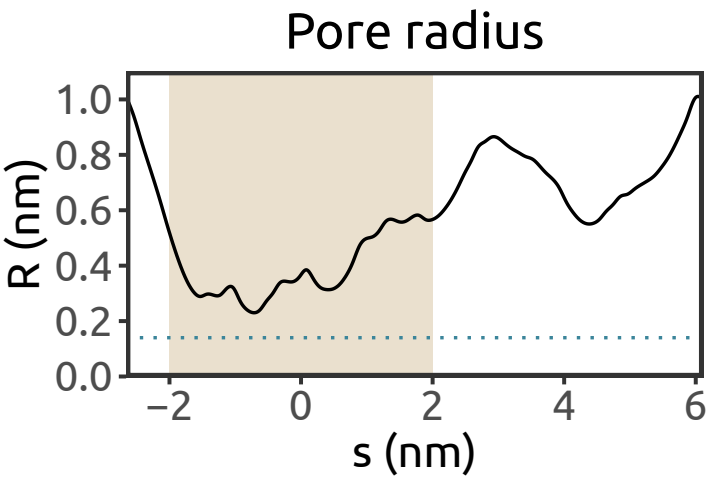
Simulation result:
hydrated channel

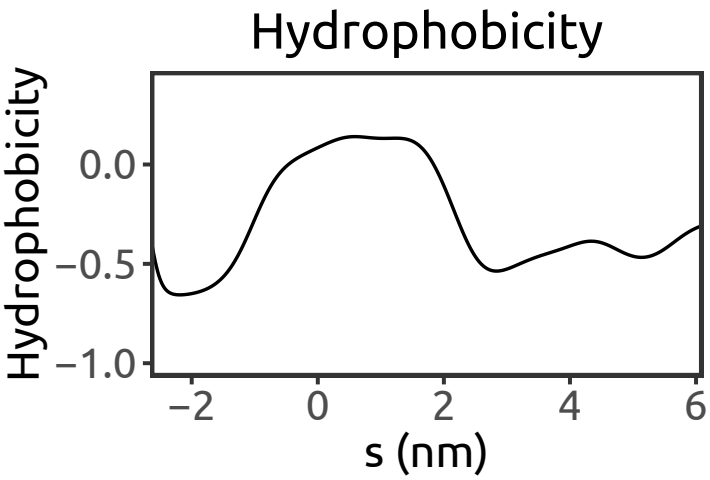
GLIC (PDB ID: 4QH5)

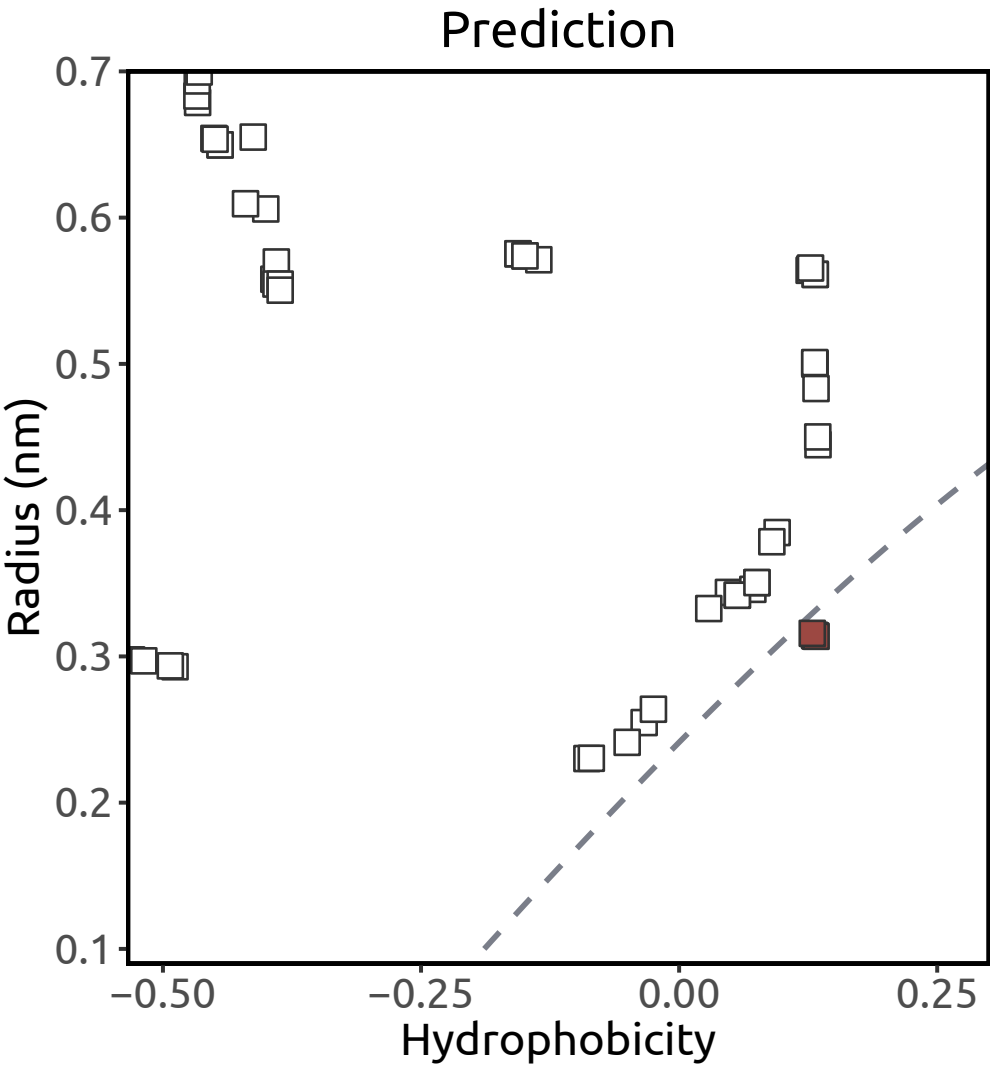
Gloeobacter violaceus

X–ray (3 Å)

Fourati et al., 2015







Heuristic score:

0.07 (n = 5)

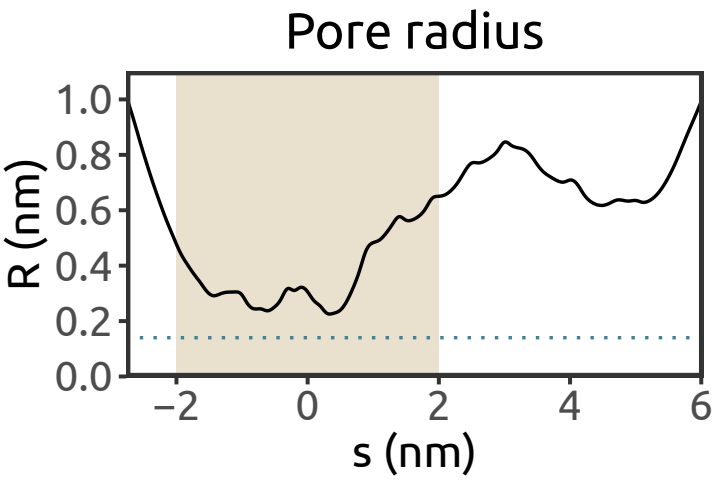
Simulation result:

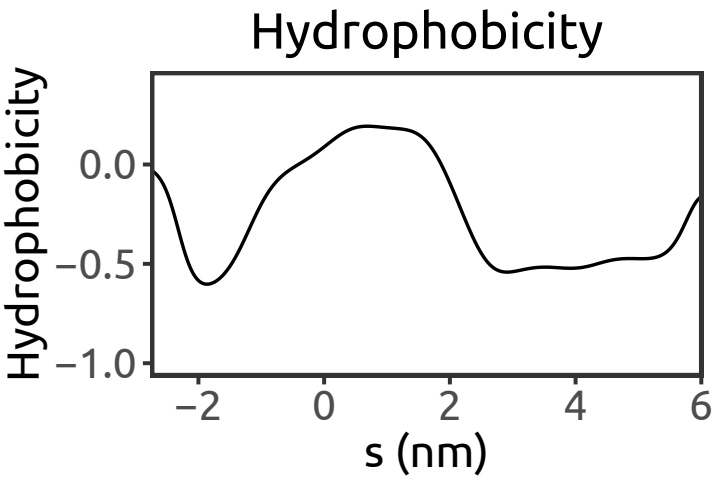
hydrated channel

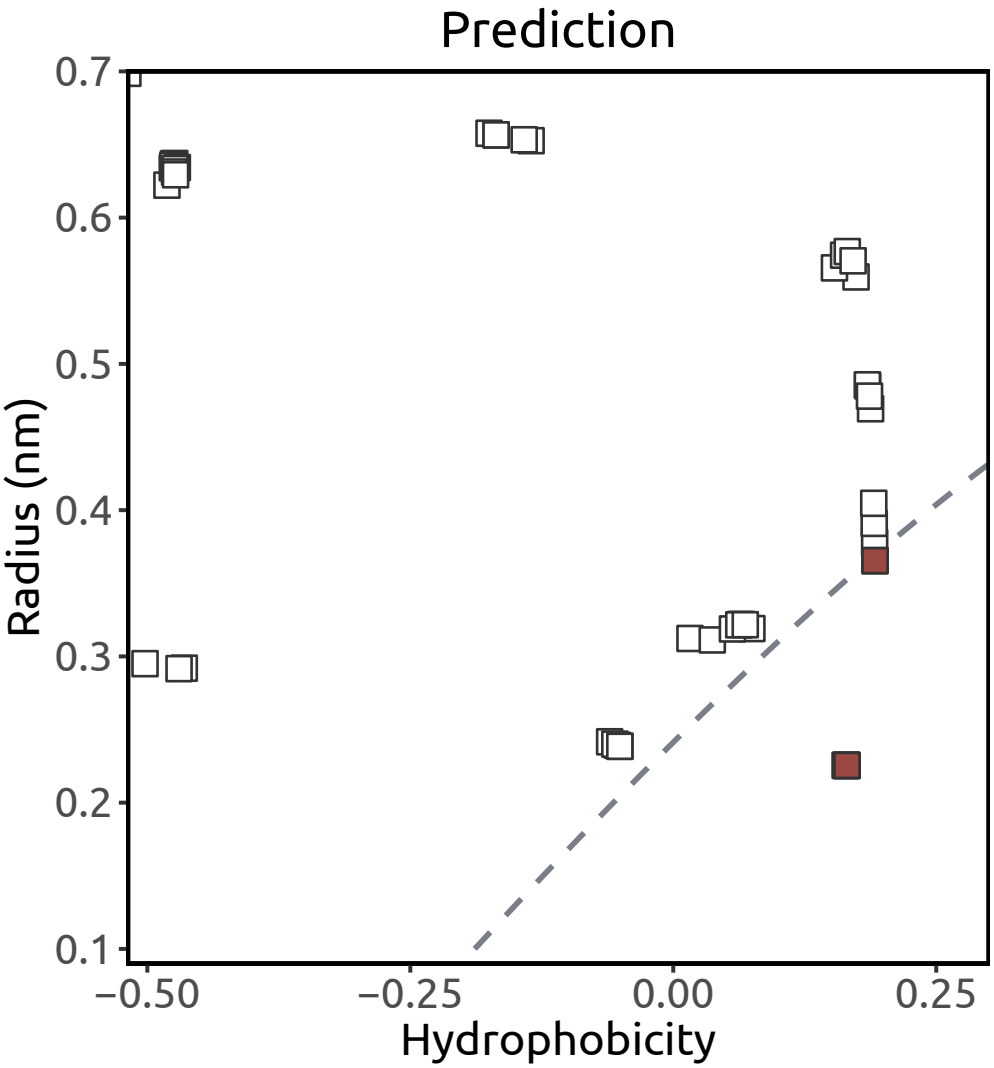
GLIC (PDB ID: 5J0Z)

Gloeobacter violaceus
X–ray (3.25 Å)

Basak et al., 2017







Heuristic score:
0.54 (n = 7)

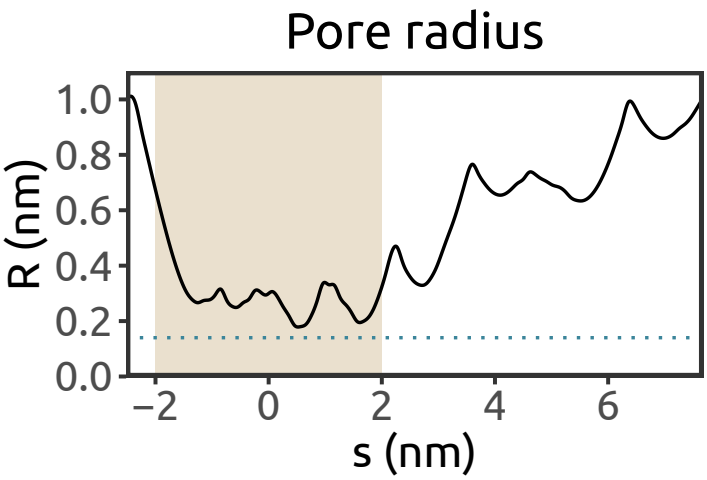
Simulation result:
hydrated channel

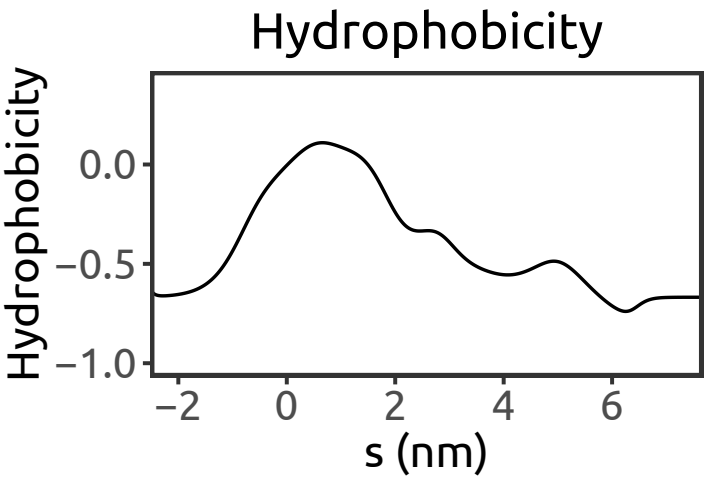
GLIC (PDB ID: 5L47)

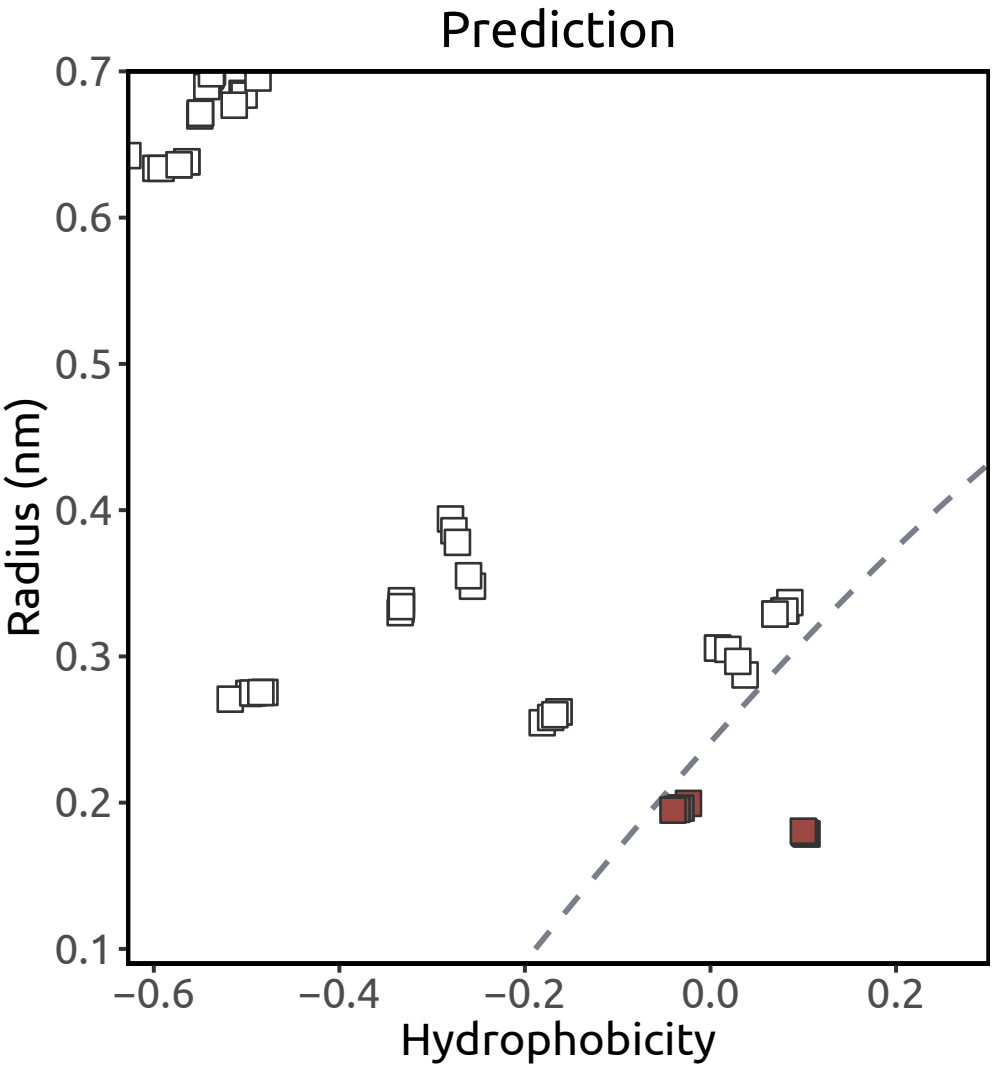
Gloeobacter violaceus

X–ray (3.3 Å)

Fourati et al., 2017







Heuristic score:

0.63 (n = 10)

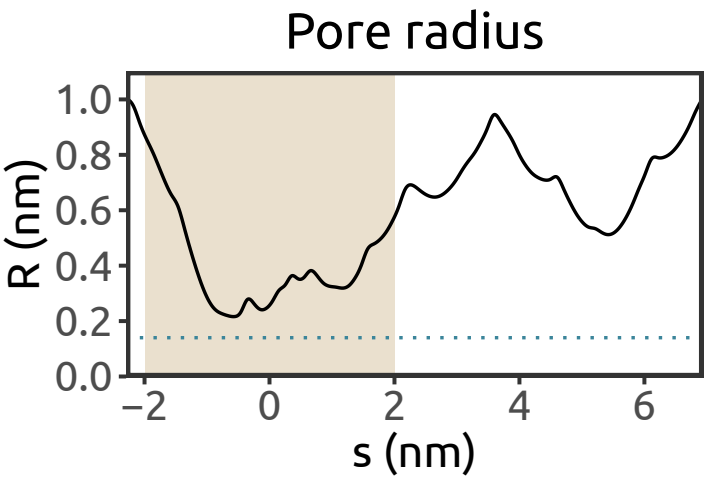
Simulation result:

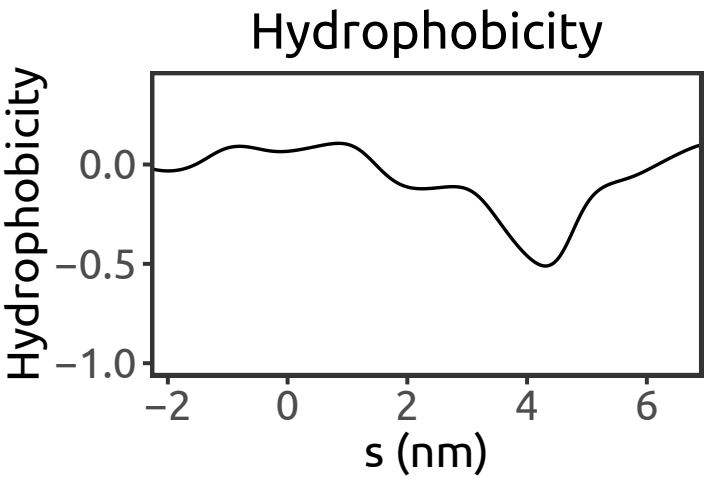
barrier to water

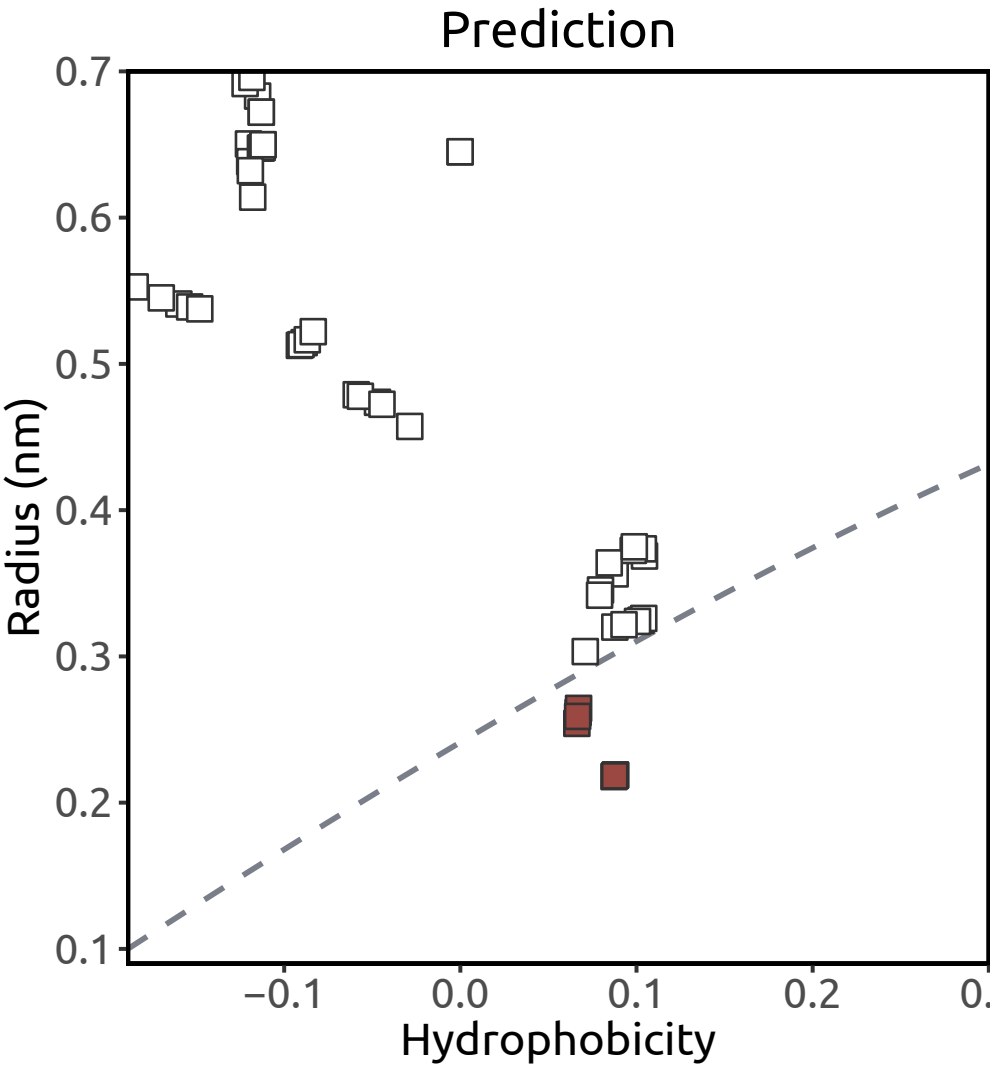
GluCl (PDB ID: 3RHW)

Caenorhabditis elegans
X–ray (3.26 Å)

Pan et al., 2012







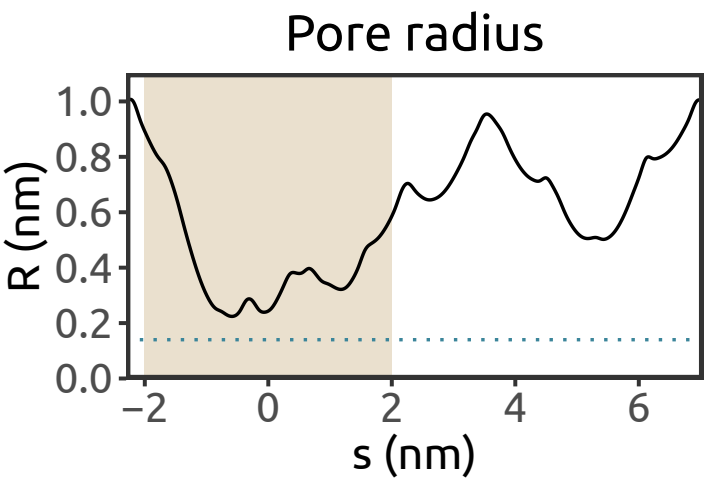
Heuristic score:
0.44 (n = 9)

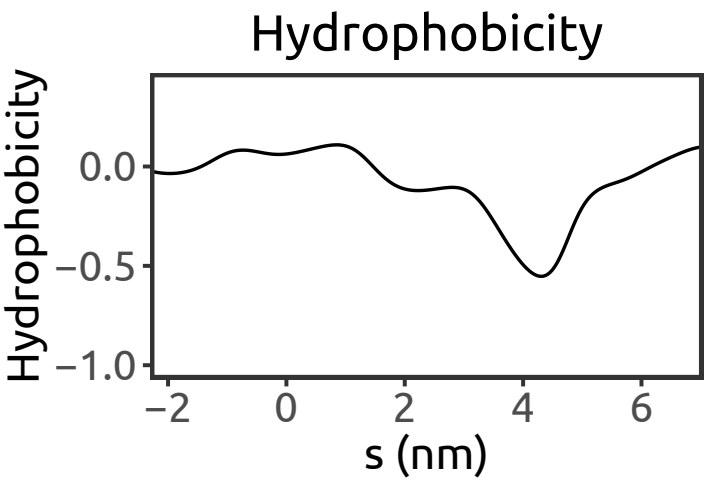
Simulation result:
hydrated channel

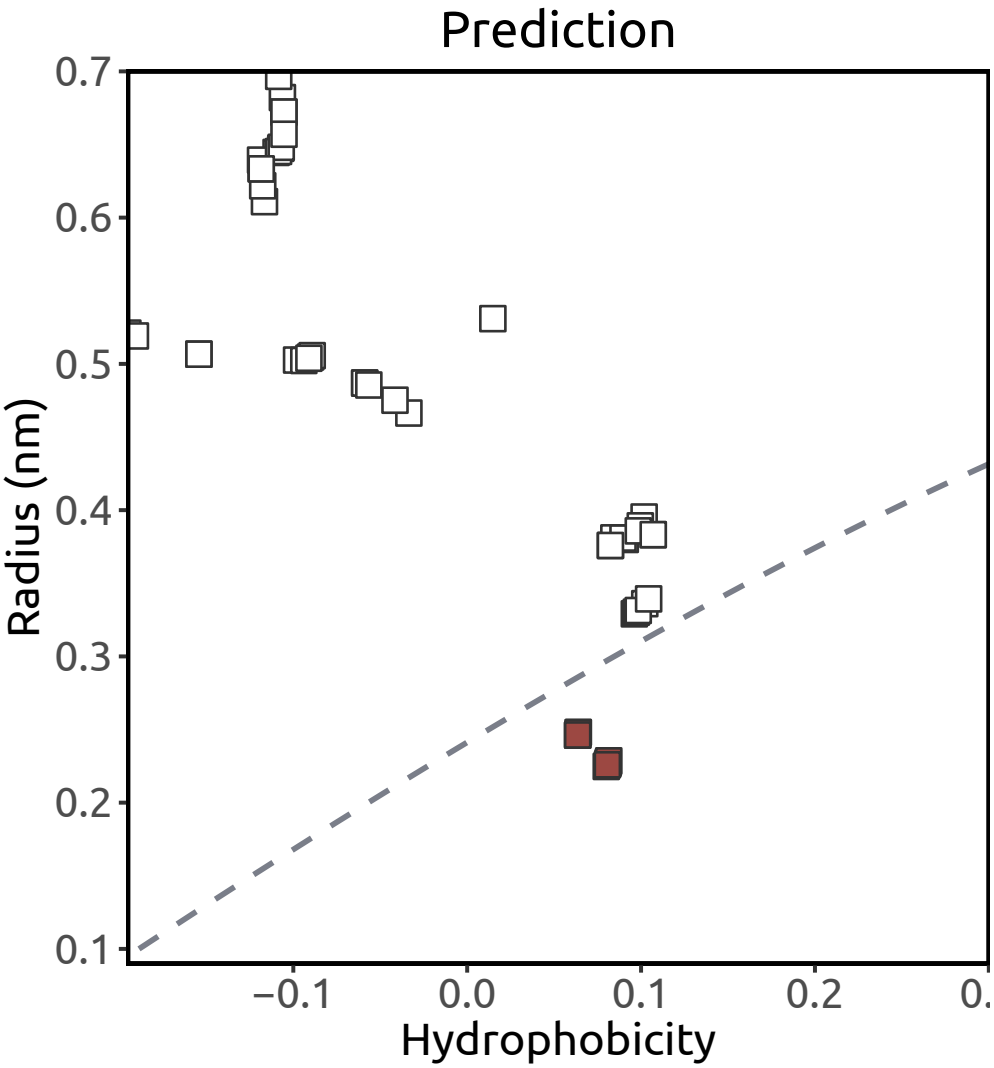
GluCl (PDB ID: 3RIF)

Caenorhabditis elegans
X–ray (3.35 Å)

Hibbs & Gounaux, 2011







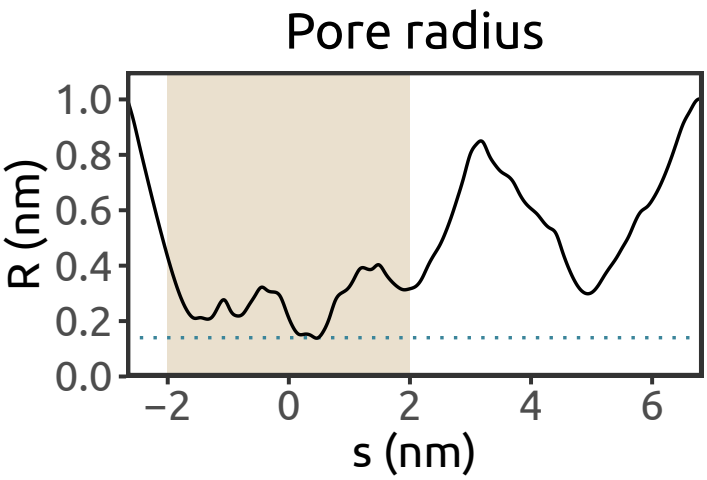
Heuristic score:
0.45 (n = 10)

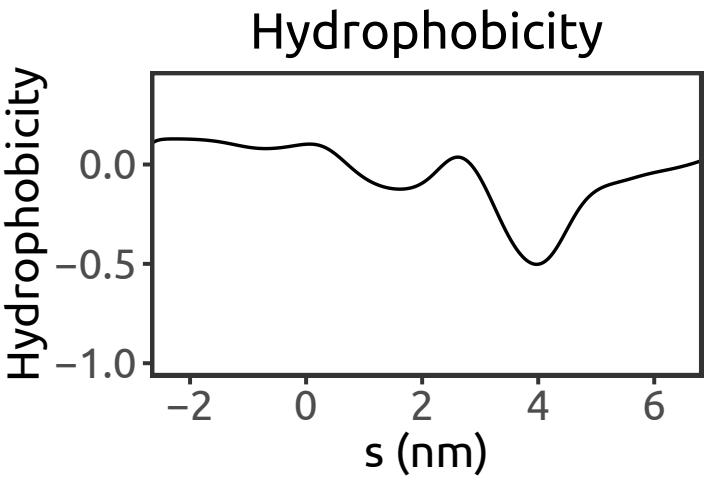
Simulation result:
hydrated channel

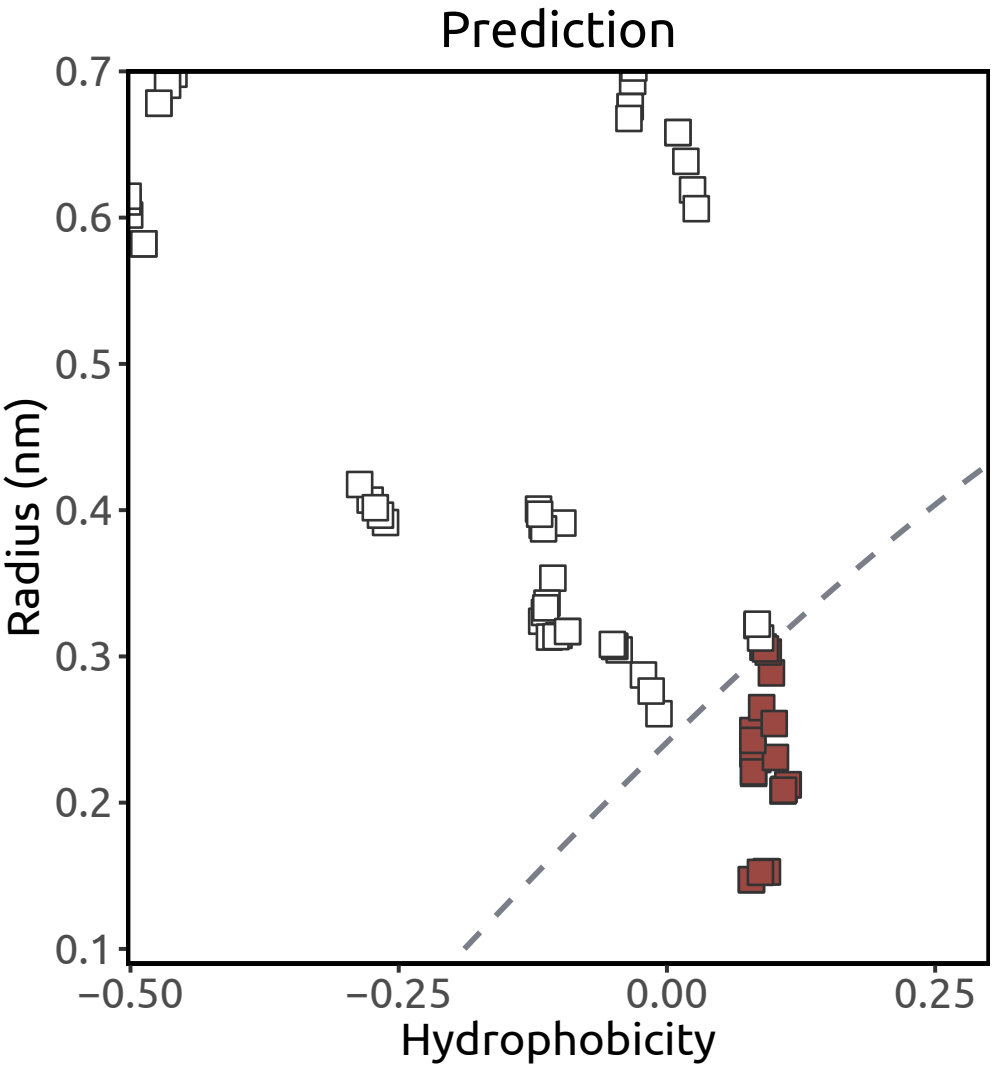
GluCl (PDB ID: 4TNV)

Caenorhabditis elegans
X–ray (3.6 Å)

Althoff et al., 2014







Heuristic score:
1.55 (n = 22)

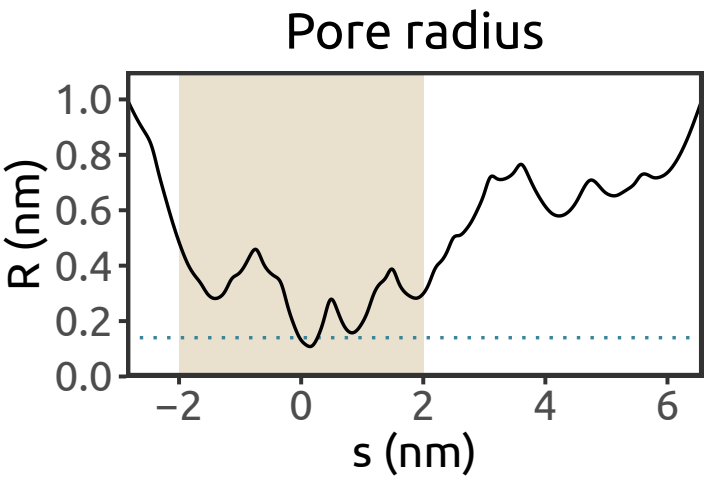
Simulation result:
barrier to water

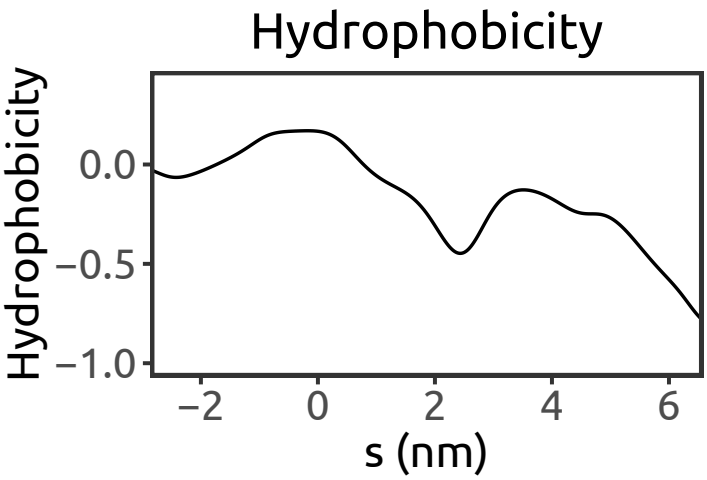
GlyR (PDB ID: 3JAD)

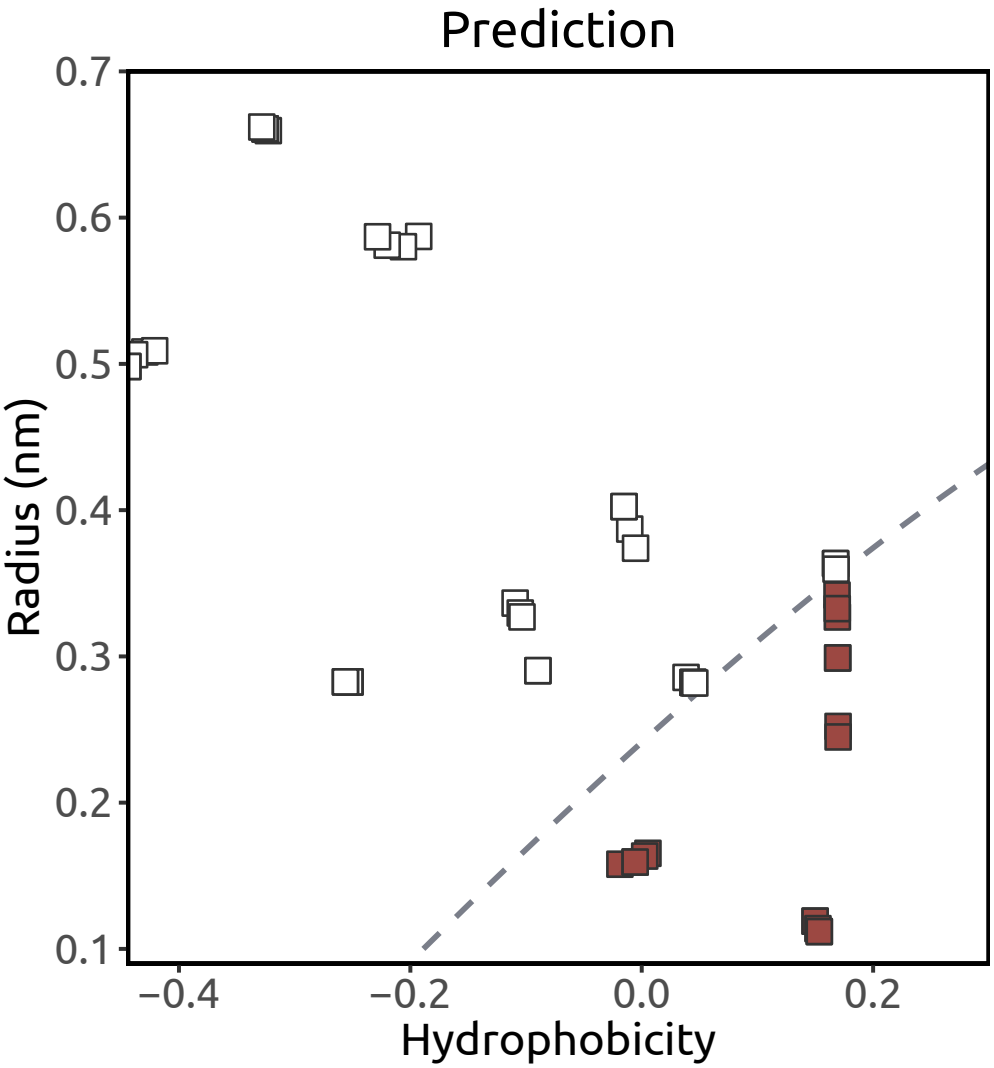
Danio rerio

cryo–EM (3.9 Å)

Du et al., 2015







Heuristic score:

1.59 (n = 17)

Simulation result:

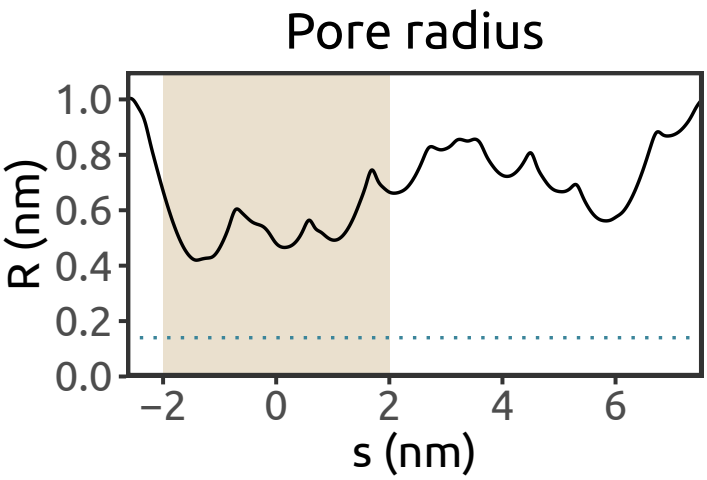
barrier to water

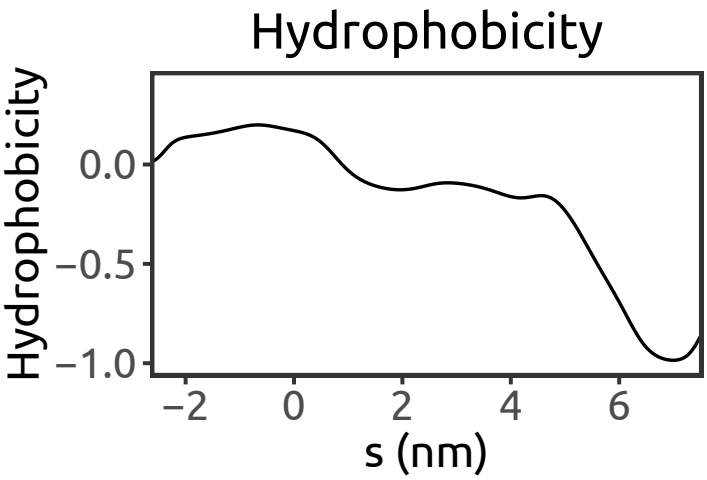
GlyR (PDB ID: 3JAE)

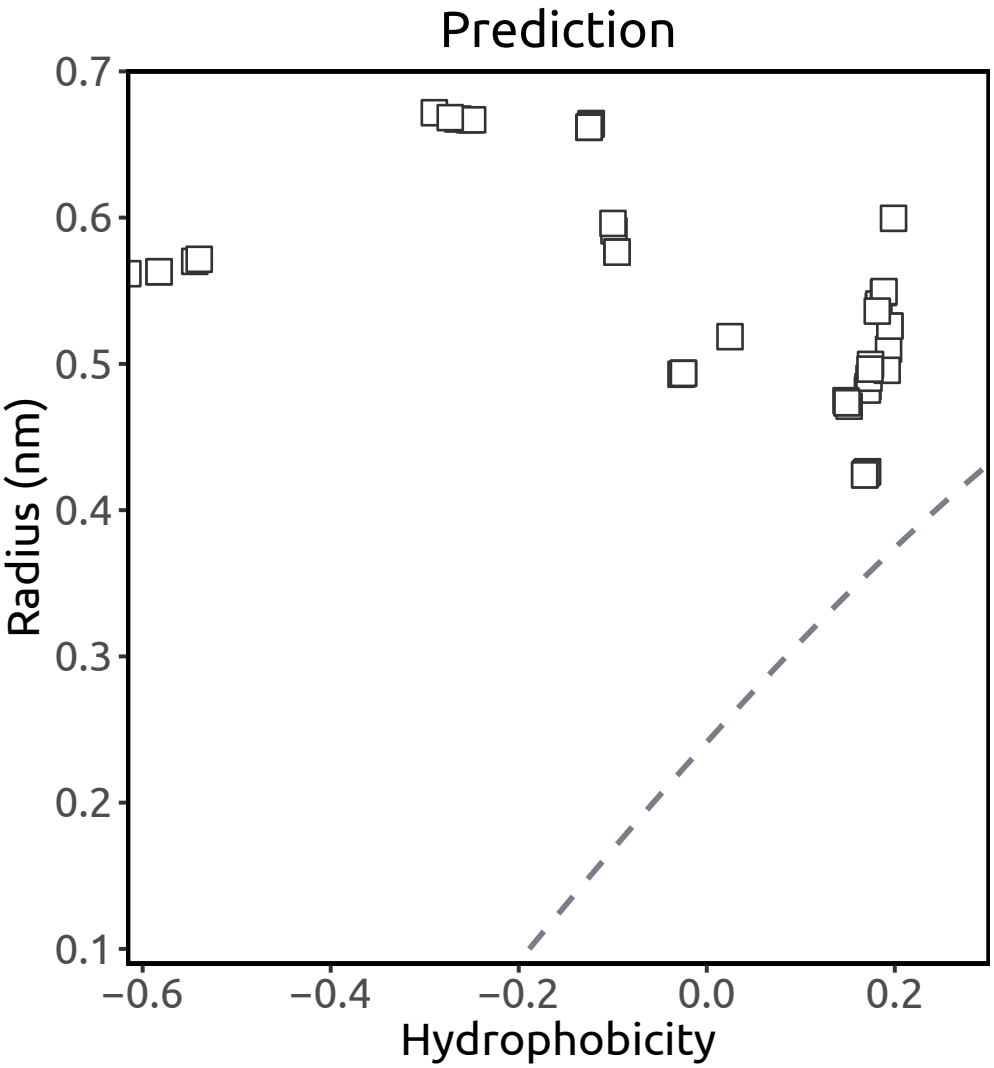
Danio rerio

cryo–EM (3.9 Å)

Du et al., 2015







Heuristic score:

0 (n = 0)

Simulation result:

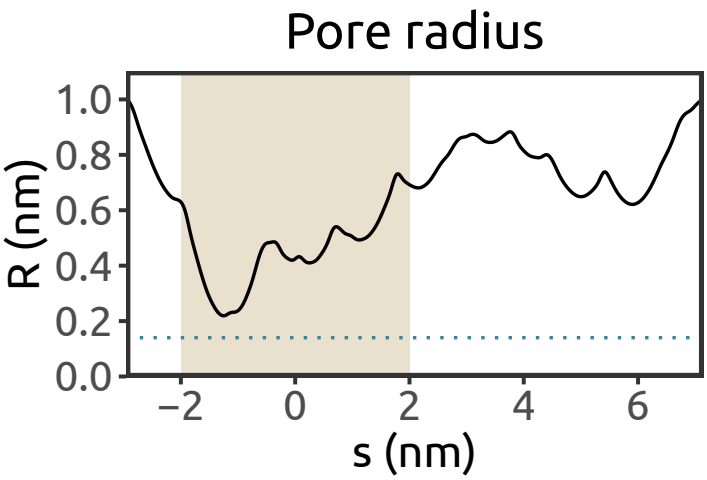
hydrated channel

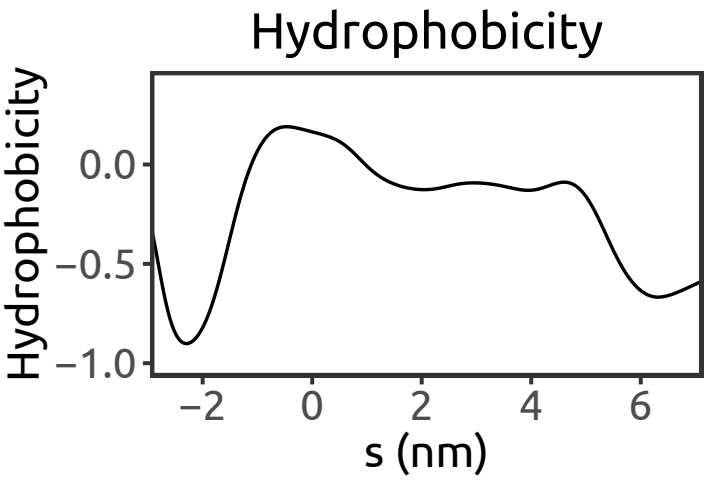
GlyR (PDB ID: 3JAF)

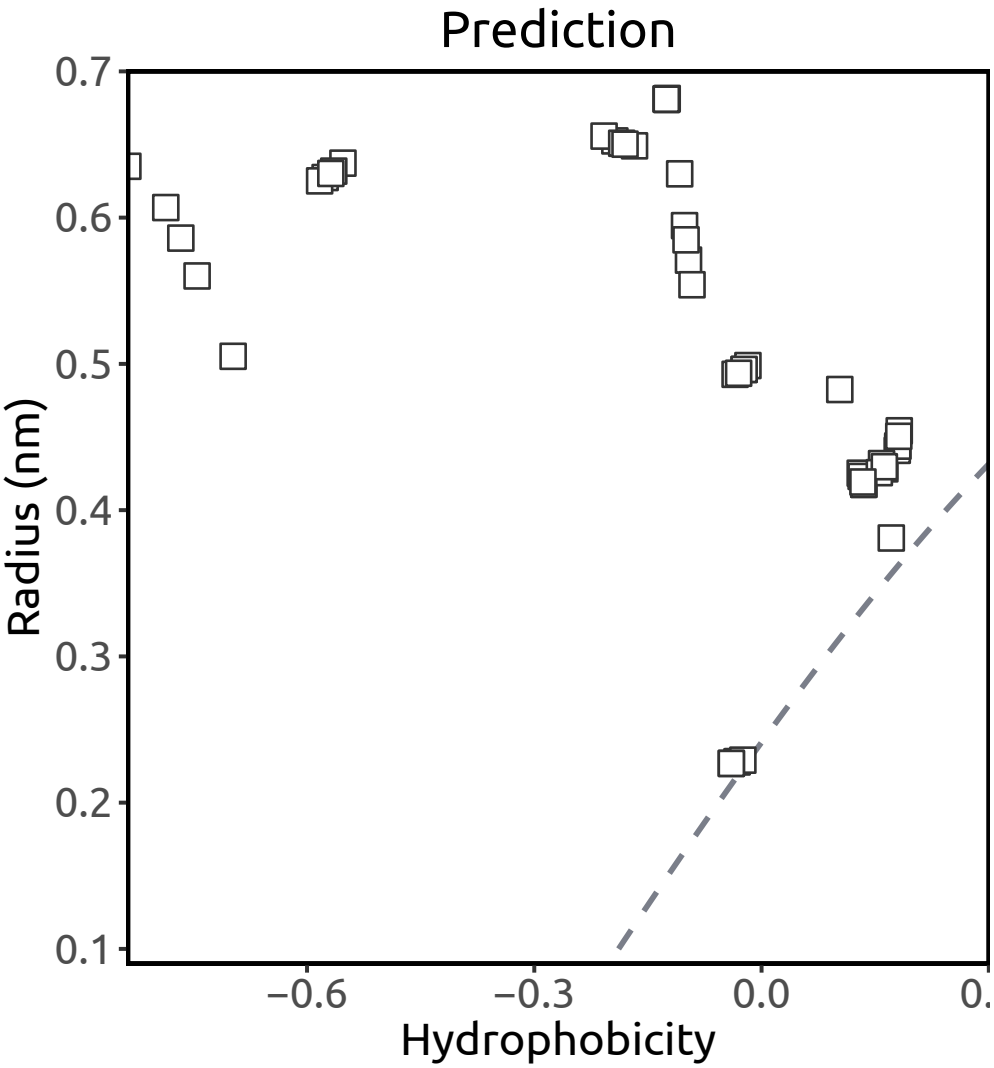
Danio rerio

cryo–EM (3.8 Å)

Du et al., 2015







Heuristic score:

0 (n = 0)

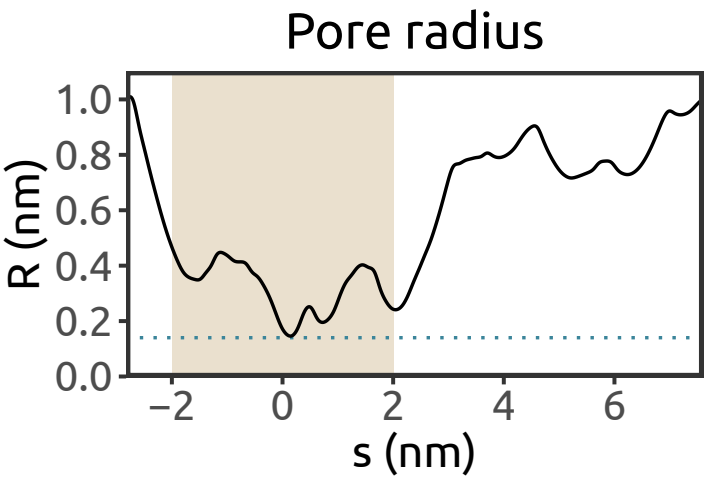
Simulation result:

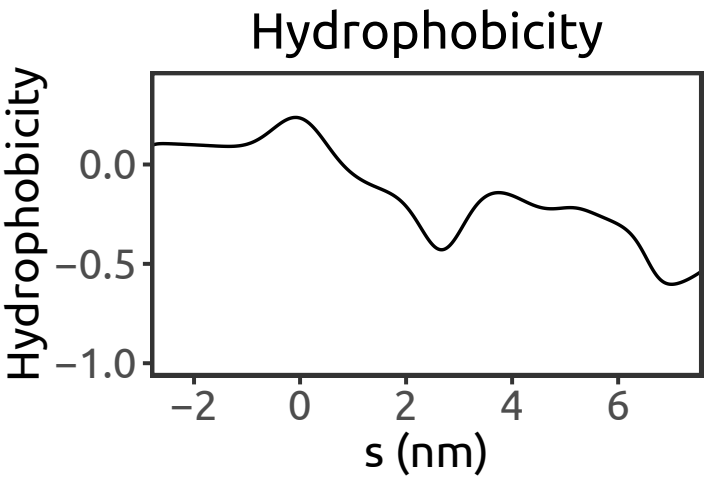
hydrated channel

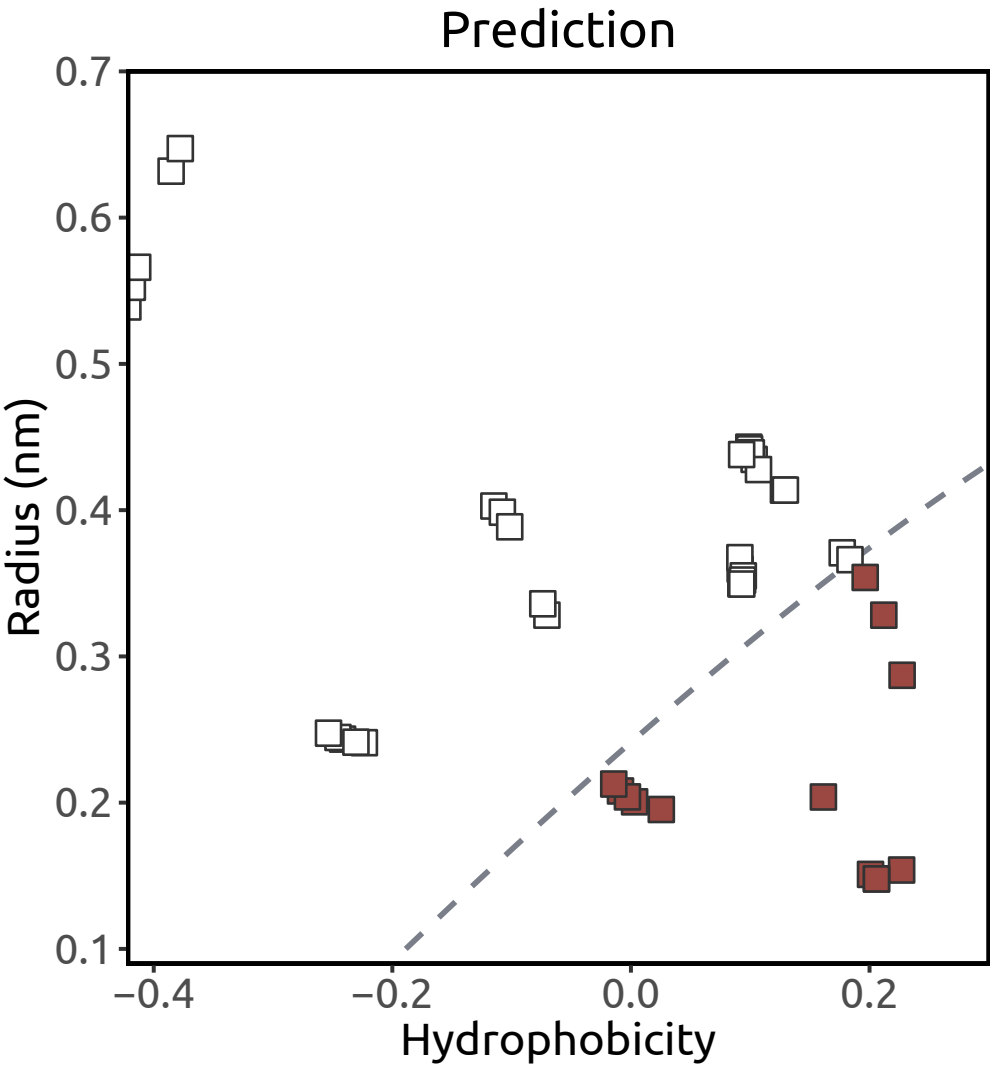
GlyR (PDB ID: 5CFB)

Homo sapiens
X–ray (3.04 Å)

Huang et al., 2015







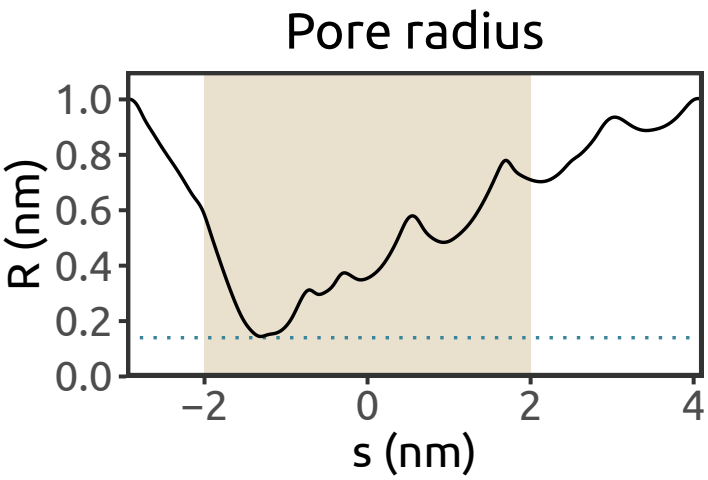
Heuristic score:
1.2 (n = 13)

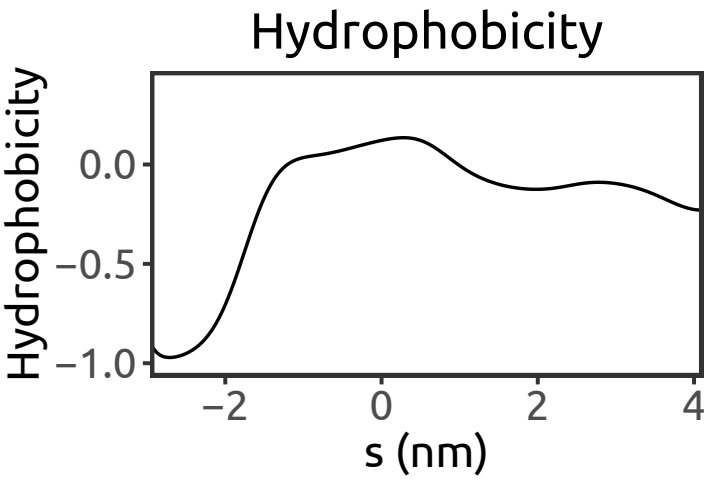
Simulation result:
barrier to water

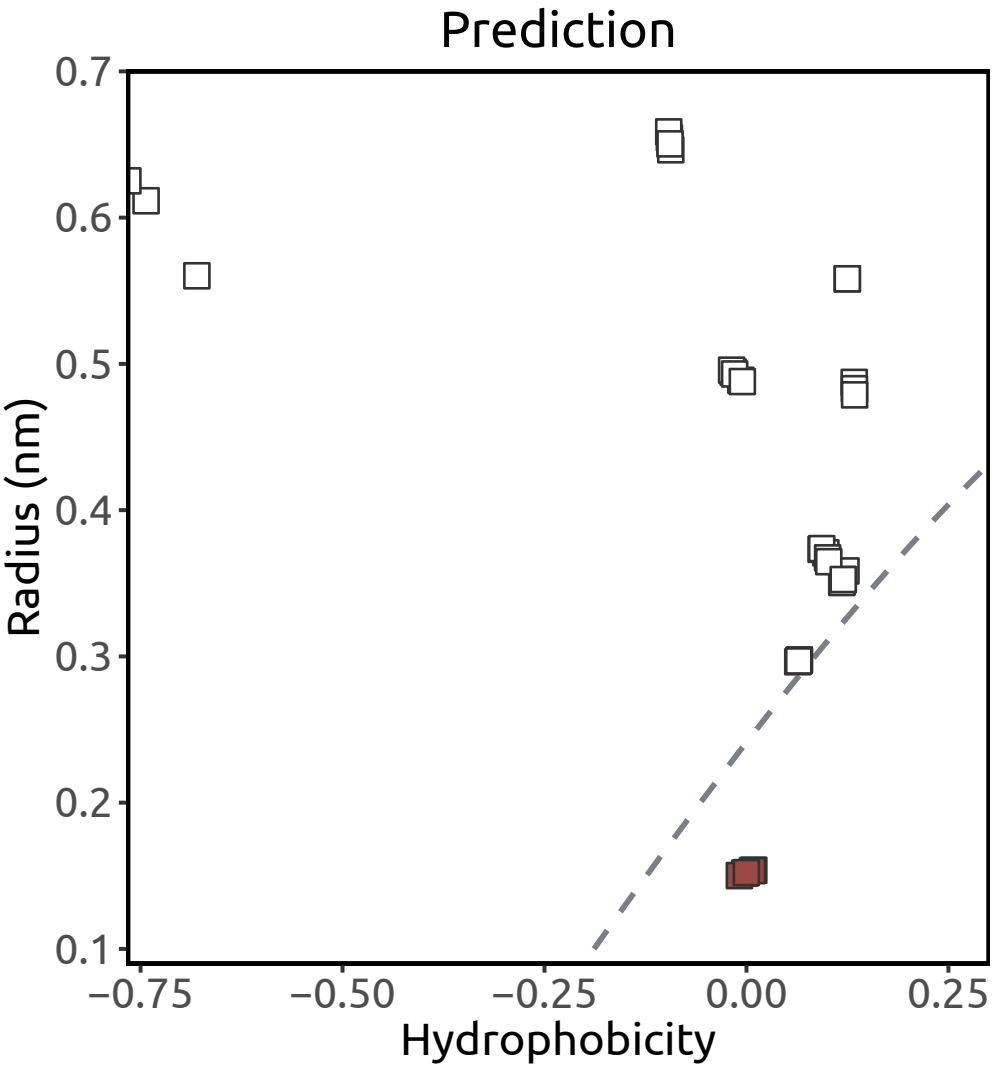
GlyR (PDB ID: 5VDH)

Homo sapiens
X–ray (2.85 Å)

Huang et al., 2017







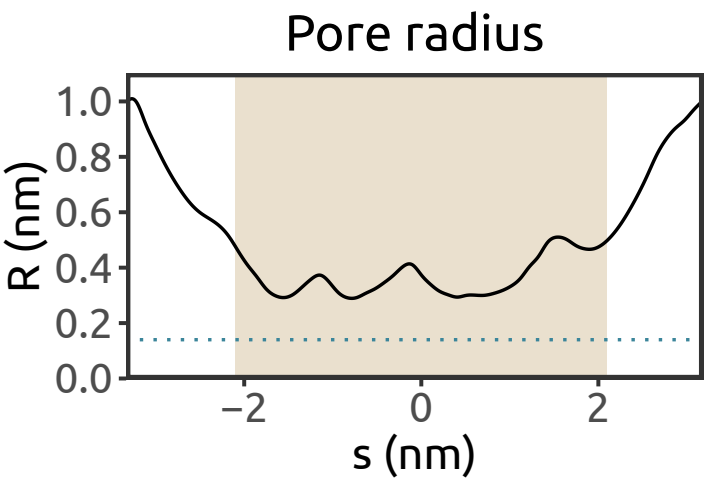
Heuristic score:
0.36 (n = 5)

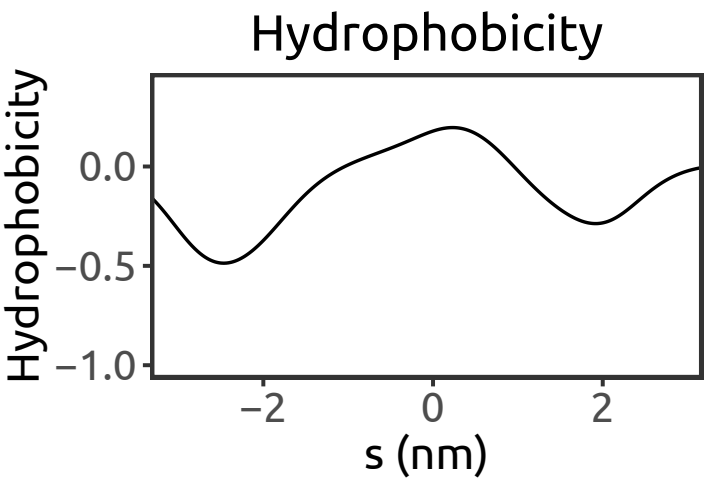
Simulation result:
barrier to water

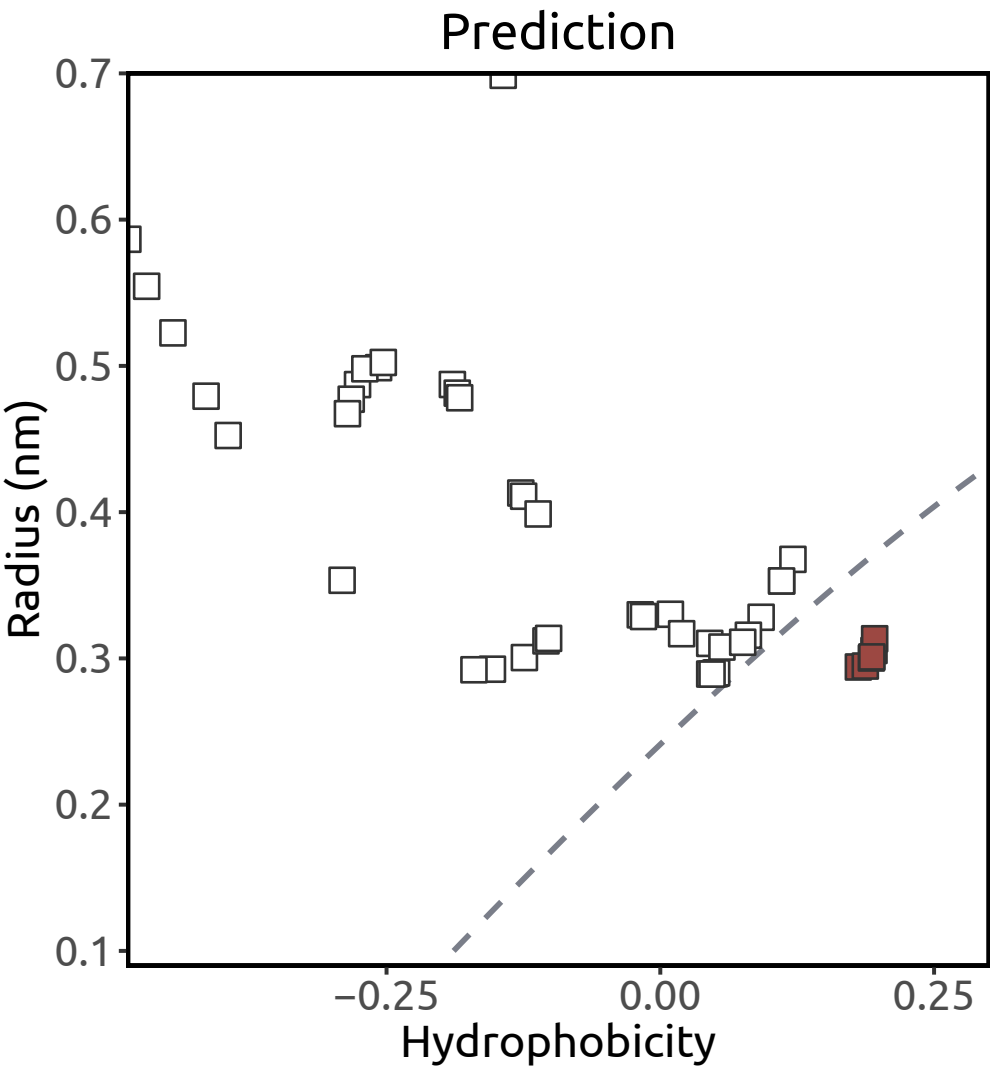
nAChR (PDB ID: 1OED)

Torpedo marmorata
EM (4 Å)

Miyazawa et al., 2003







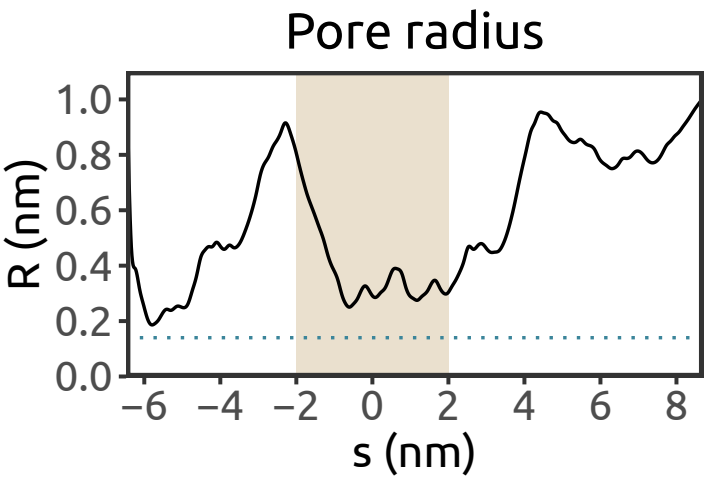
Heuristic score:
0.34 (n = 6)

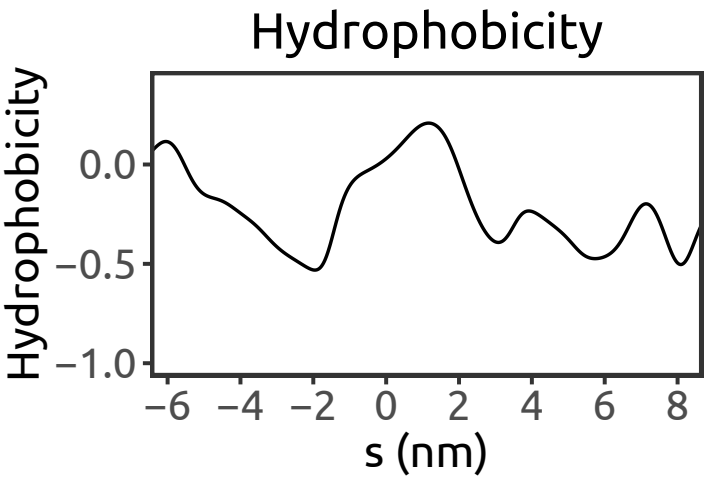
Simulation result:
barrier to water

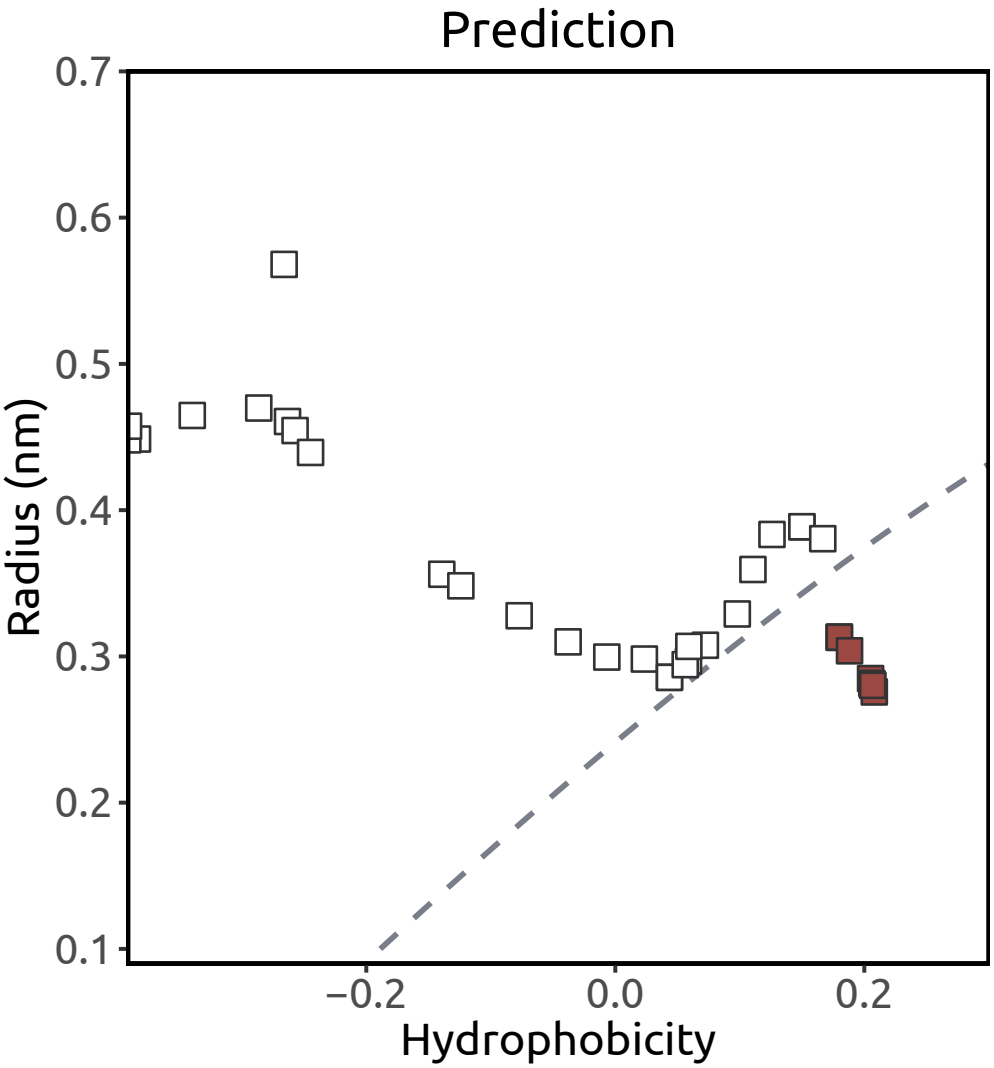
nAChR (PDB ID: 2BG9)

Torpedo marmorata
EM (4 Å)

Unwin, 2005







Heuristic score:
0.59 (n = 9)

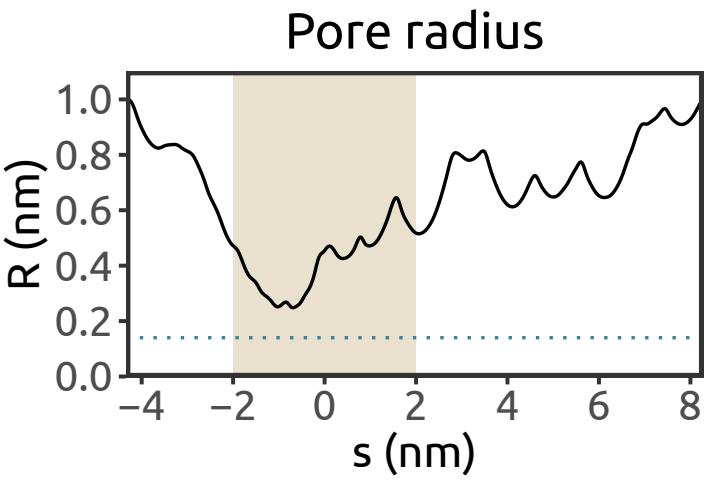
Simulation result:
barrier to water

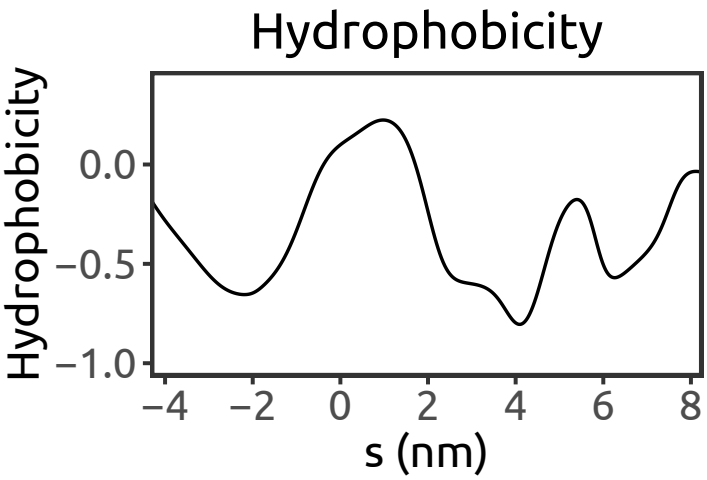
nAChR (PDB ID: 5KXI)

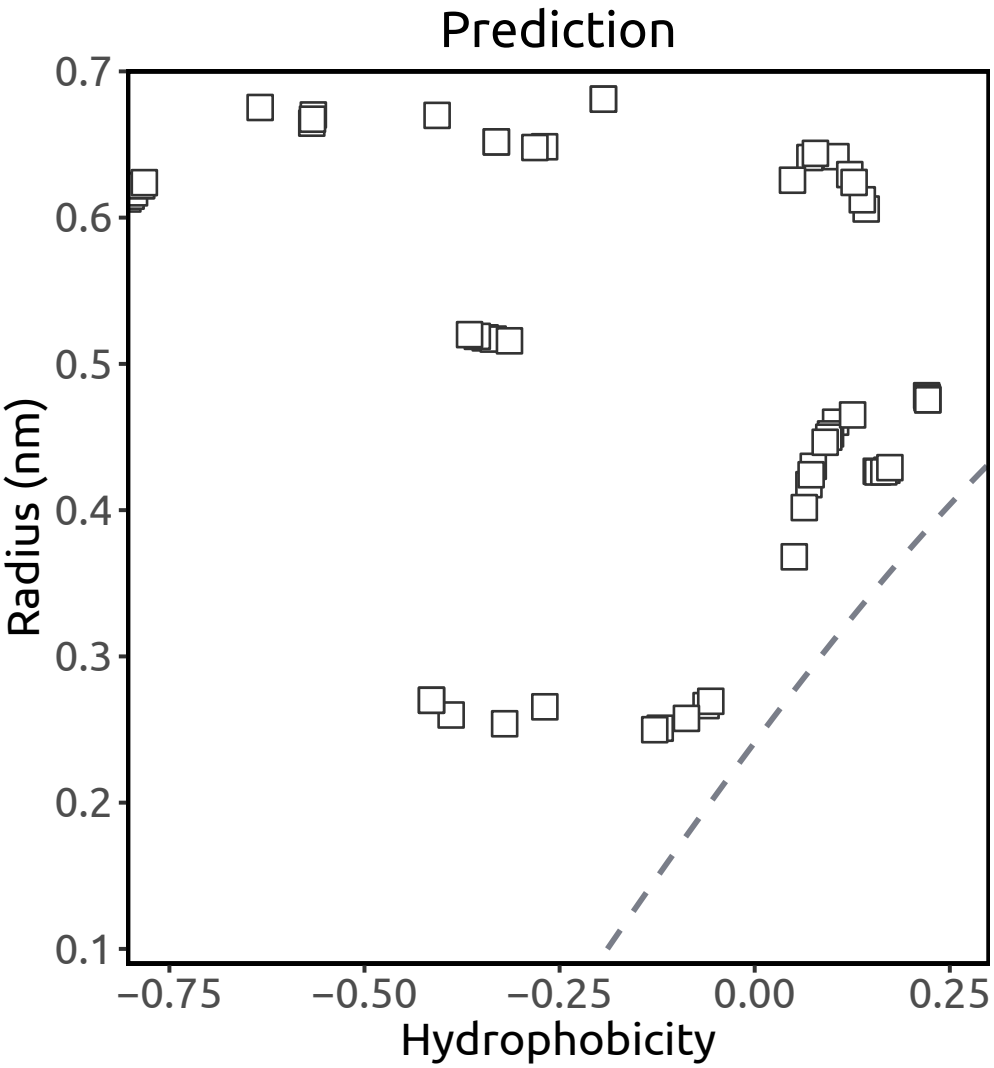
Homo sapiens

X–ray (3.94 Å)

Morales–Perez et al., 2016







Heuristic score:

0 (n = 0)

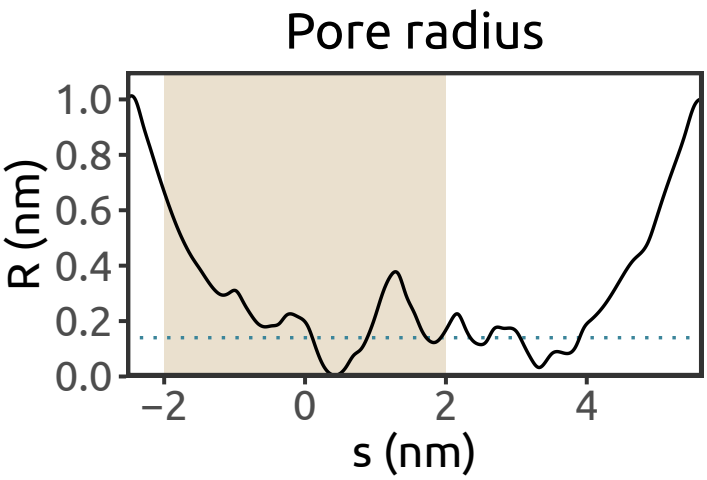
Simulation result:

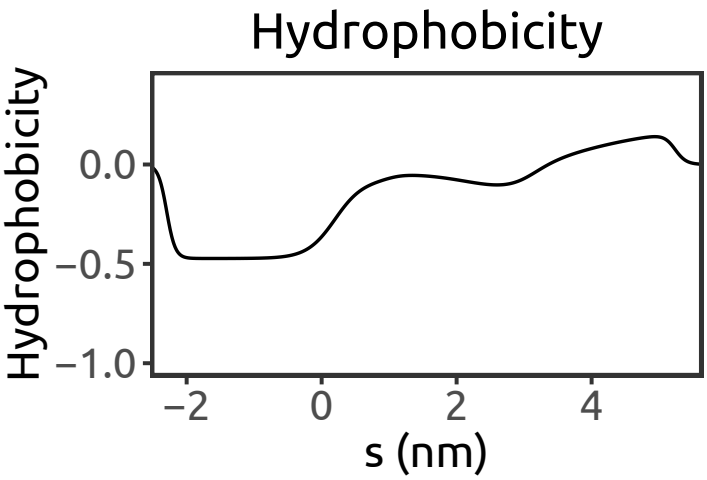
hydrated channel

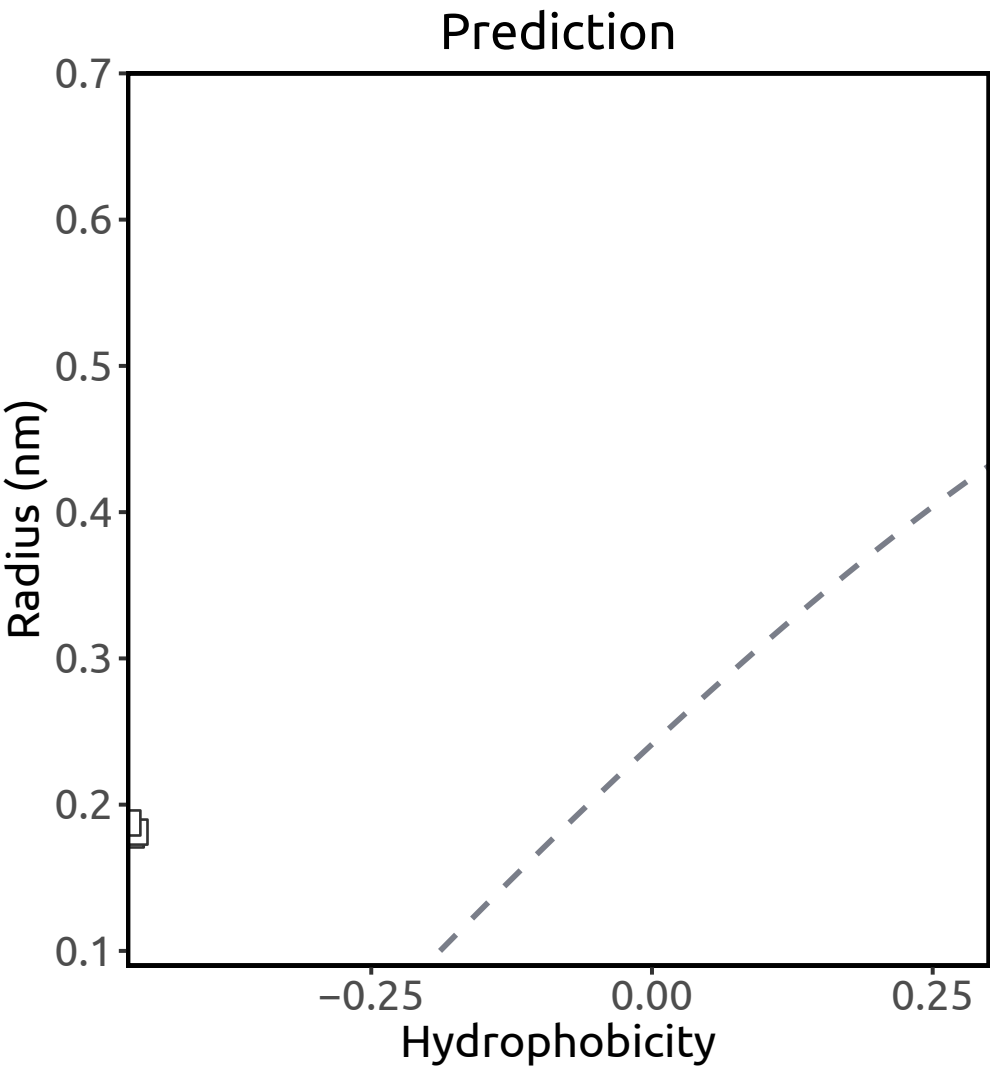
GluA (PDB ID: 5WEK)

Rattus norvegicus
cryo–EM (4.6 Å)

Twomey et al., 2017







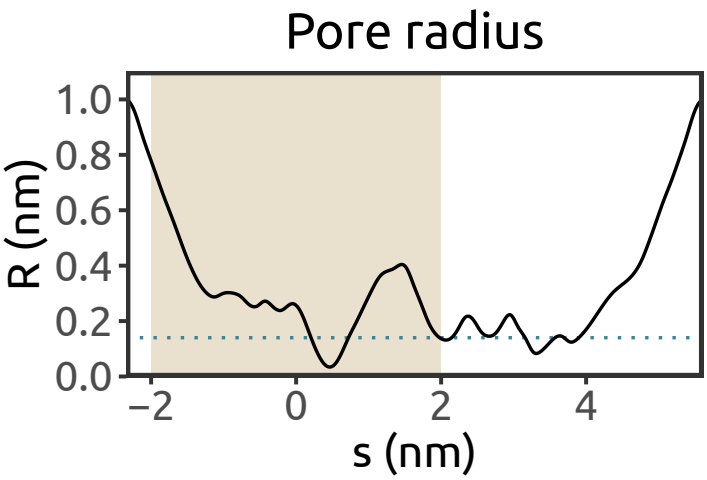
Heuristic score:
0.09 (n = 1)

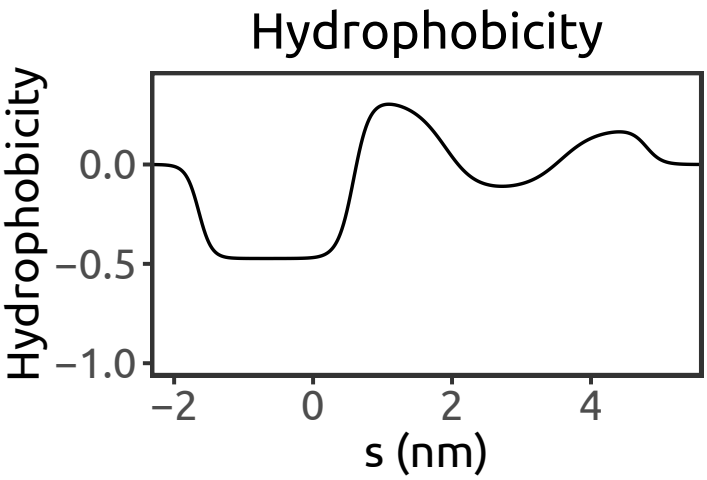
Simulation result:
barrier to water

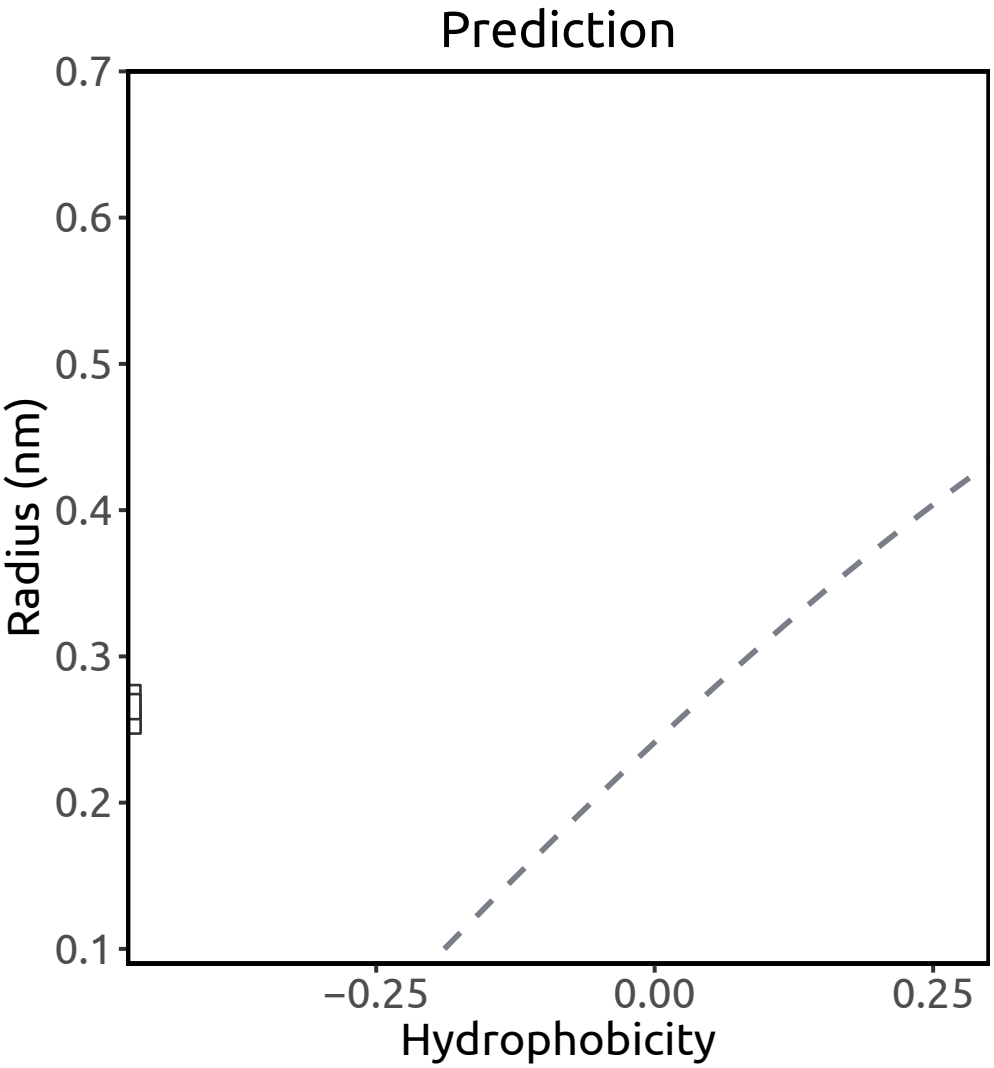
GluA (PDB ID: 5WEL)

Rattus norvegicus
cryo–EM (4.4 Å)

Twomey et al., 2017







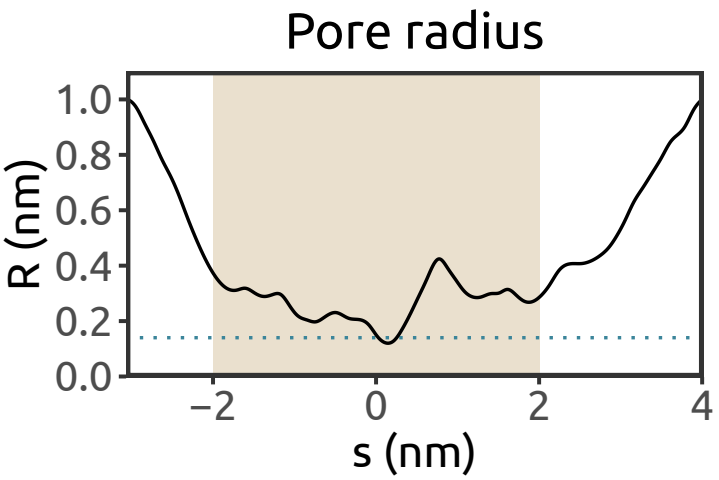
Heuristic score:
0 (n = 0)

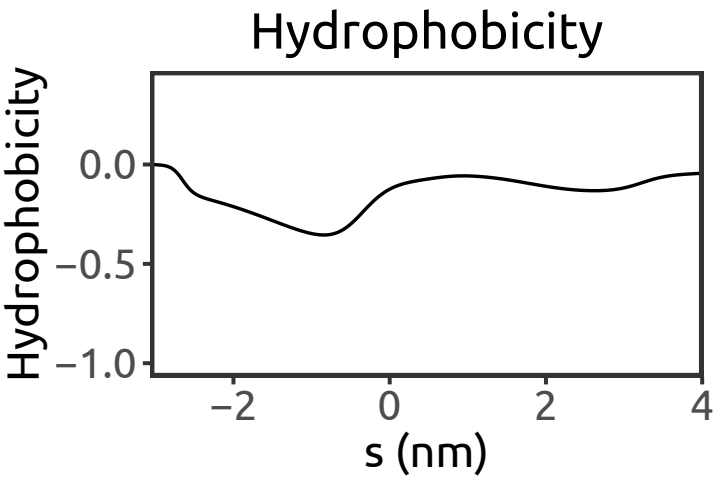
Simulation result:
barrier to water

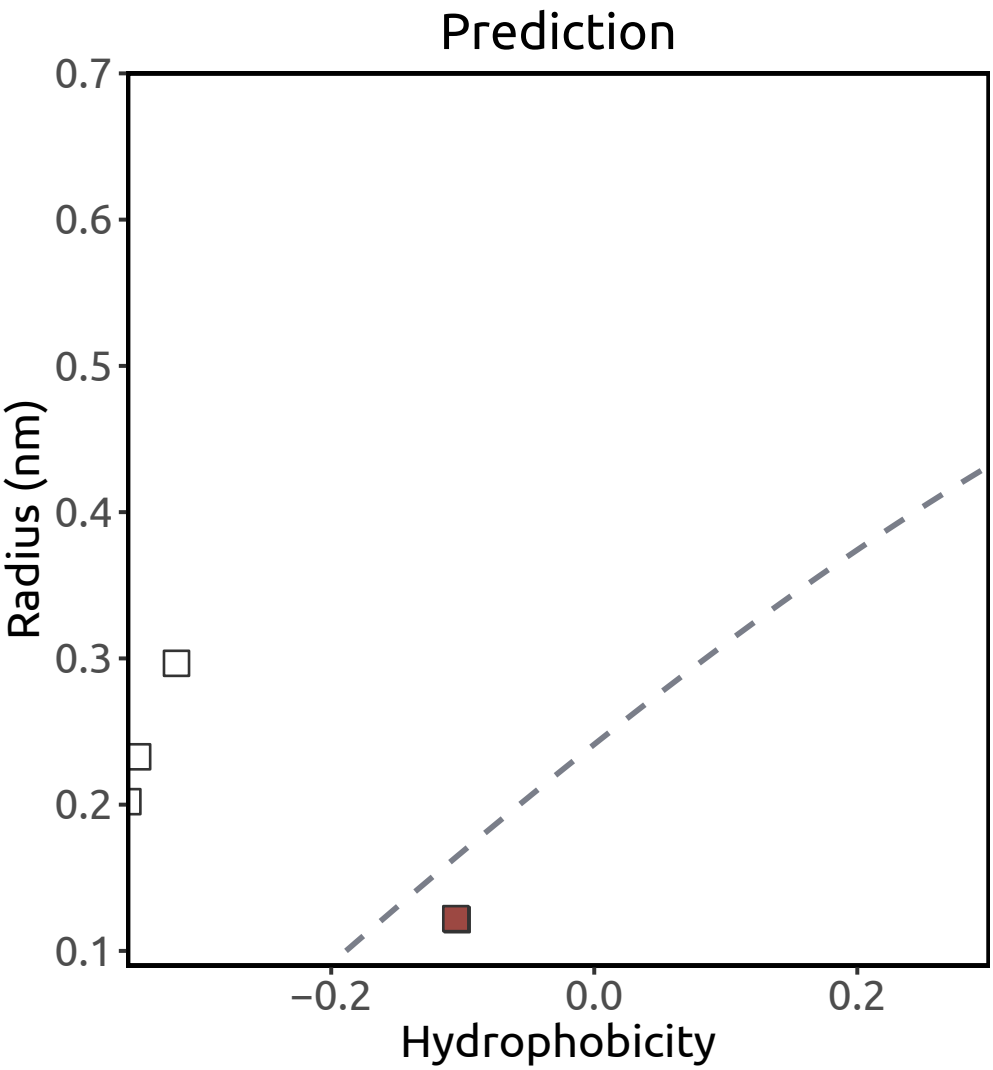
GluA (PDB ID: 5WEO)

Rattus norvegicus
cryo–EM (4.2 Å)

Twomey et al., 2017







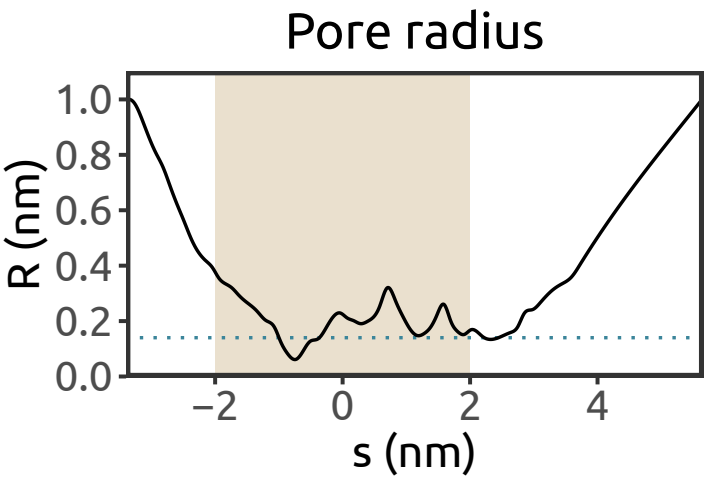
Heuristic score:
0.07 (n = 2)

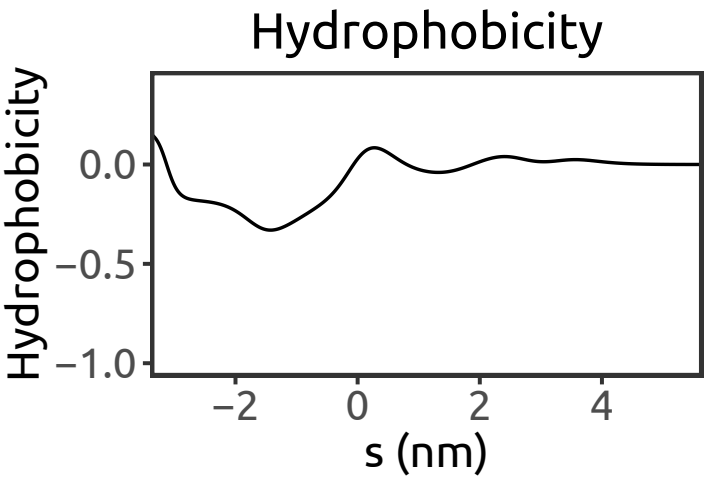
Simulation result:
hydrated channel

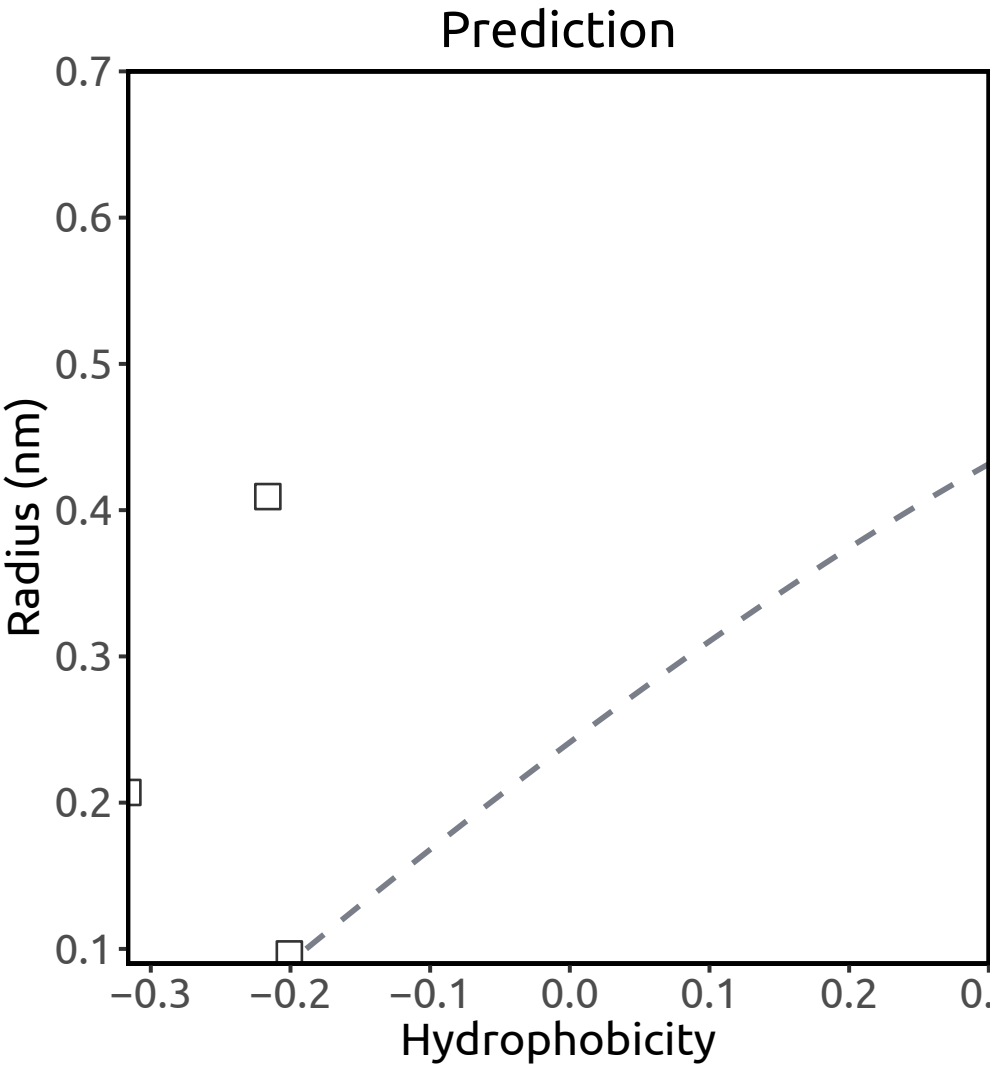
GluN (PDB ID: 5UOW)

Xenopus laevis
cryo–EM (4.5 Å)

Lü et al., 2017







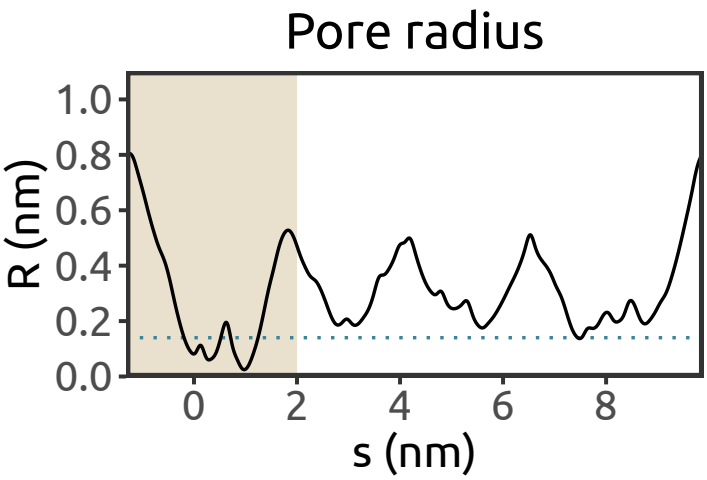
Heuristic score:
0 (n = 0)

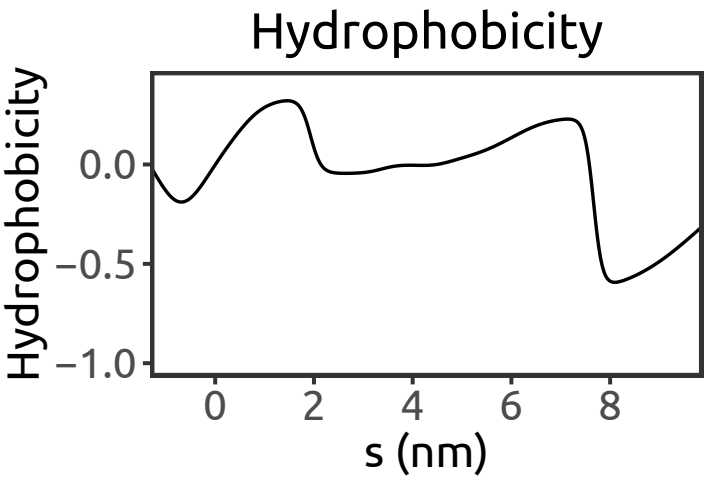
Simulation result:
hydrated channel

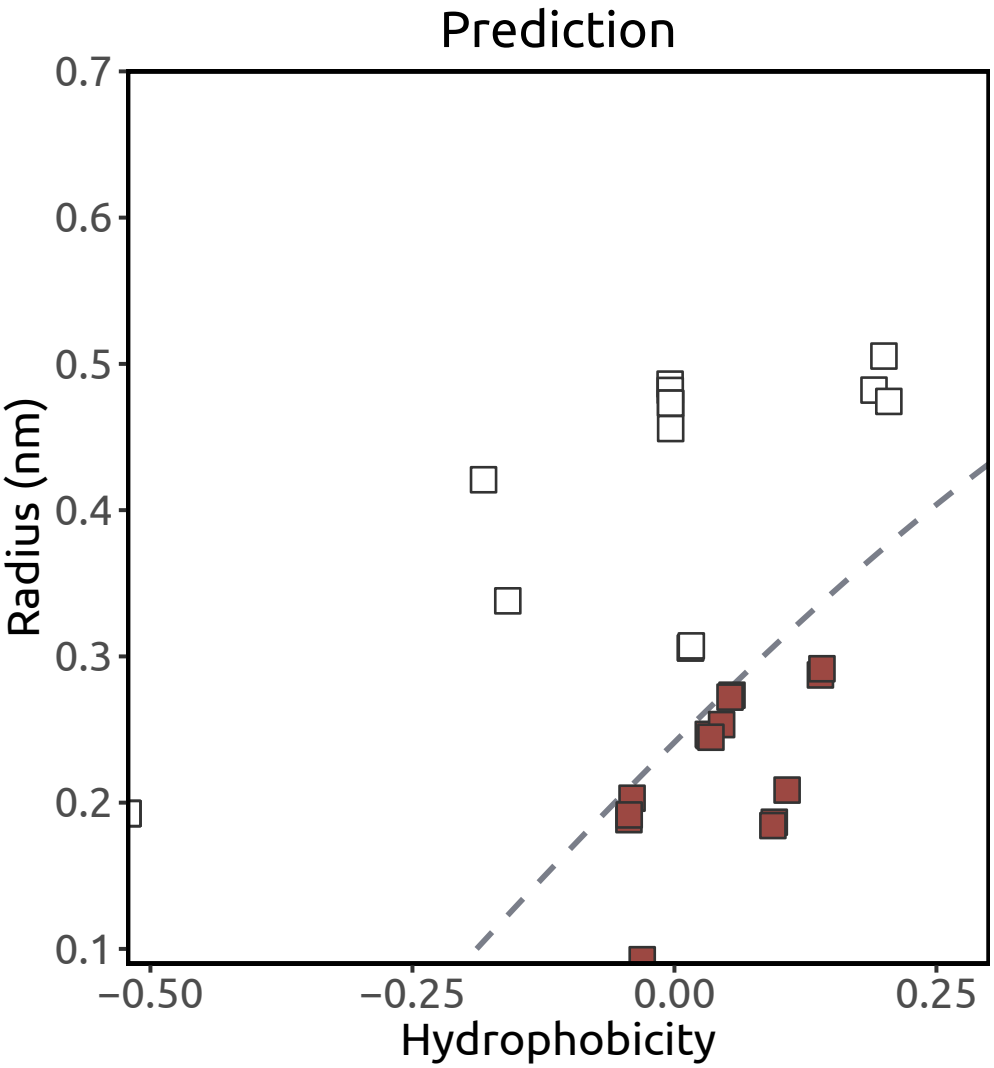
P2X3 (PDB ID: 5SVJ)

Homo sapiens
X–ray (2.98 Å)

Mansoor et al., 2016







Heuristic score:
2.49 (n = 23)

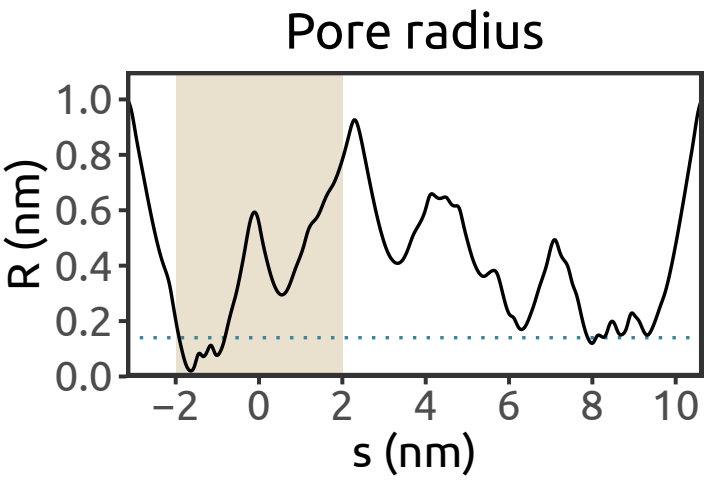
Simulation result:
barrier to water

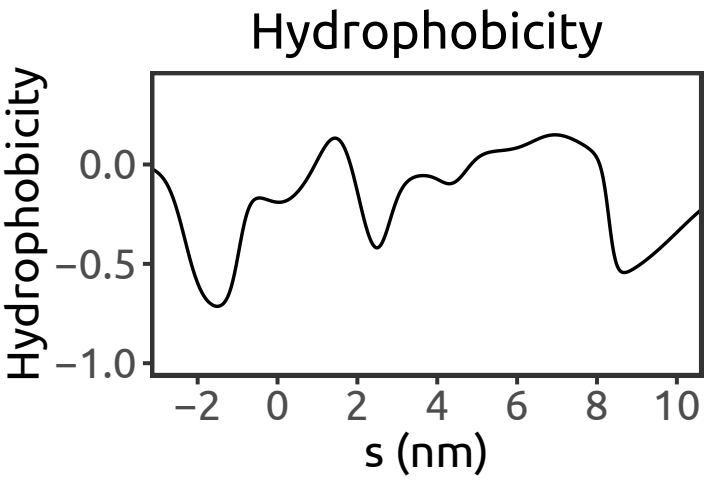
P2X3 (PDB ID: 5SVK)

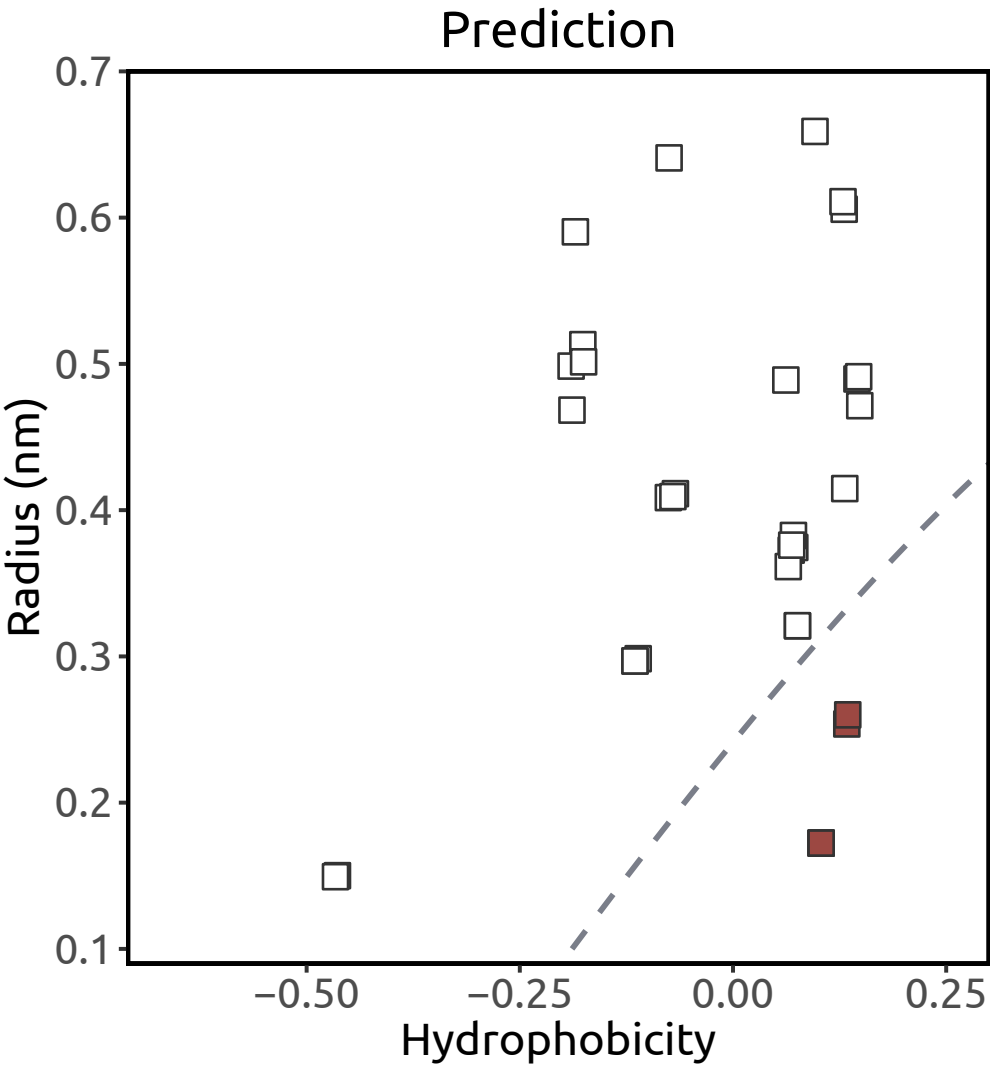
Homo sapiens

X–ray (2.77 Å)

Mansoor et al., 2016







Heuristic score:

0.47 (n = 5)

Simulation result:

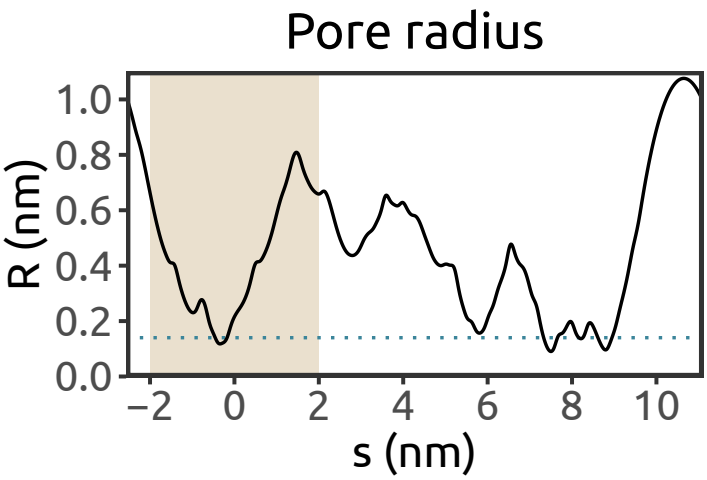
barrier to water

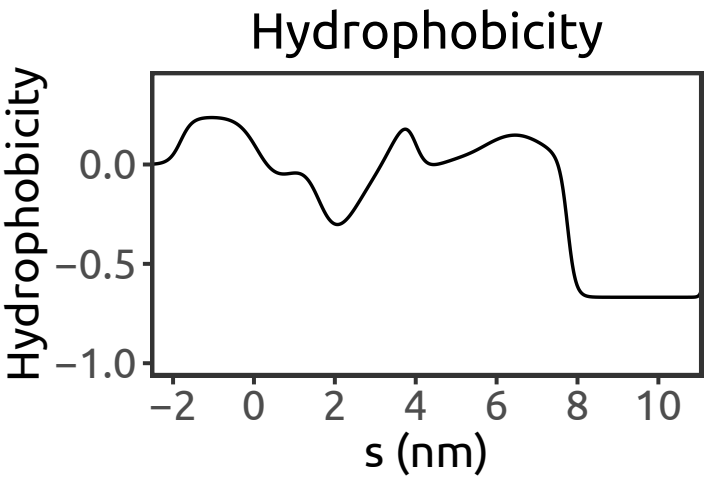
P2X3 (PDB ID: 5SVL)

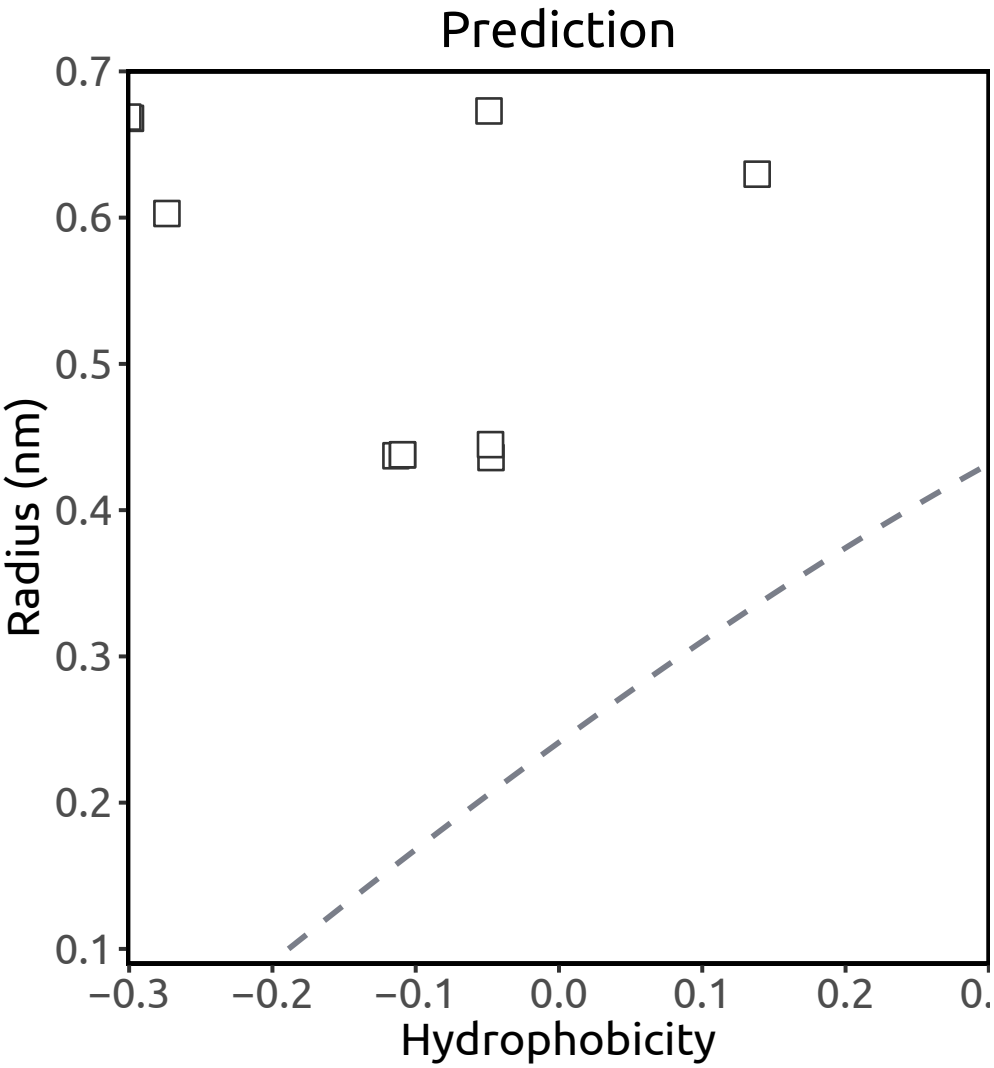
Homo sapiens

X–ray (2.9 Å)

Mansoor et al., 2016







Heuristic score:

0 (n = 0)

Simulation result:

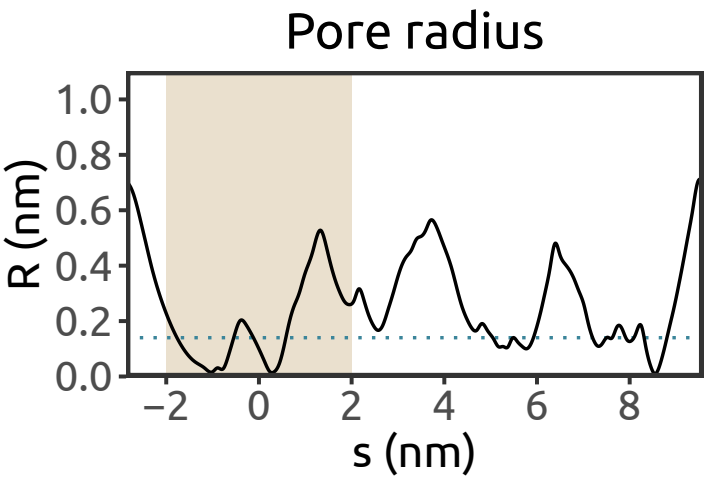
hydrated channel

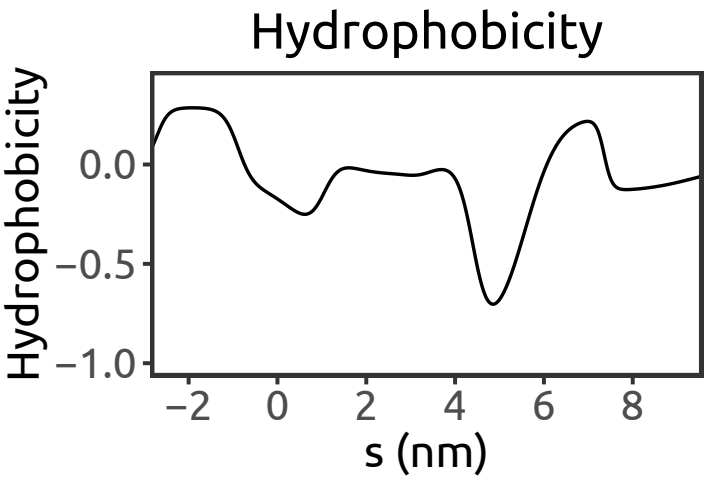
P2X4 (PDB ID: 3H9V)

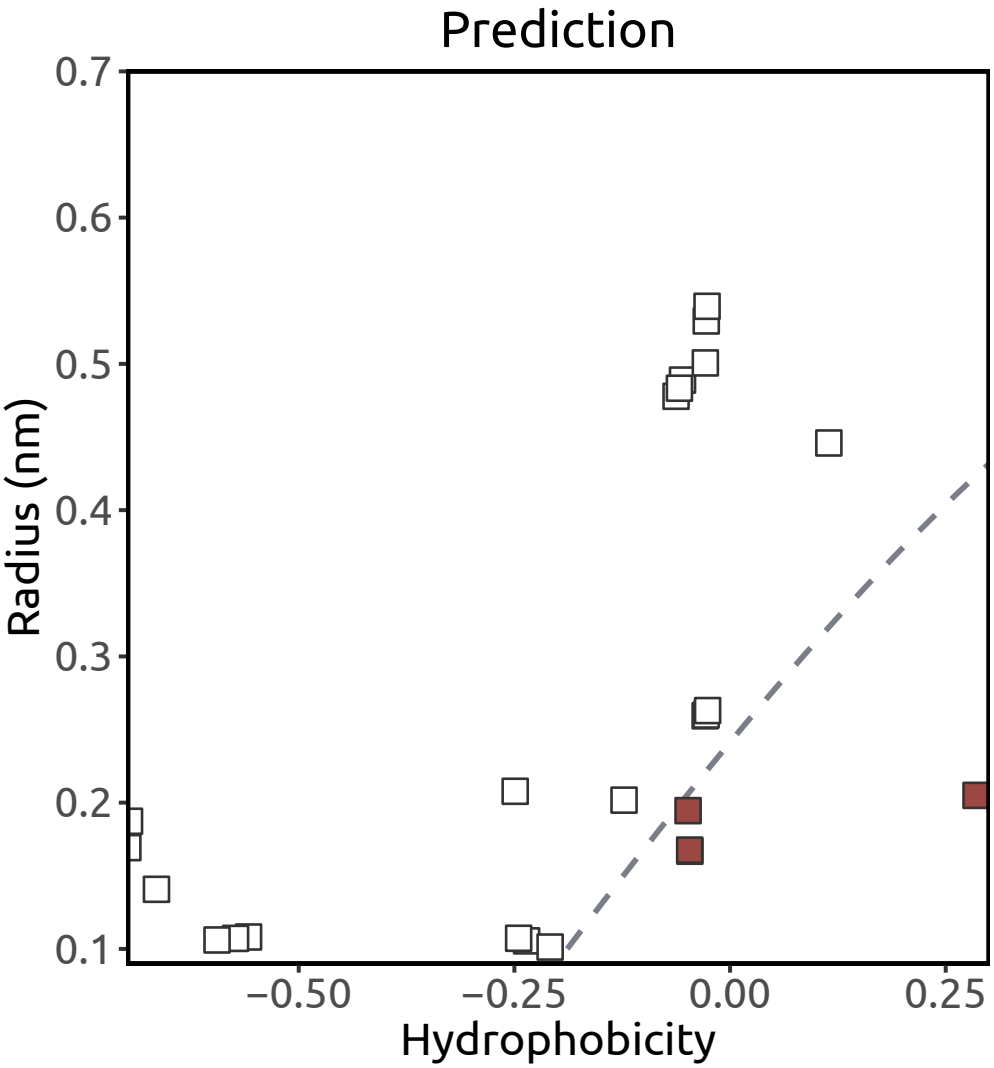
Danio rerio

X–ray (3.1 Å)

Kawate et al., 2009







Heuristic score:

0.94 (n = 9)

Simulation result:

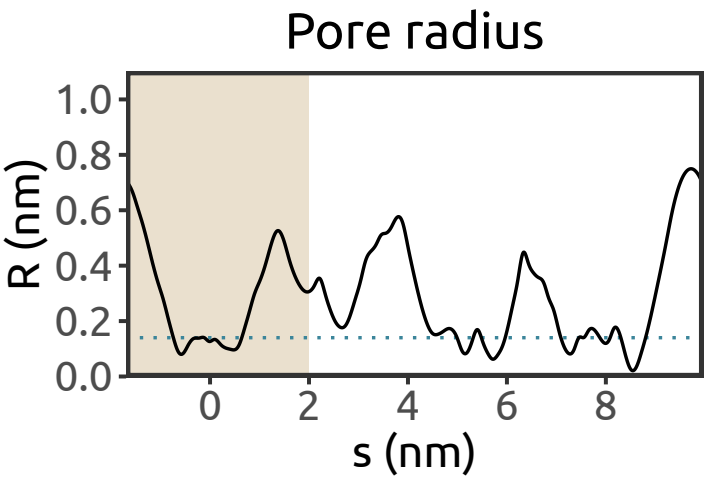
barrier to water

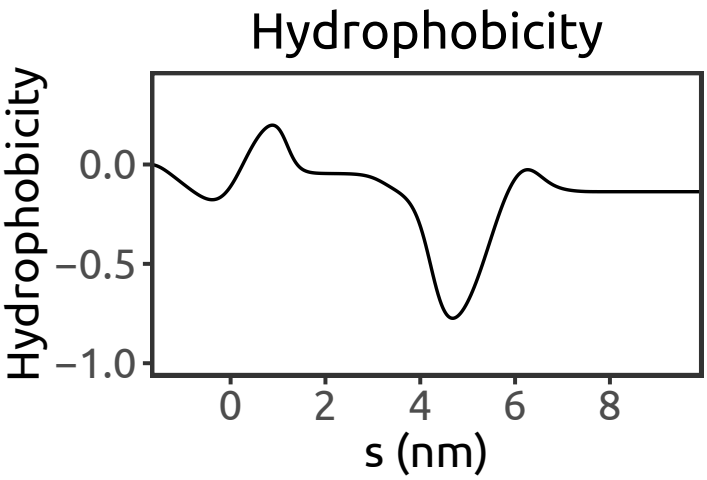
P2X4 (PDB ID: 3I5D)

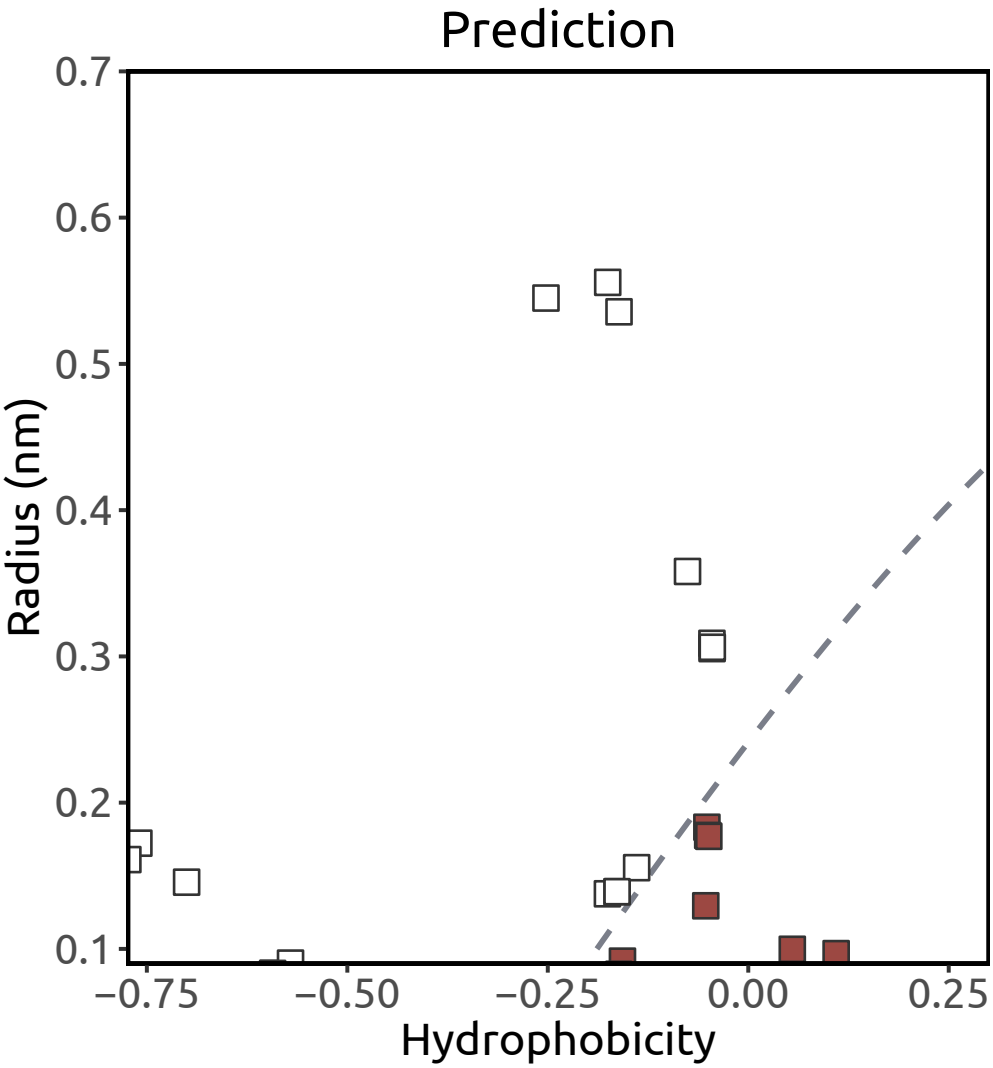
Danio rerio

X–ray (3.46 Å)

Kawate et al., 2009







Heuristic score:

0.8 (n = 12)

Simulation result:

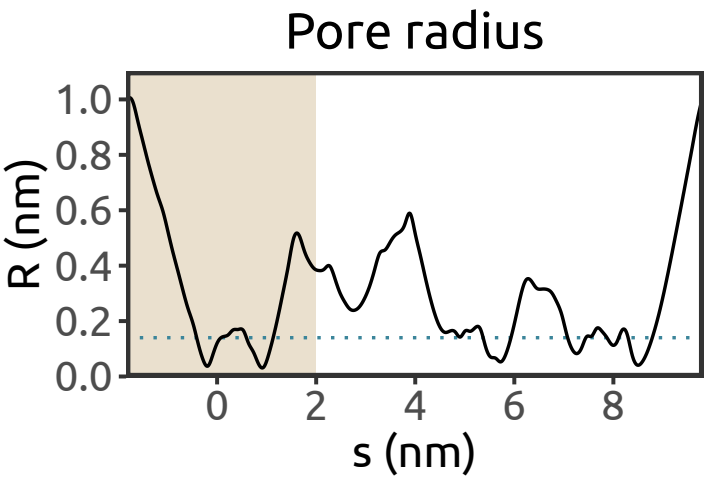
barrier to water

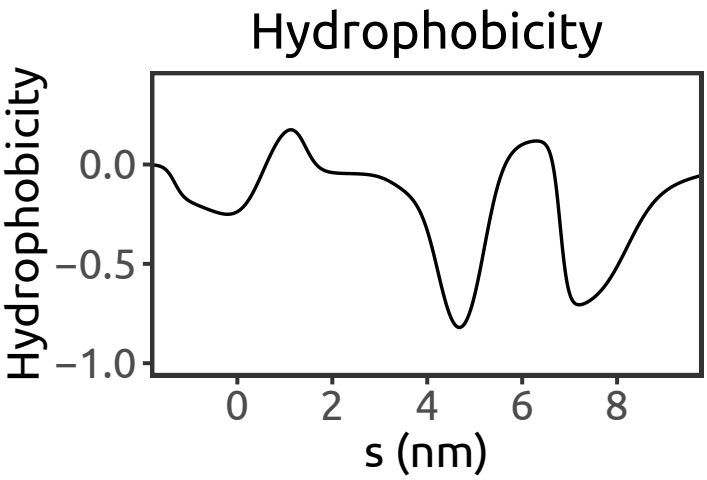
P2X4 (PDB ID: 4DW0)

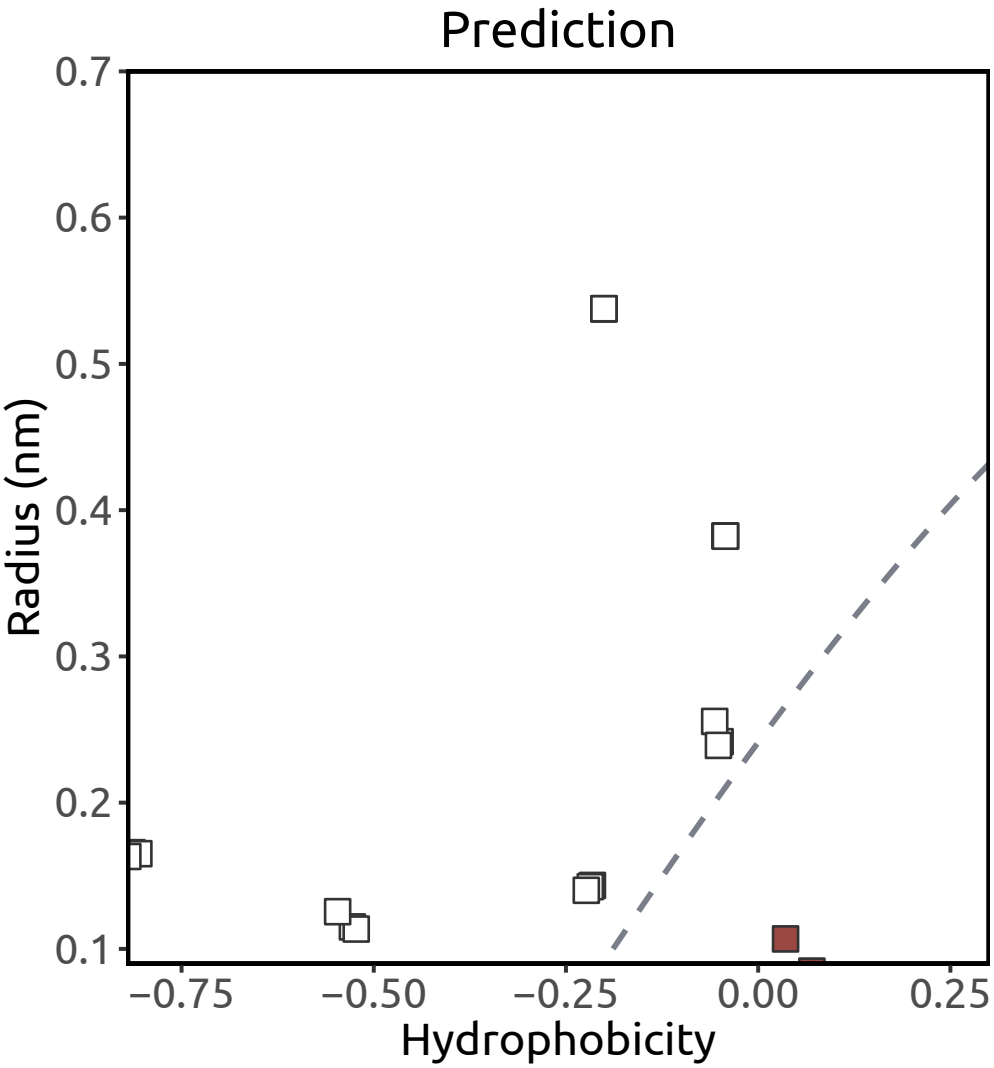
Danio rerio

X–ray (2.9 Å)

Hattori & Gouaux, 2012







Heuristic score:

0.92 (n = 6)

Simulation result:

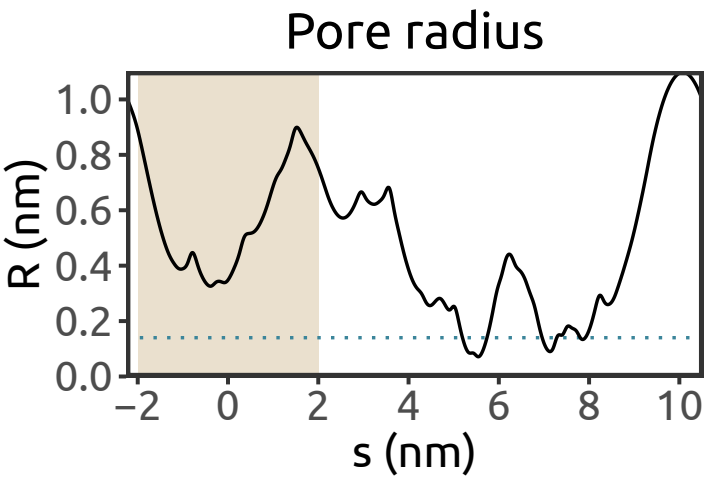
barrier to water

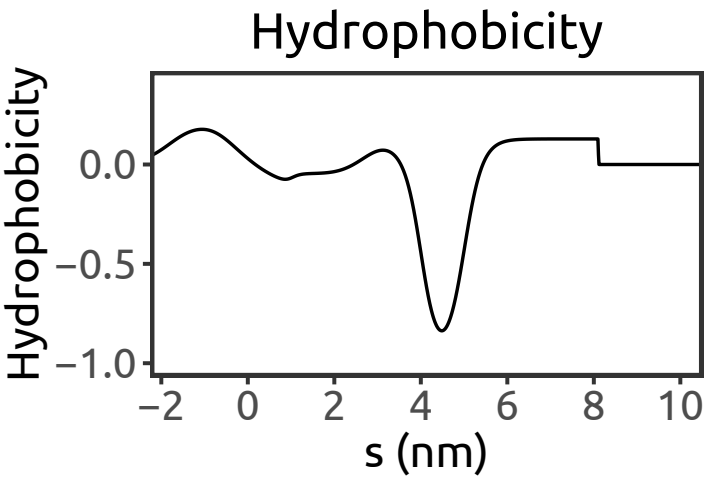
P2X4 (PDB ID: 4DW1)

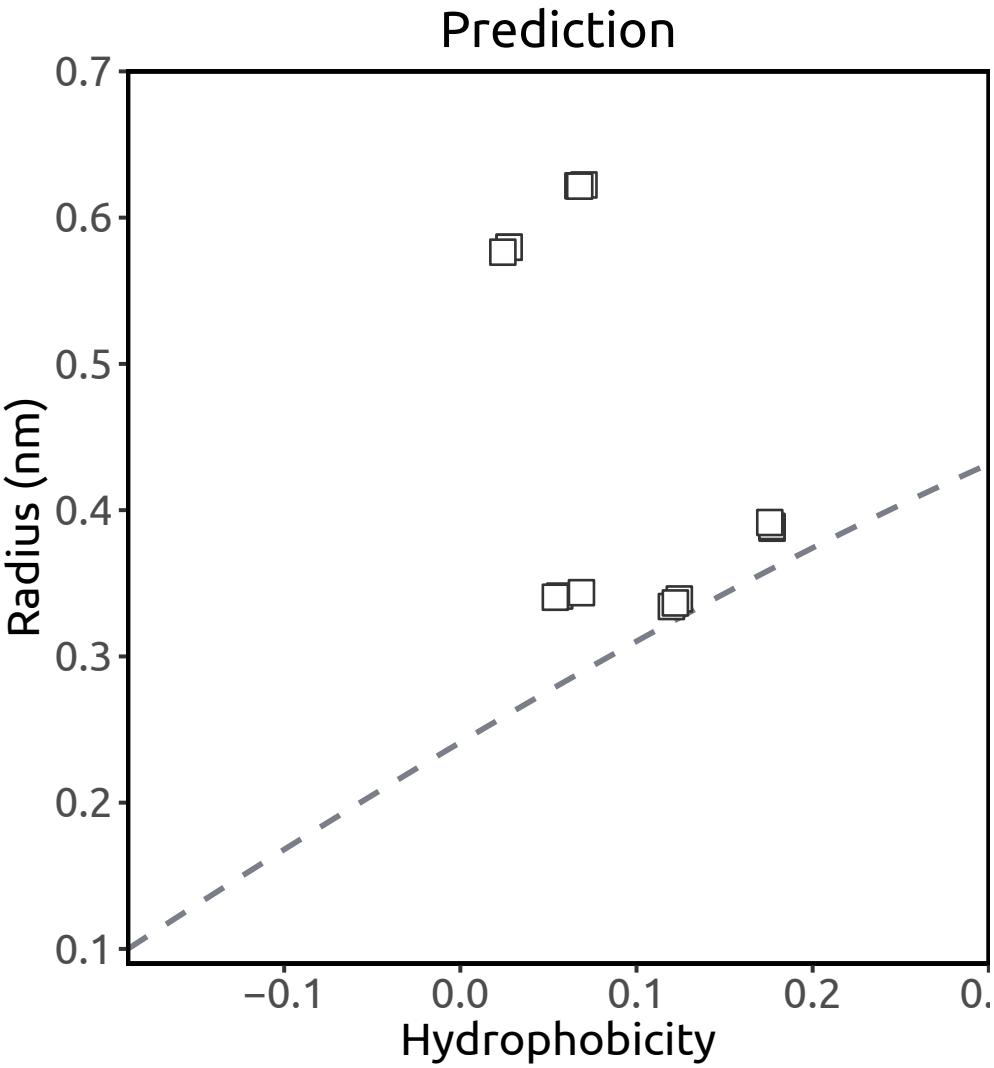
Danio rerio

X–ray (2.8 Å)

Hattori & Gouaux, 2012







Heuristic score:

0 (n = 0)

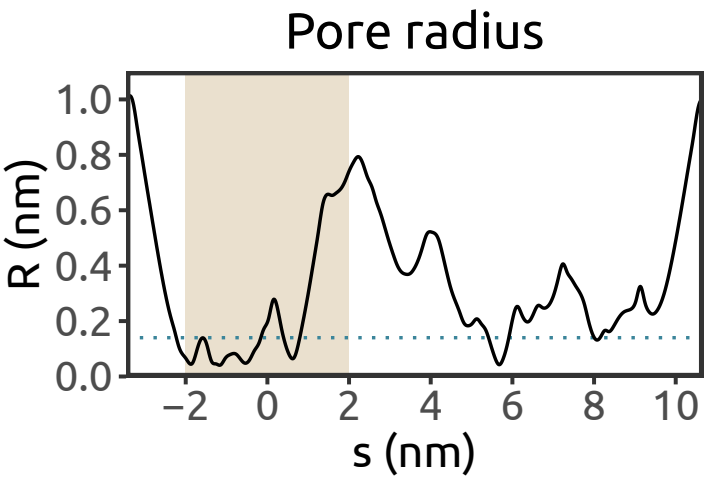
Simulation result:

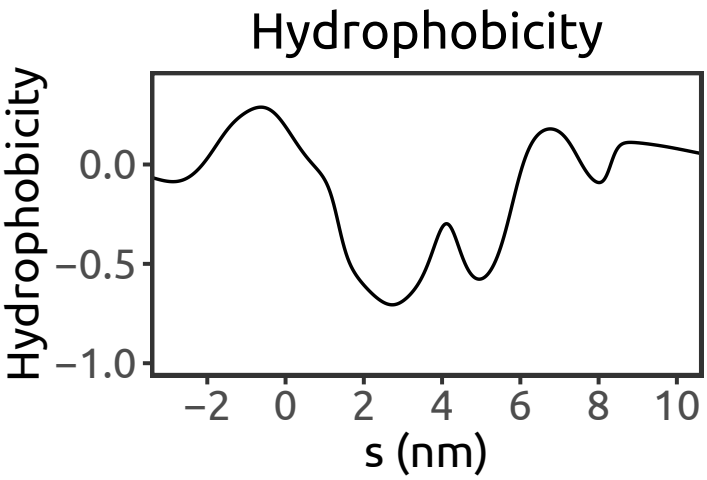
hydrated channel

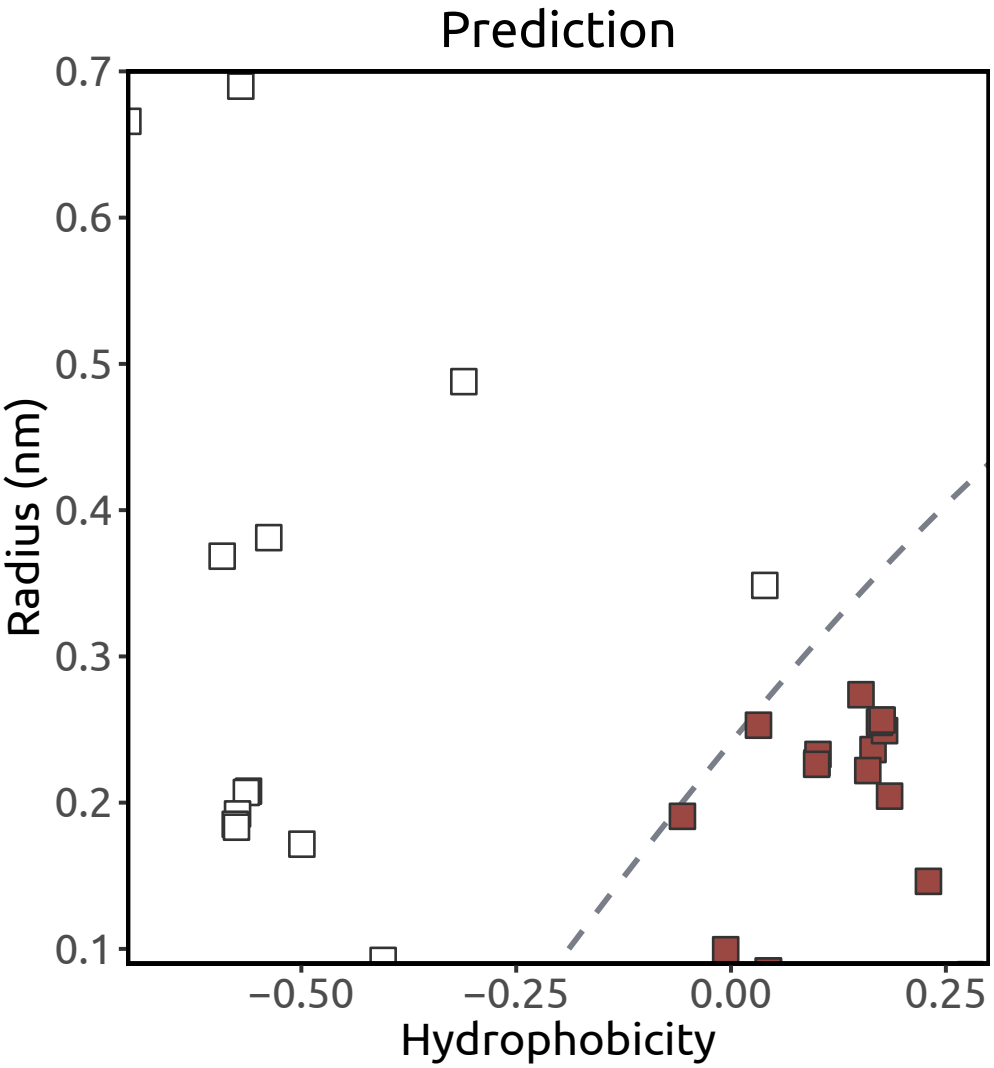
P2X7 (PDB ID: 5XW6)

Gallus gallus
X–ray (3.1 Å)

Kasuya et al., 2017







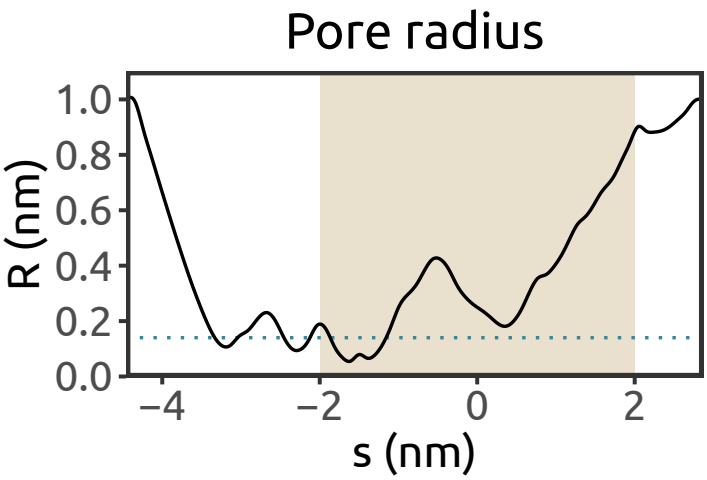
Heuristic score:
3.62 (n = 25)

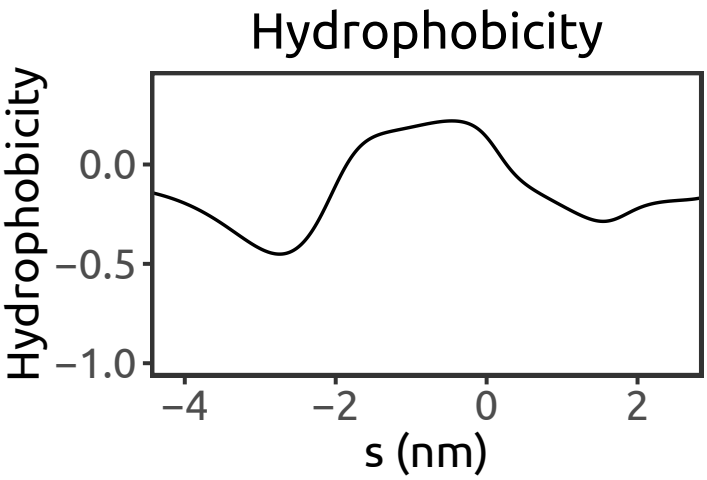
Simulation result:
barrier to water

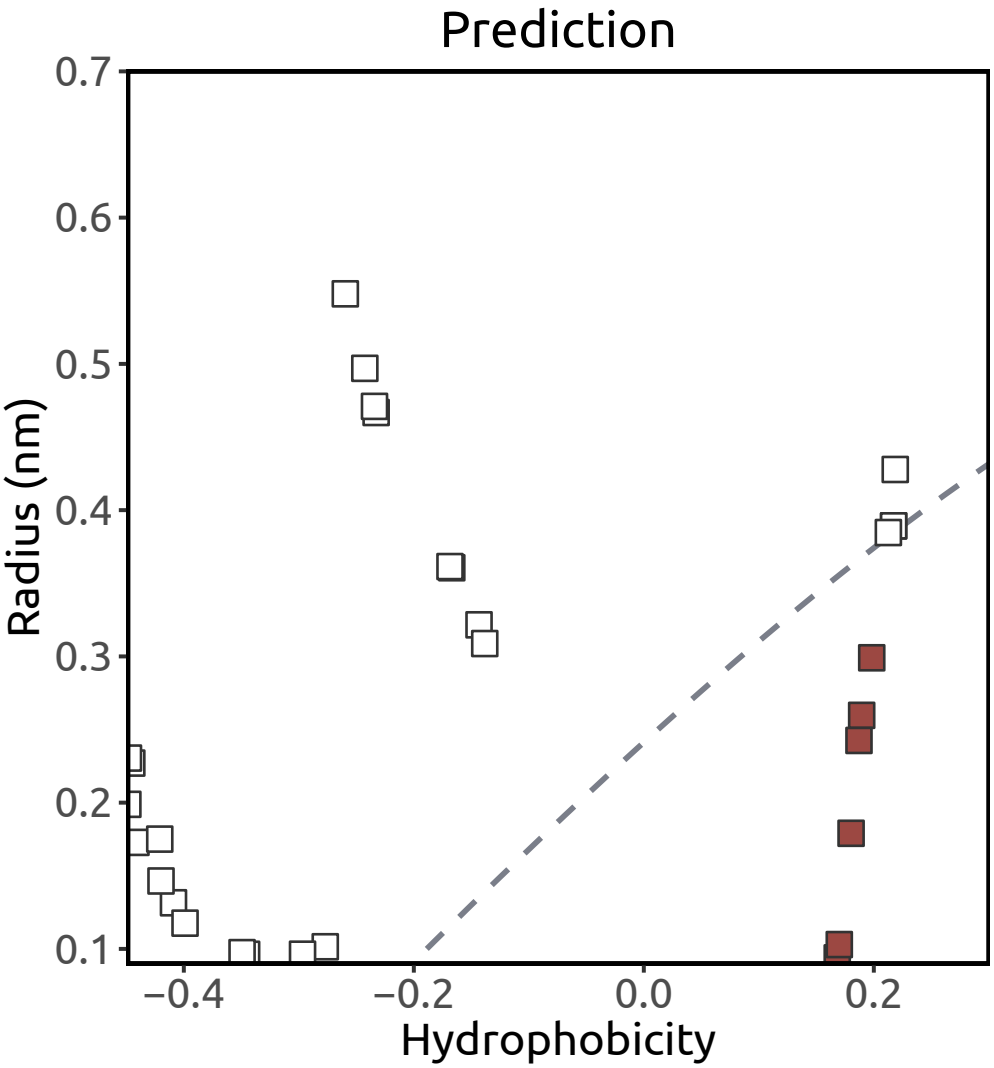
NOMPC (PDB ID: 5VKQ)

Drosophila melanogaster
cryo–EM (3.55 Å)

Jin et al., 2017







Heuristic score:
2.14 (n = 12)

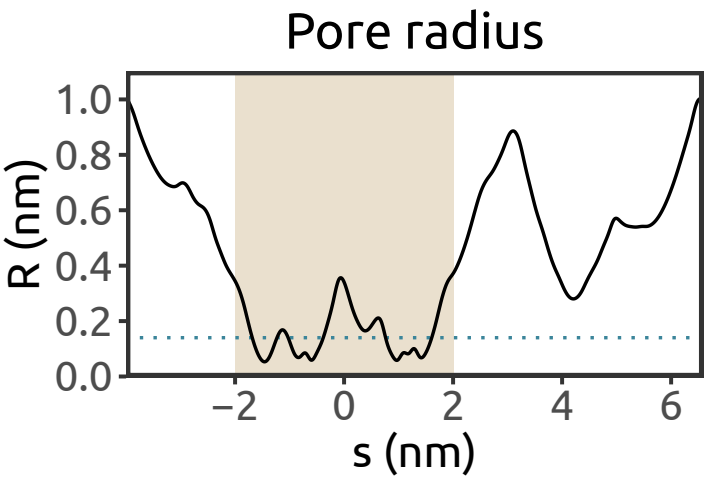
Simulation result:
barrier to water

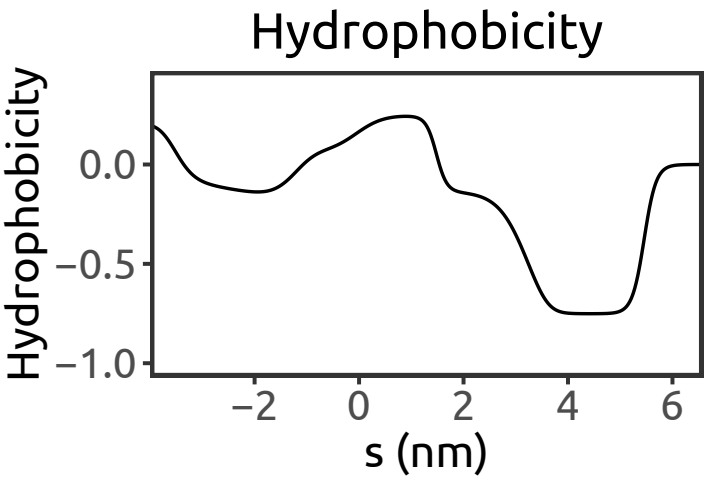
PKD2 (PDB ID: 5K47)

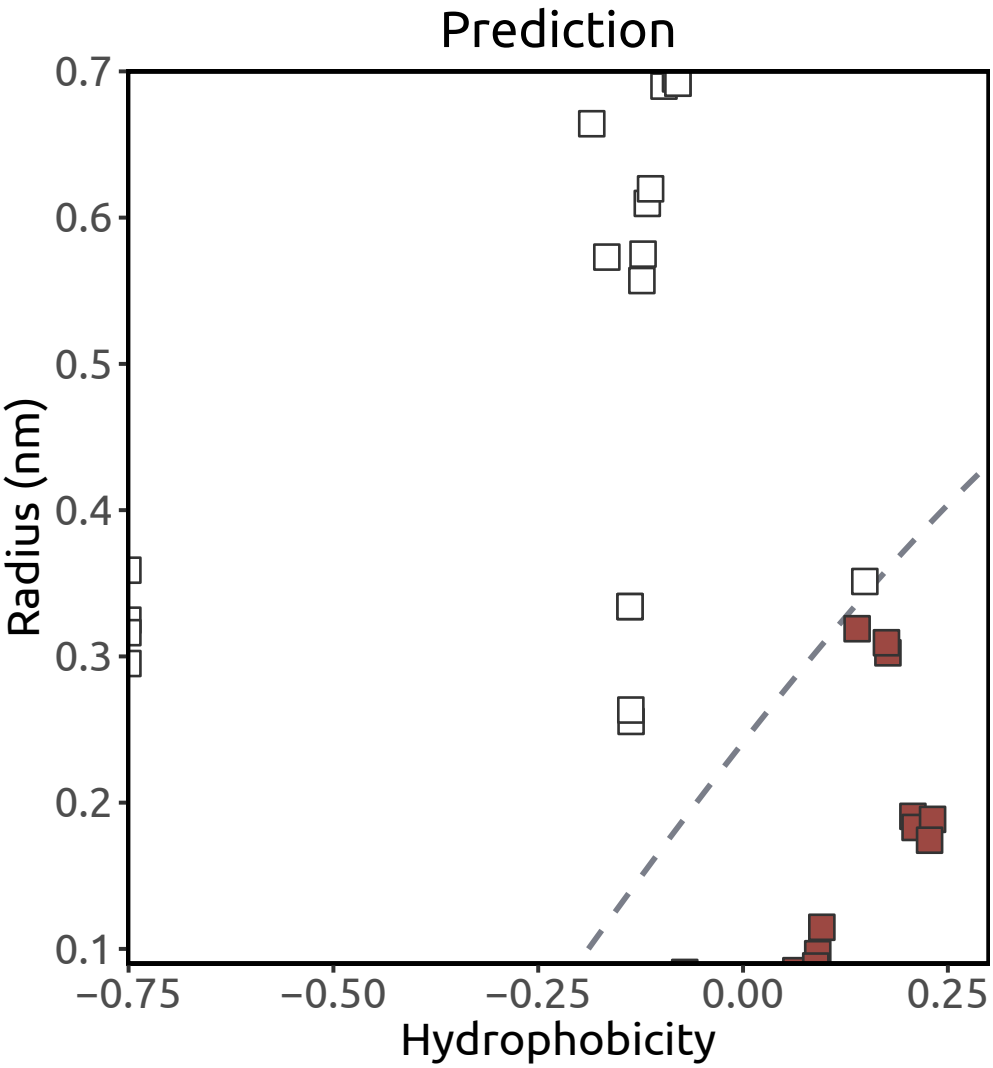
Homo sapiens

cryo–EM (4.22 Å)

Grieben et al., 2017







Heuristic score:

2.49 (n = 19)

Simulation result:

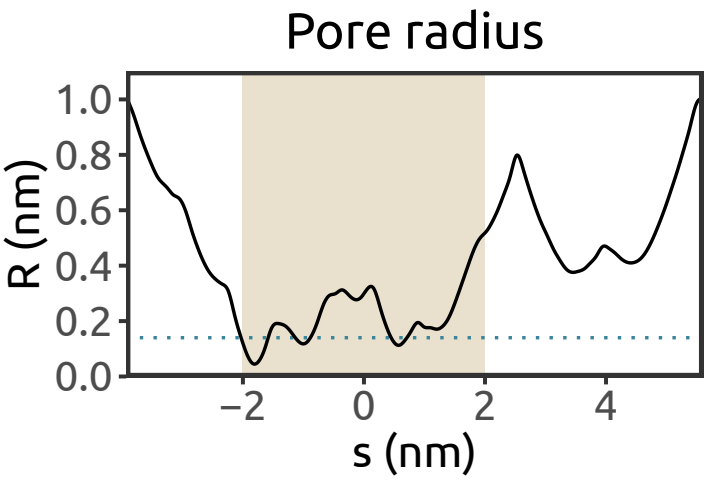
barrier to water

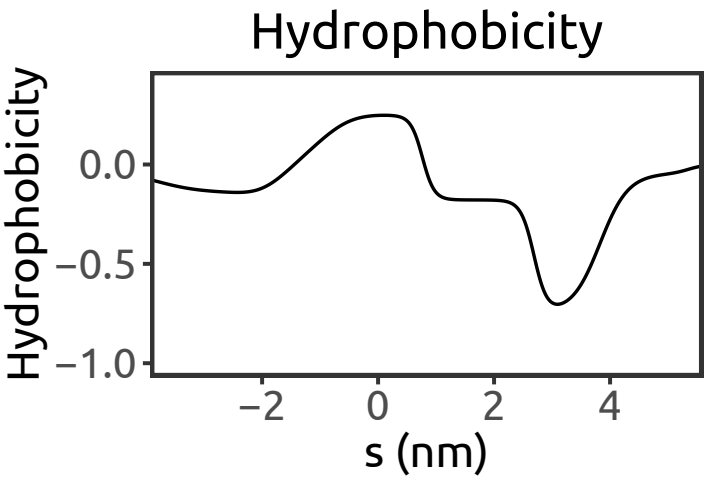
PKD2 (PDB ID: 5MKE)

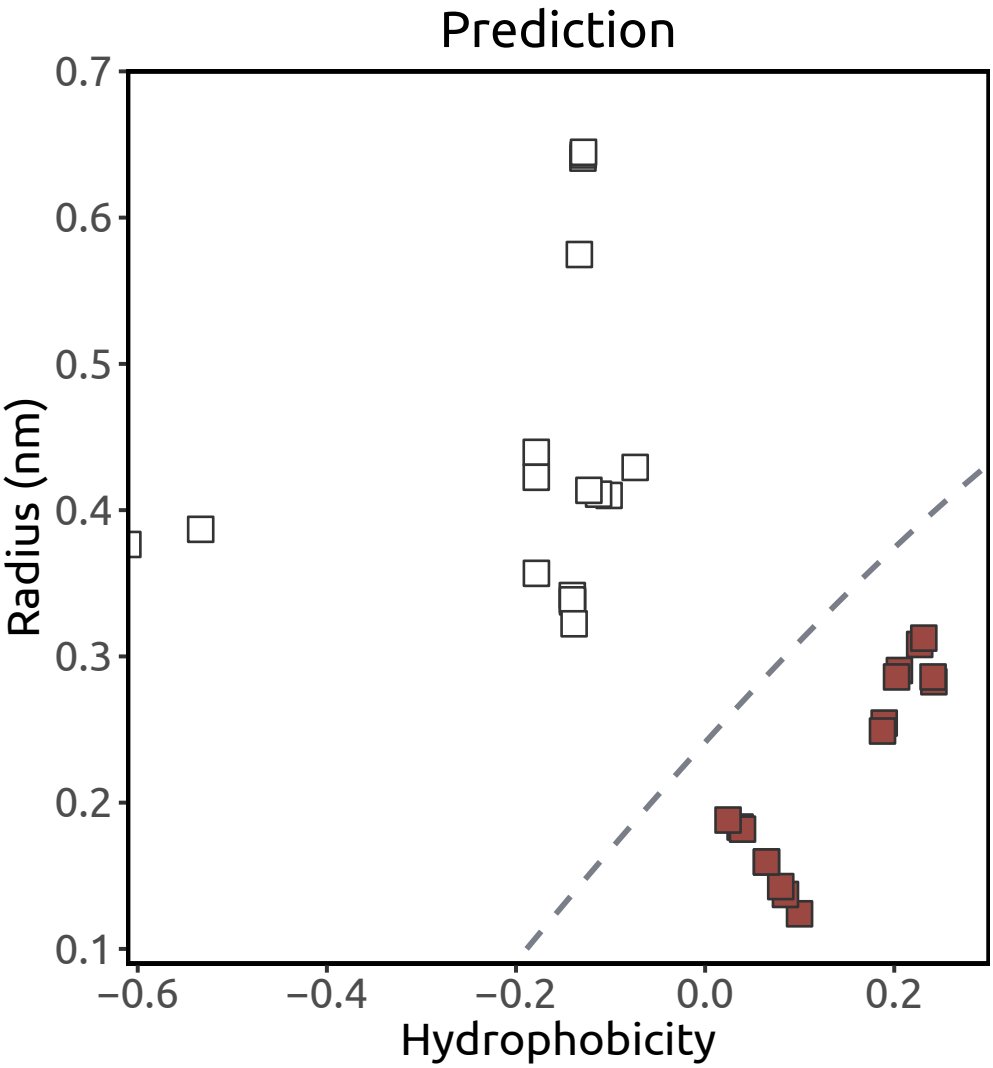
Homo sapiens

cryo–EM (4.3 Å)

Wilkes et al., 2017







Heuristic score:

1.91 (n = 20)

Simulation result:

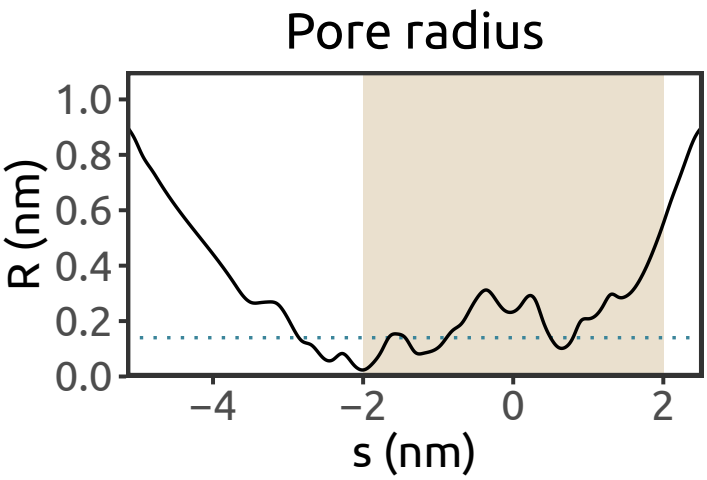
hydrated channel

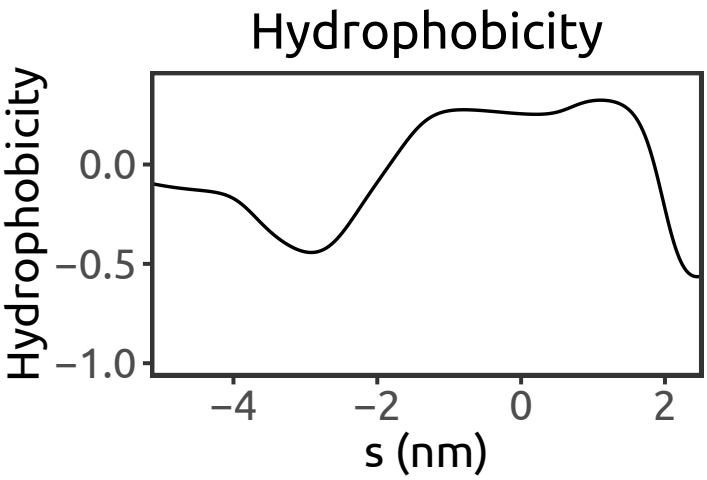
PKD2 (PDB ID: 5MKF)

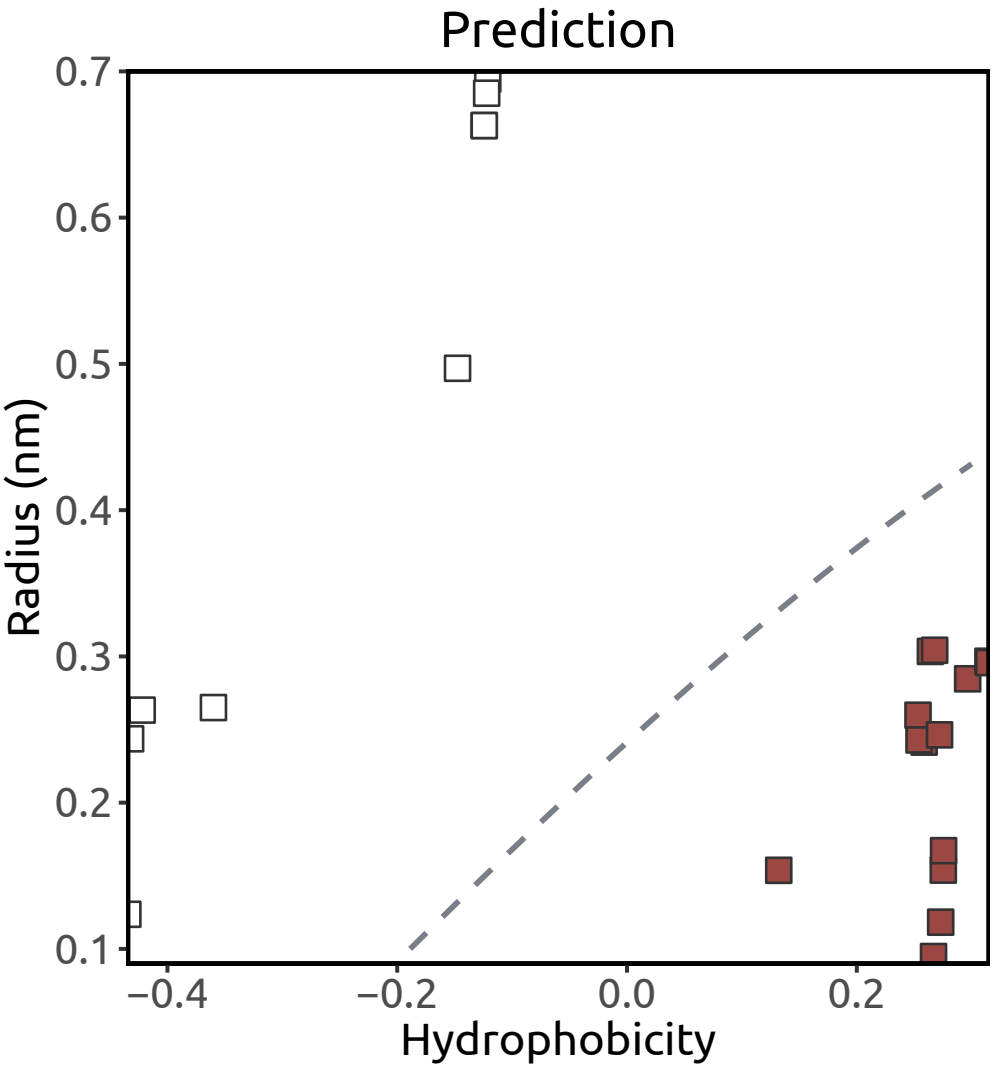
Homo sapiens

cryo–EM (4.2 Å)

Wilkes et al., 2017







Heuristic score:

2.5 (n = 16)

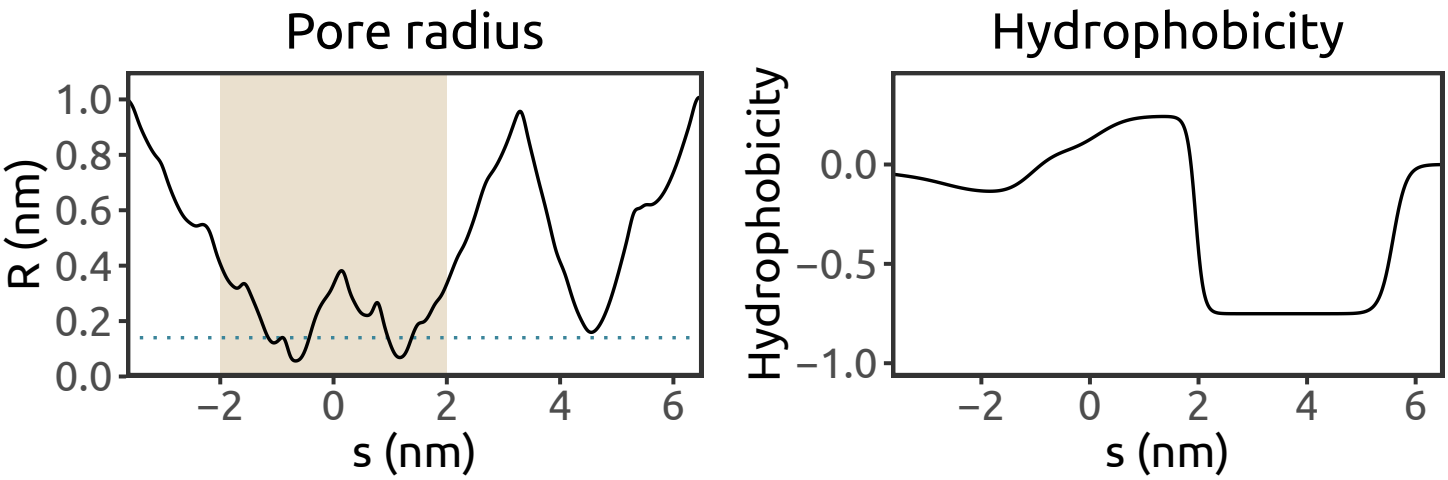
Simulation result:

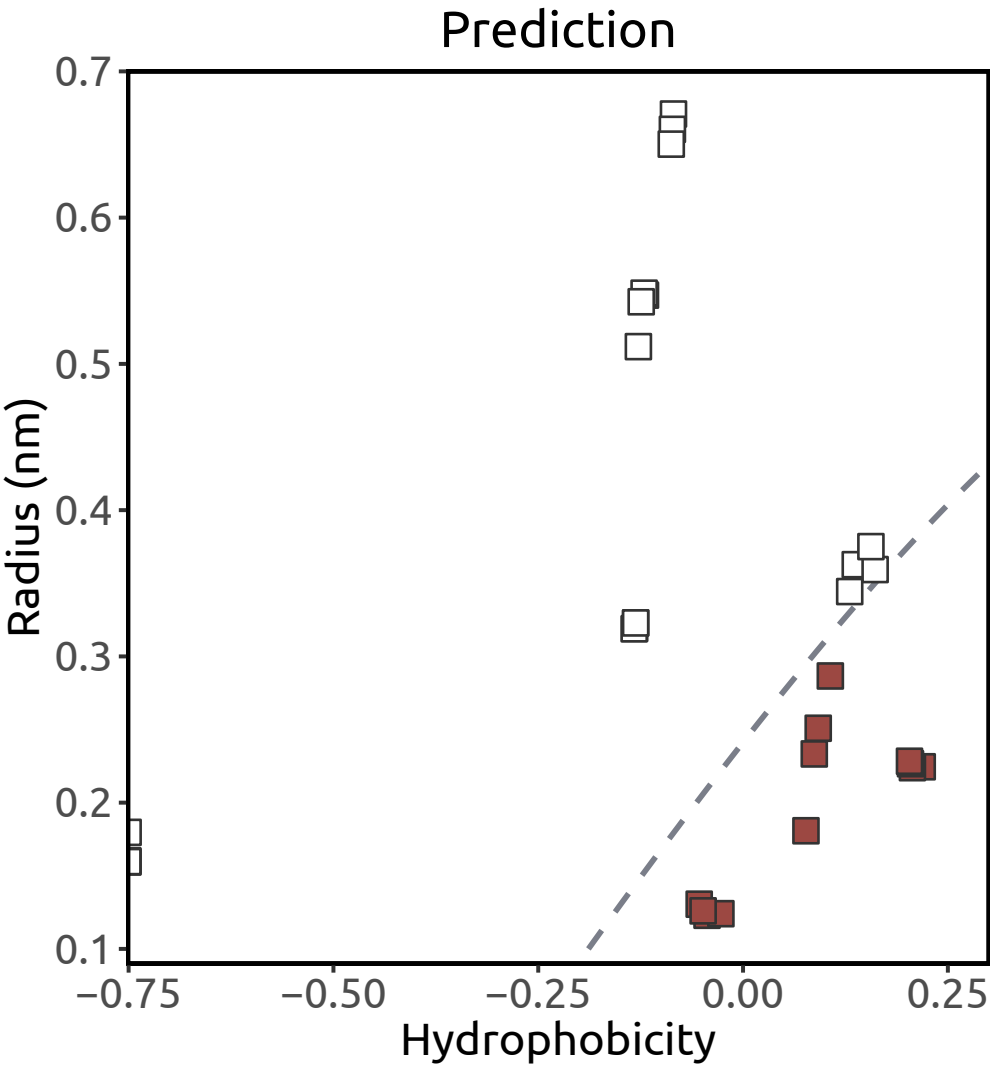
barrier to water

PKD2 (PDB ID: 5T4D)

Homo sapiens
cryo–EM (3 Å)

Shen et al., 2016





Heuristic score:
1.71 (n = 16)

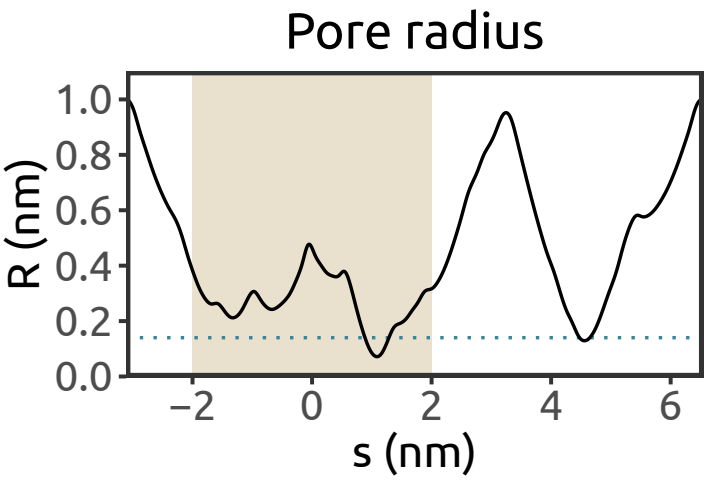
Simulation result:
barrier to water

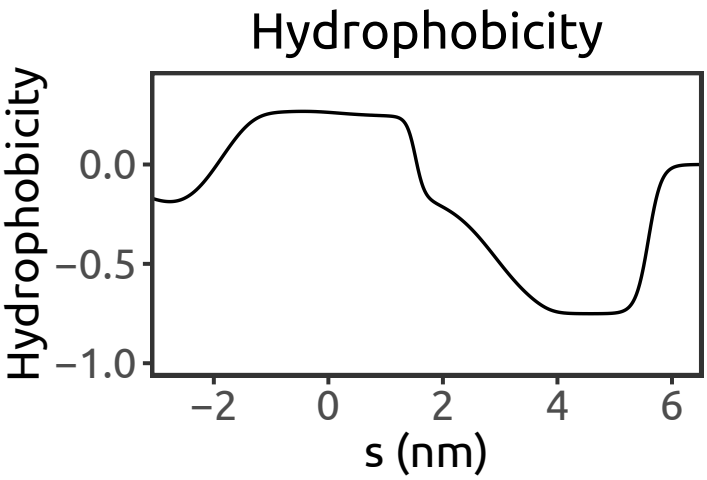
PKD2 (PDB ID: 6D1W)

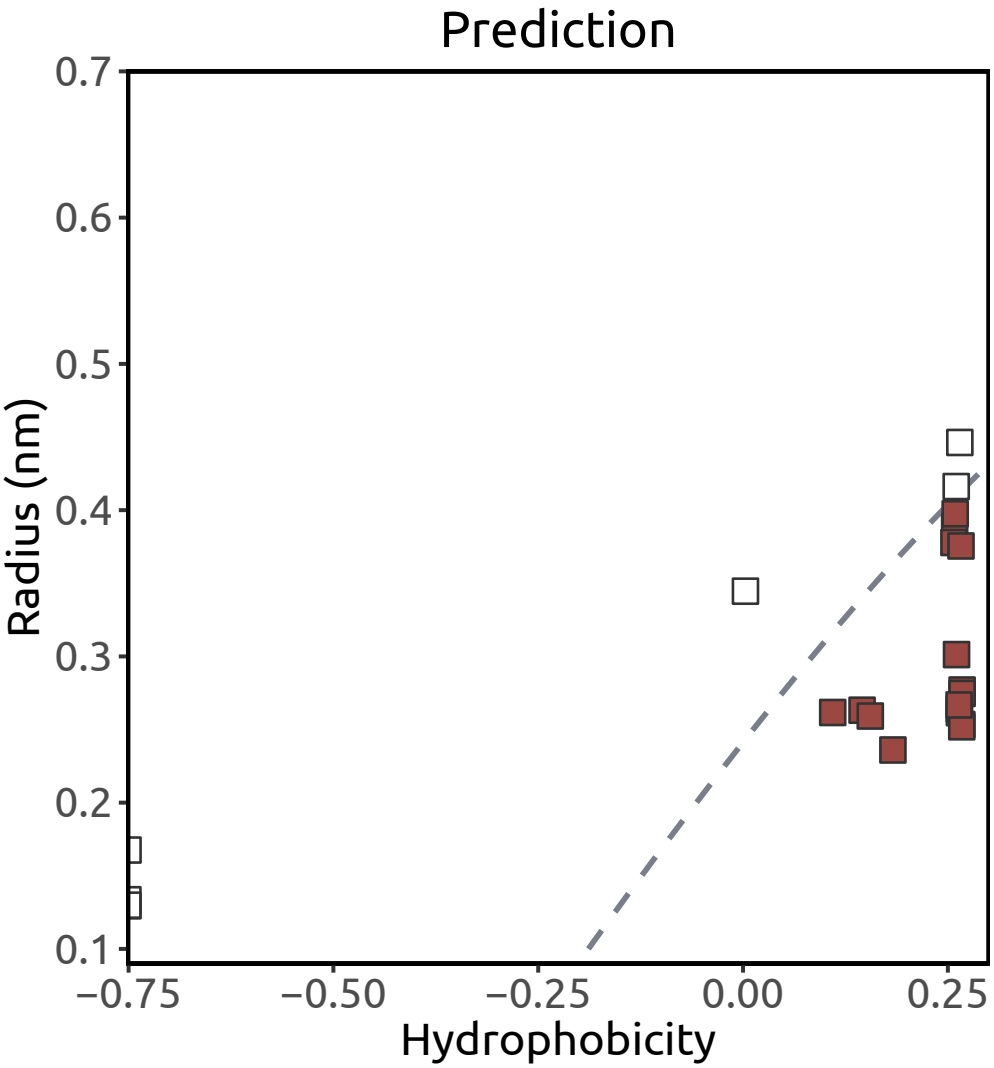
Homo sapiens

cryo–EM (3.54 Å)

Zheng et al., 2018







Heuristic score:

1.37 (n = 16)

Simulation result:

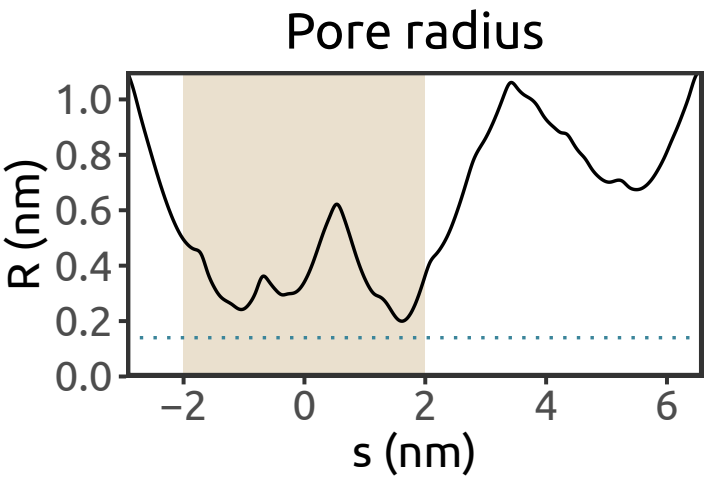
barrier to water

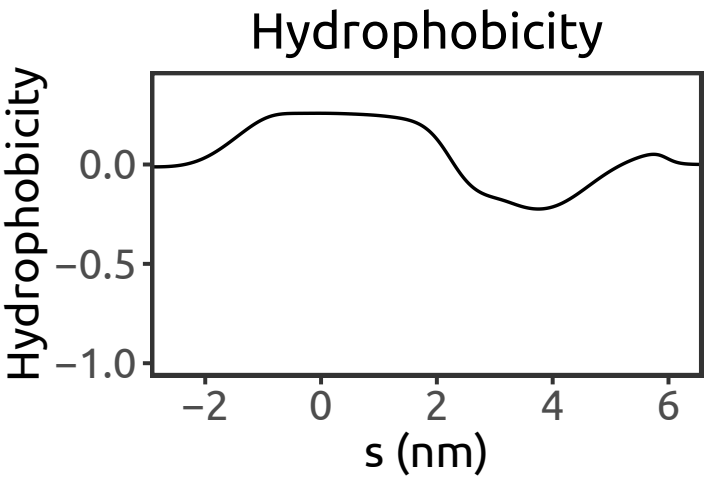
PKD2L1 (PDB ID: 5Z1W)

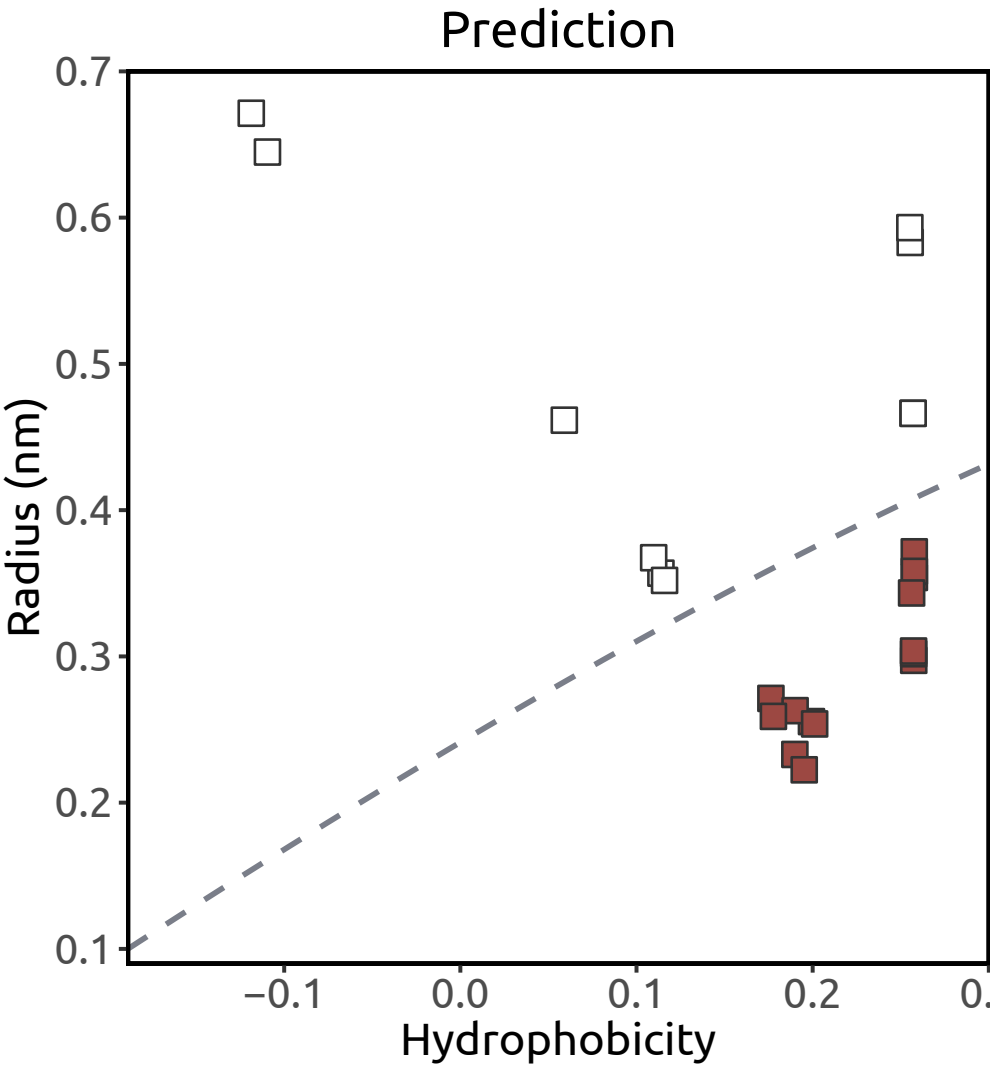
Mus musculus

cryo–EM (3.38 Å)

Su et al., 2018







Heuristic score:

1.15 (n = 14)

Simulation result:

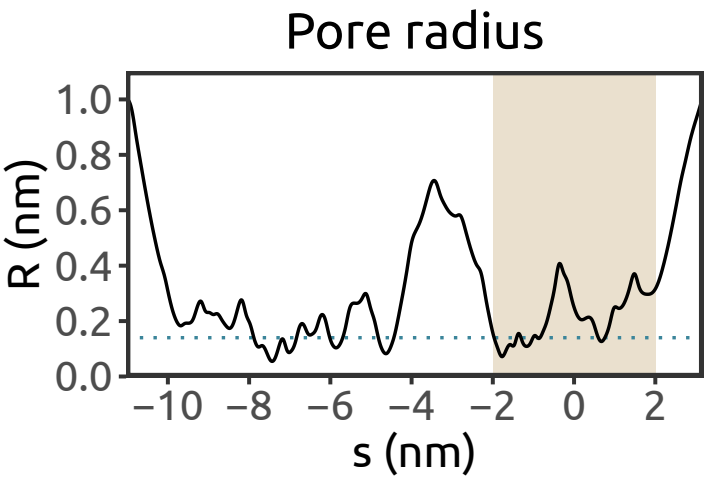
barrier to water

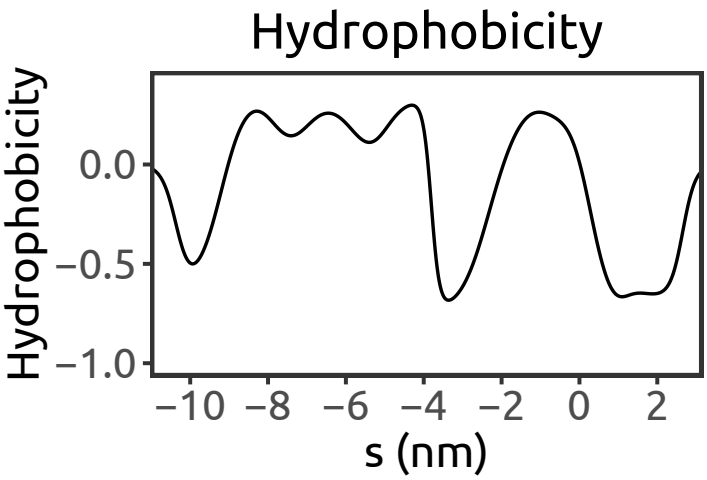
TRPA1 (PDB ID: 3J9P)

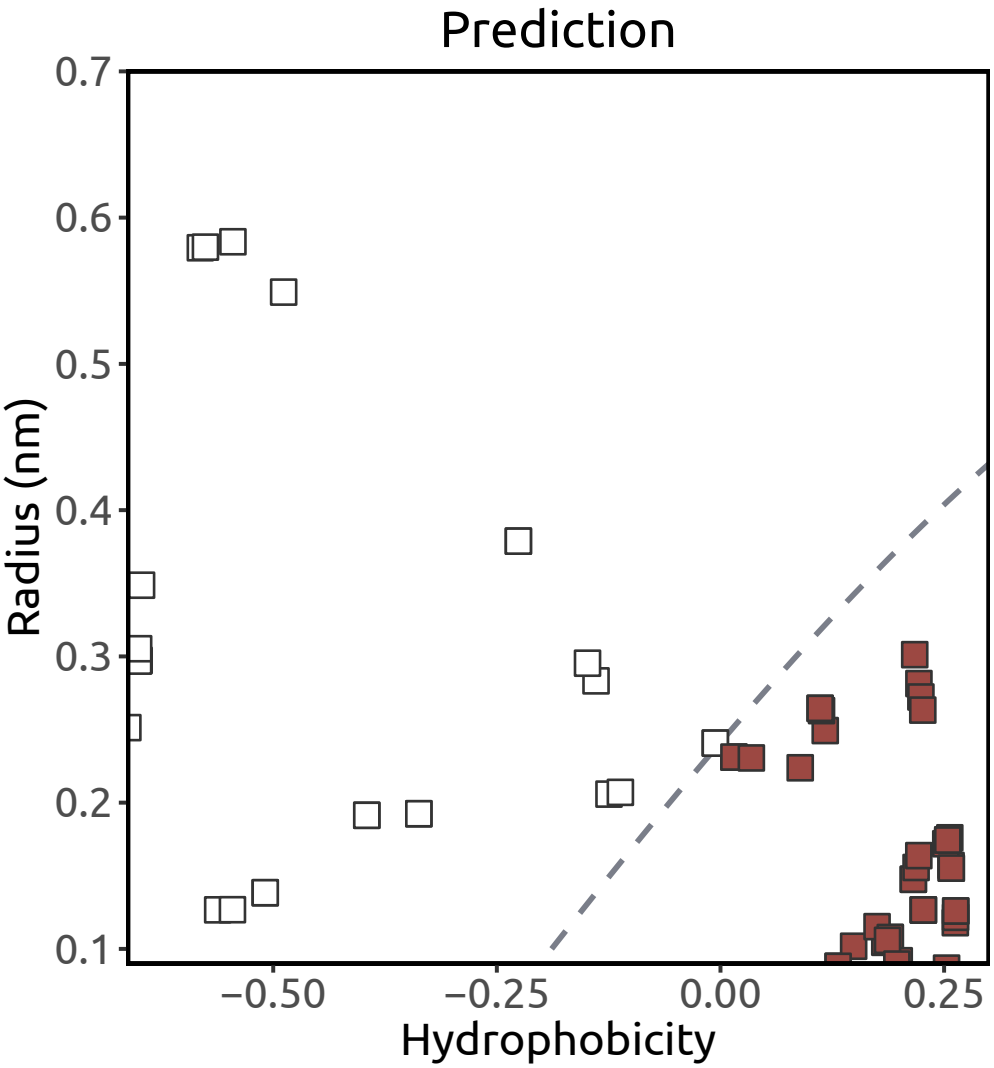
Homo sapiens

cryo–EM (4.24 Å)

Paulsen et al., 2015







Heuristic score:

8.6 (n = 48)

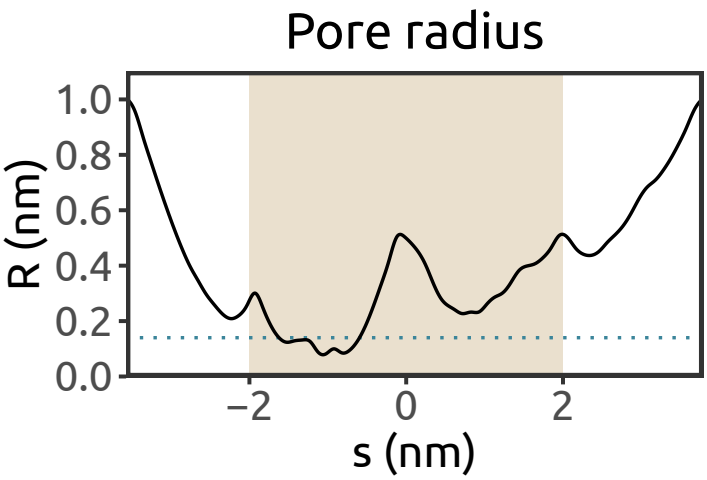
Simulation result:

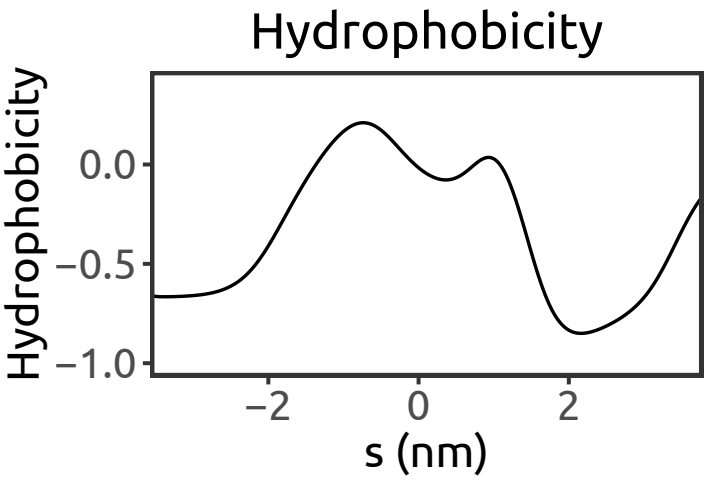
barrier to water

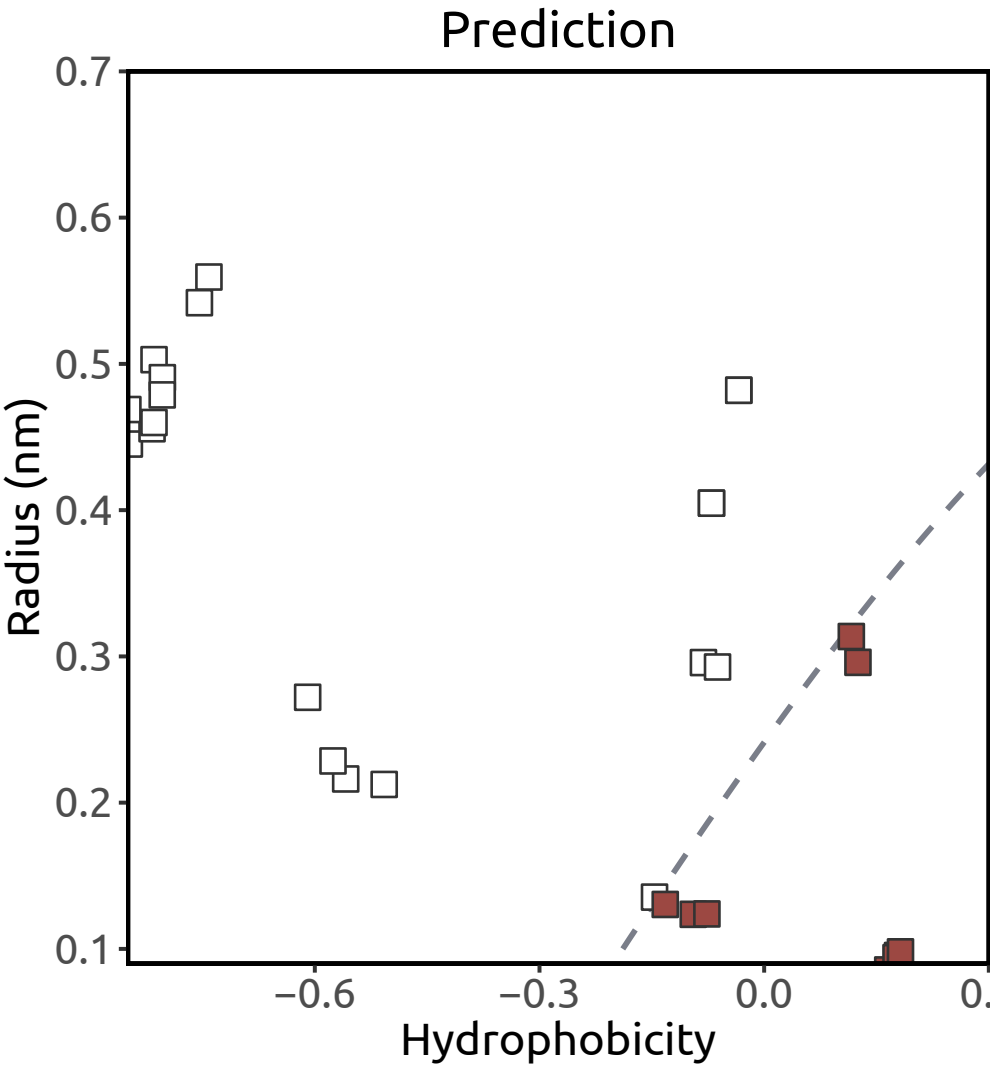
TRPM2 (PDB ID: 6CO7)

Nematostella vectensis
cryo–EM (3.07 Å)

Zhang et al., 2018







Heuristic score:
1.02 (n = 9)

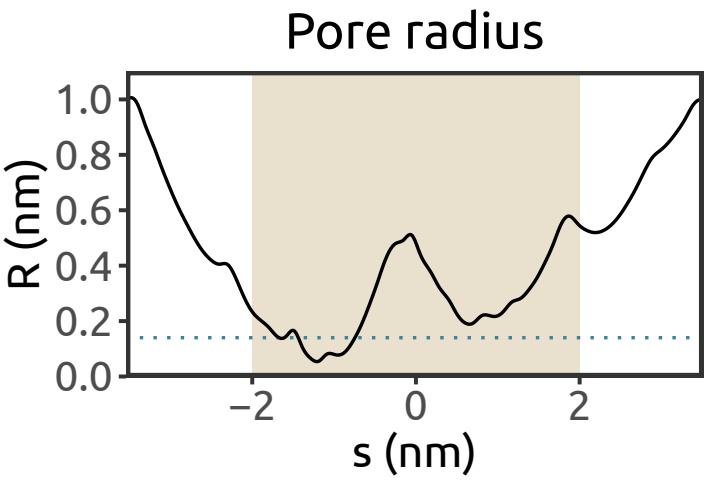
Simulation result:
barrier to water

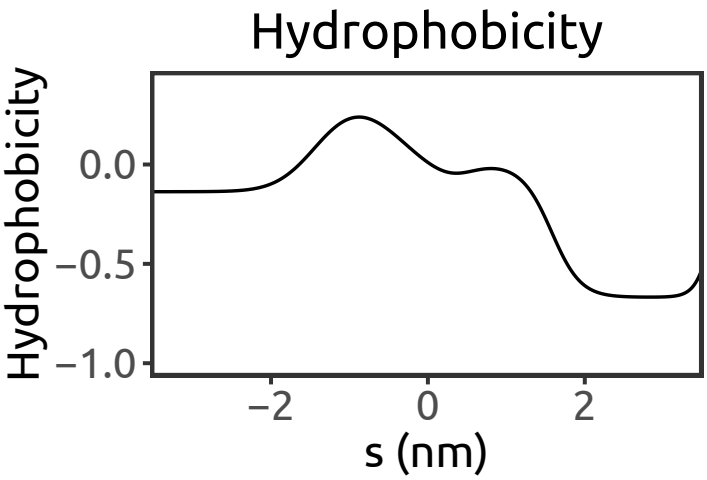
TRPM4 (PDB ID: 6BCL)

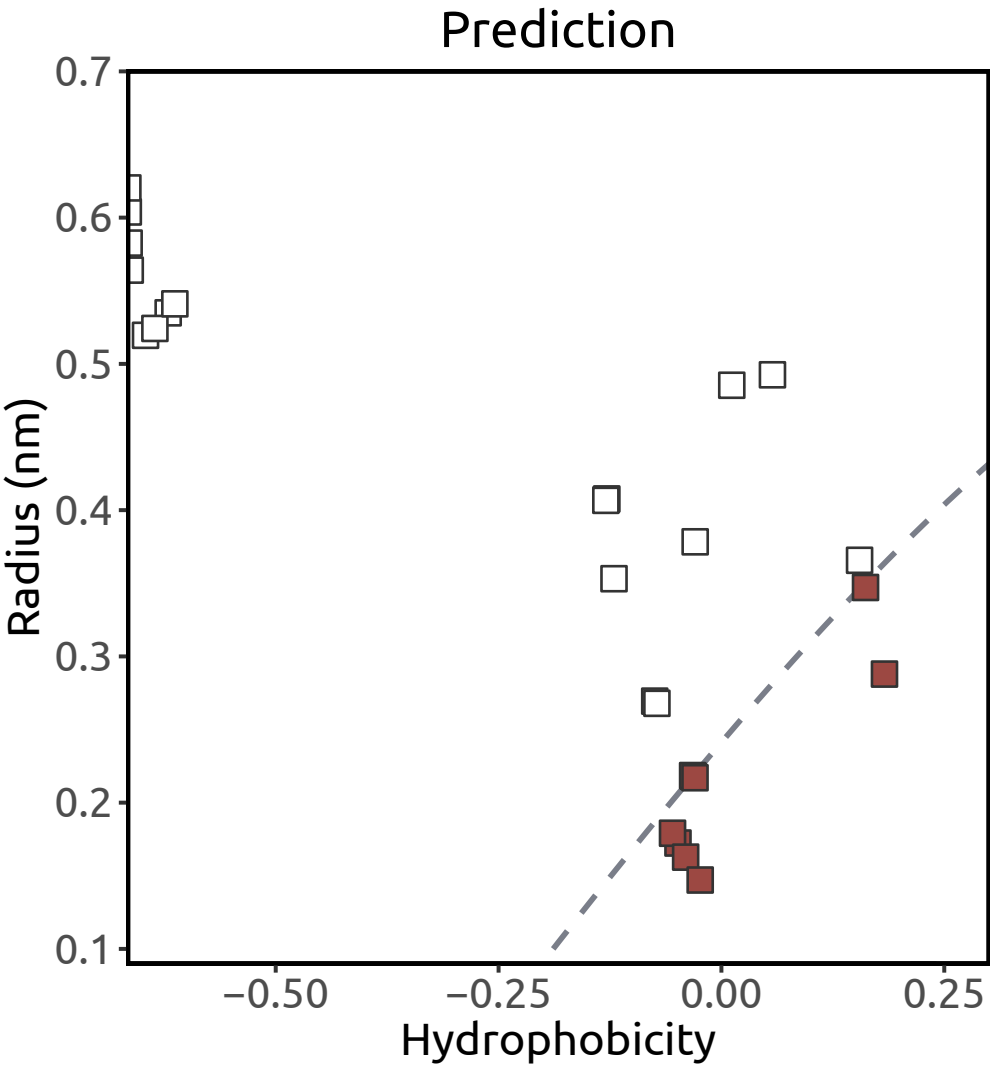
Mus musculus

cryo–EM (3.54 Å)

Guo et al., 2017







Heuristic score:

1.26 (n = 13)

Simulation result:

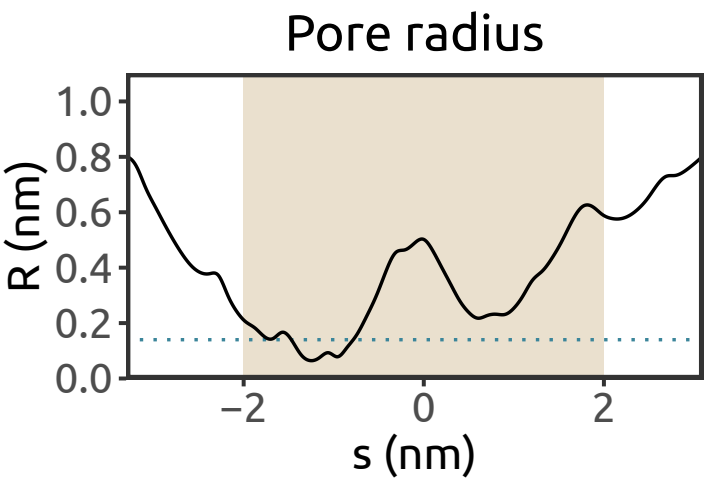
barrier to water

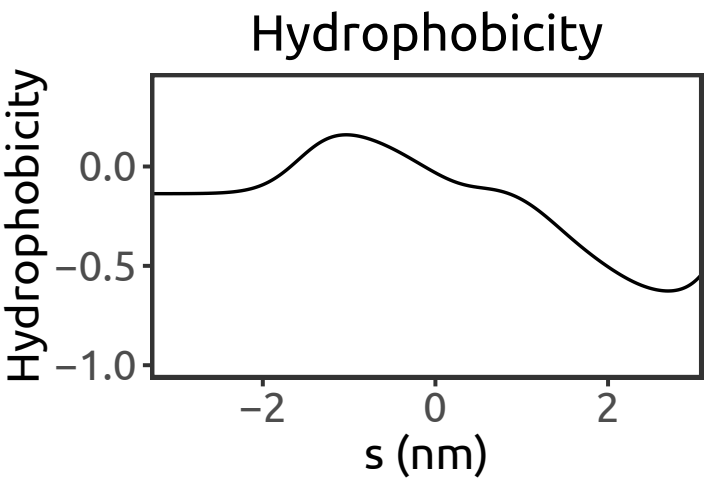
TRPM4 (PDB ID: 6BCQ)

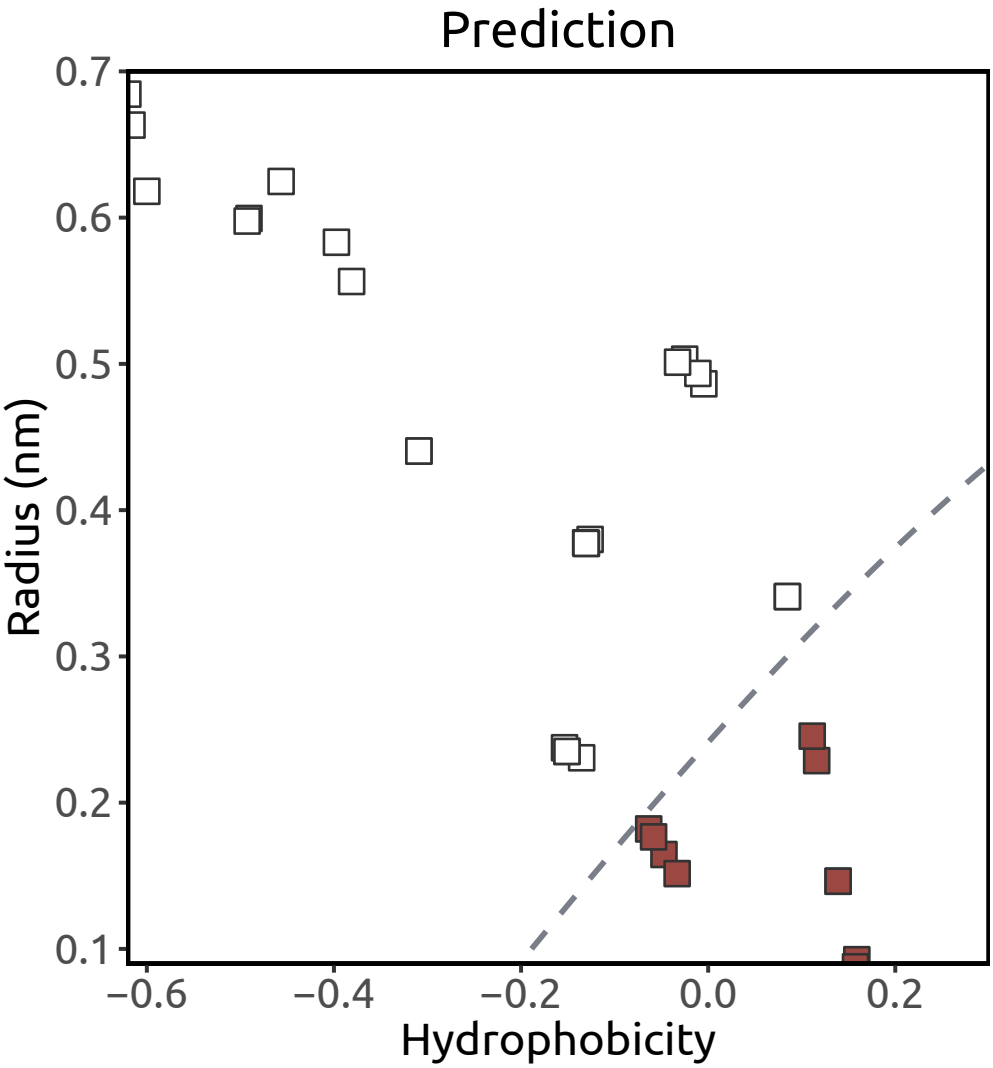
Mus musculus

cryo–EM (3.25 Å)

Guo et al., 2017







Heuristic score:

1.45 (n = 12)

Simulation result:

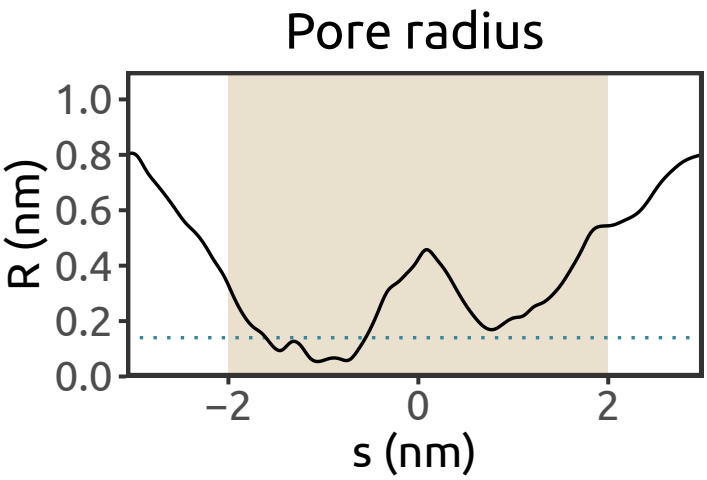
barrier to water

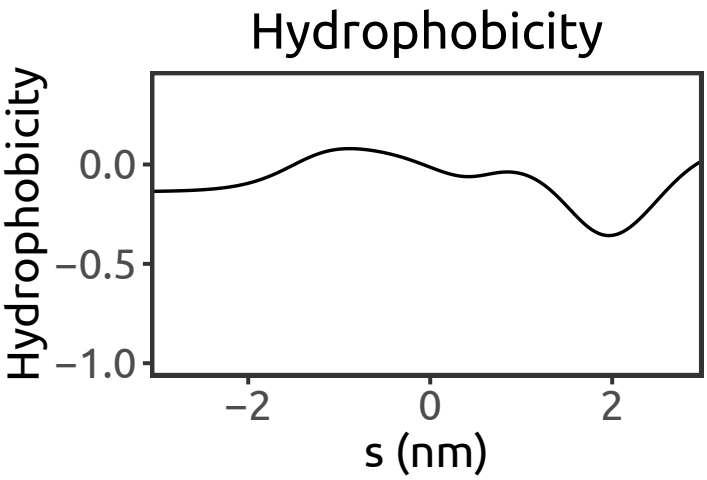
TRPM4 (PDB ID: 6BQR)

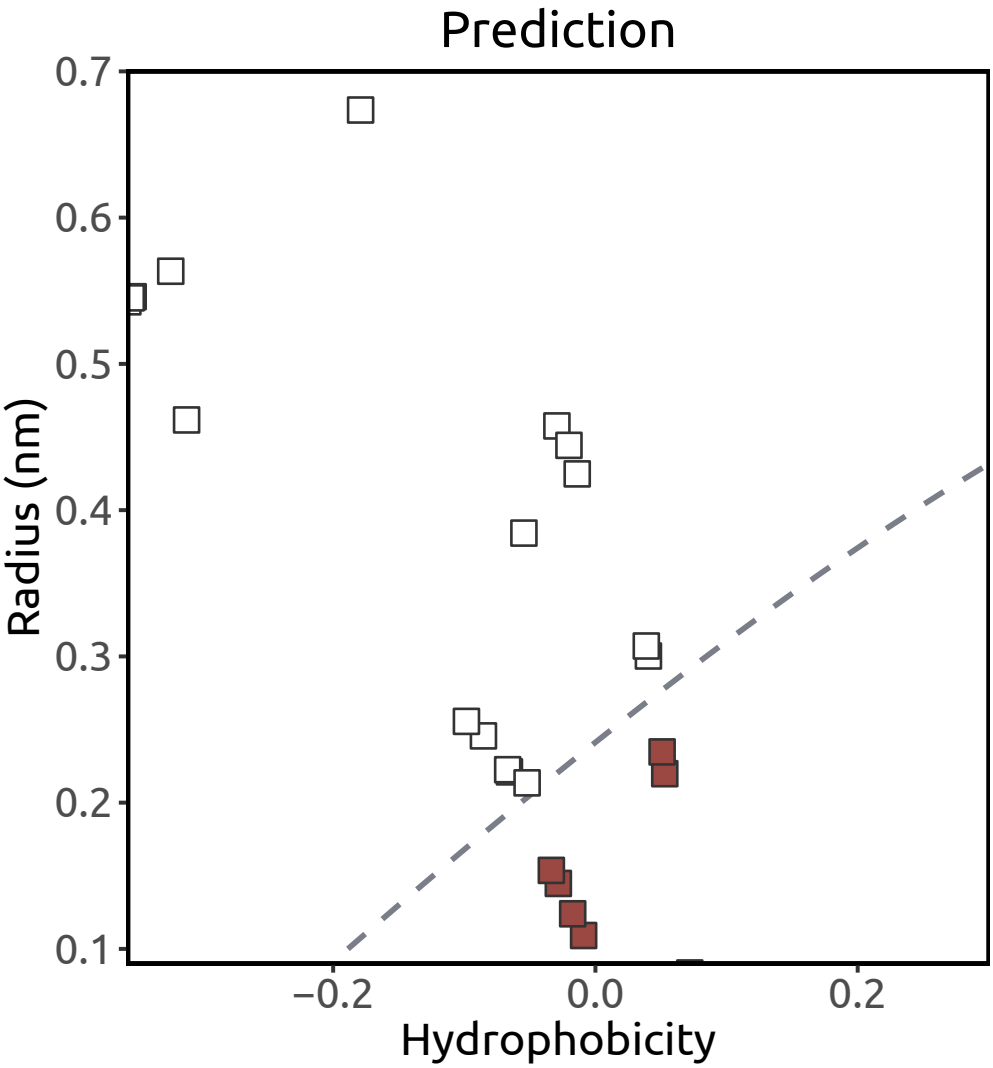
Homo sapiens

cryo–EM (3.2 Å)

Autzen et al., 2018







Heuristic score:

1.87 (n = 14)

Simulation result:

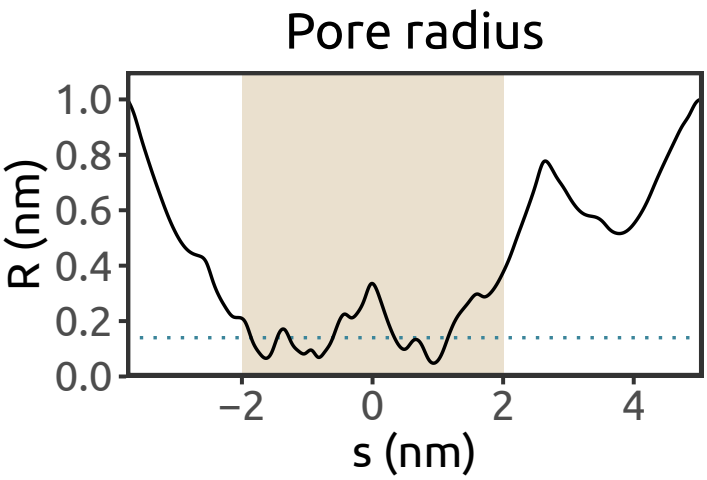
barrier to water

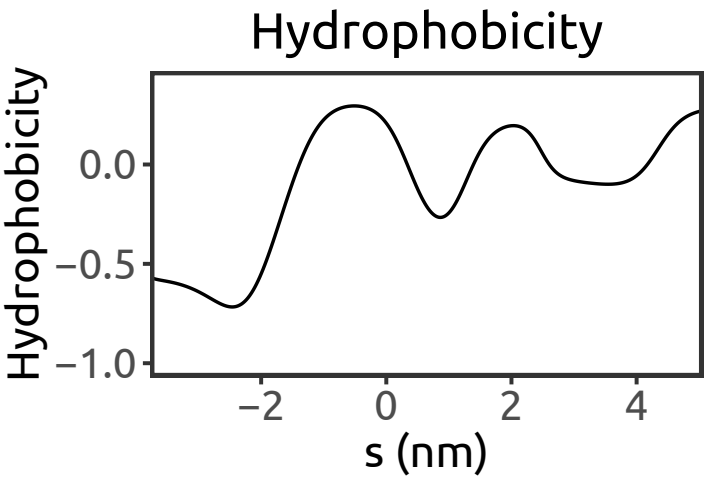
TRPML1 (PDB ID: 5WJ5)

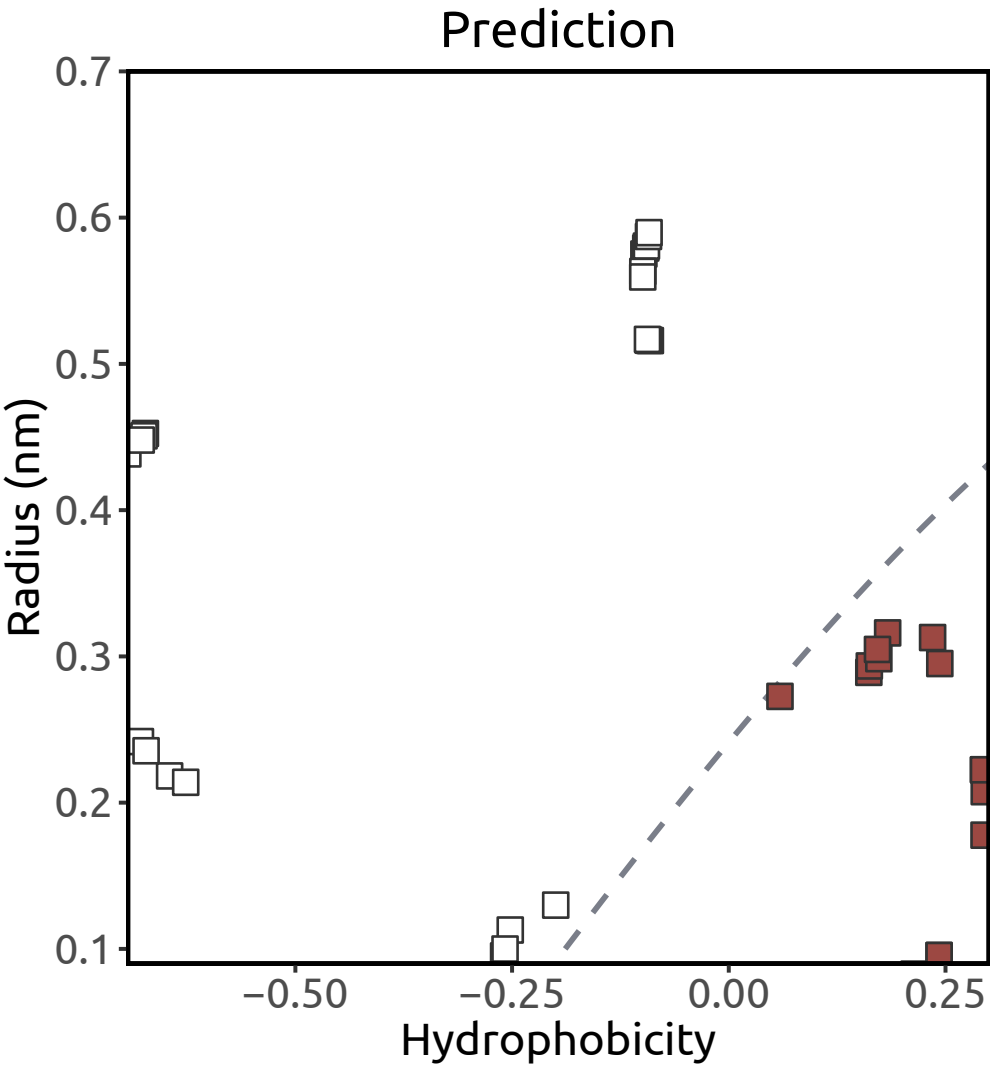
Homo sapiens

cryo–EM (3.72 Å)

Schmiege et al., 2017







Heuristic score:

2.22 (n = 17)

Simulation result:

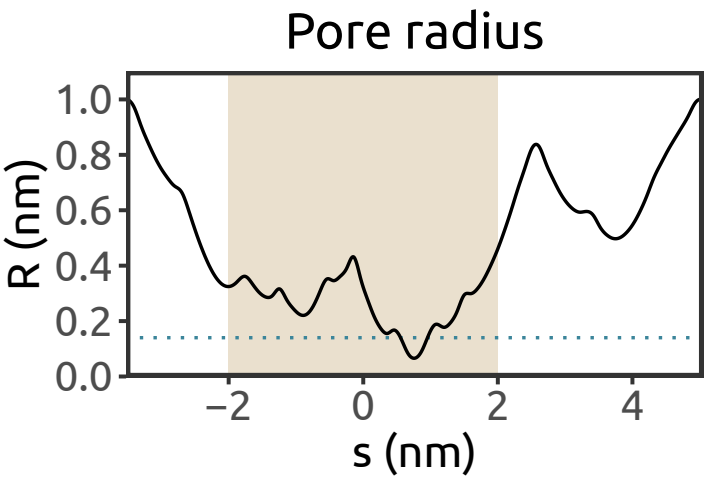
barrier to water

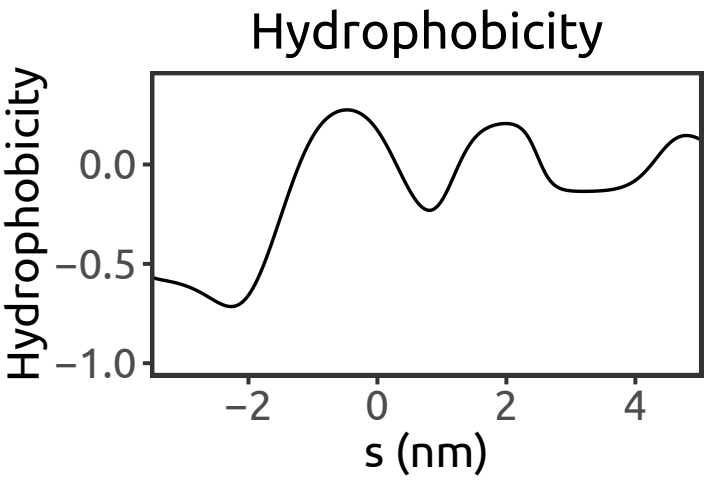
TRPML1 (PDB ID: 5WJ9)

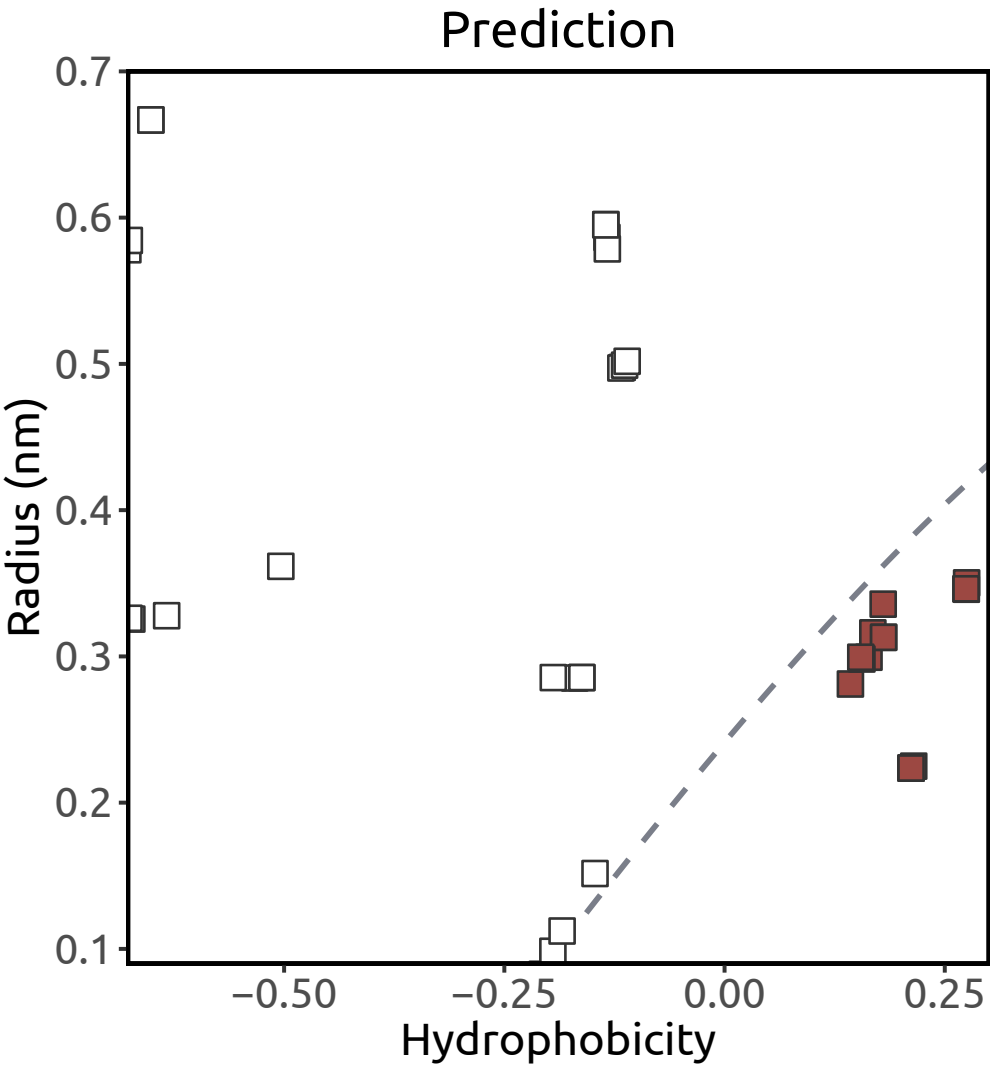
Homo sapiens

cryo–EM (3.49 Å)

Schmiege et al., 2017







Heuristic score:

1.09 (n = 16)

Simulation result:

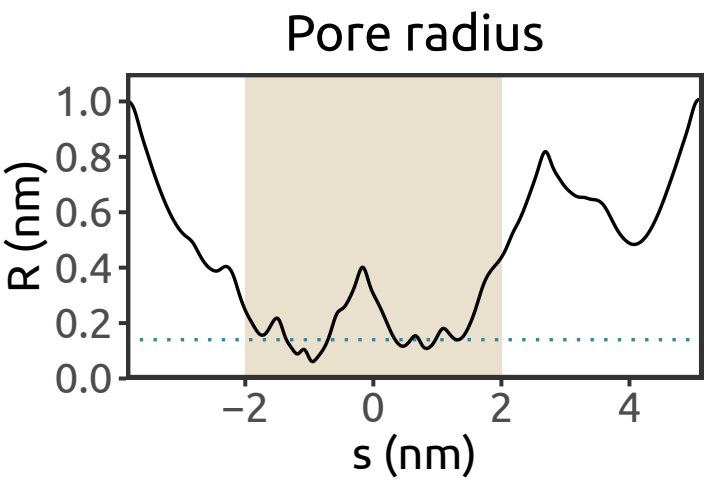
hydrated channel

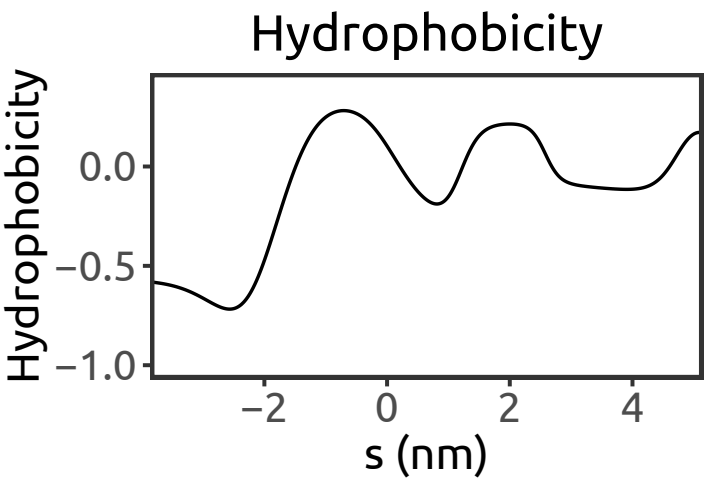
TRPML1 (PDB ID: 5WPV)

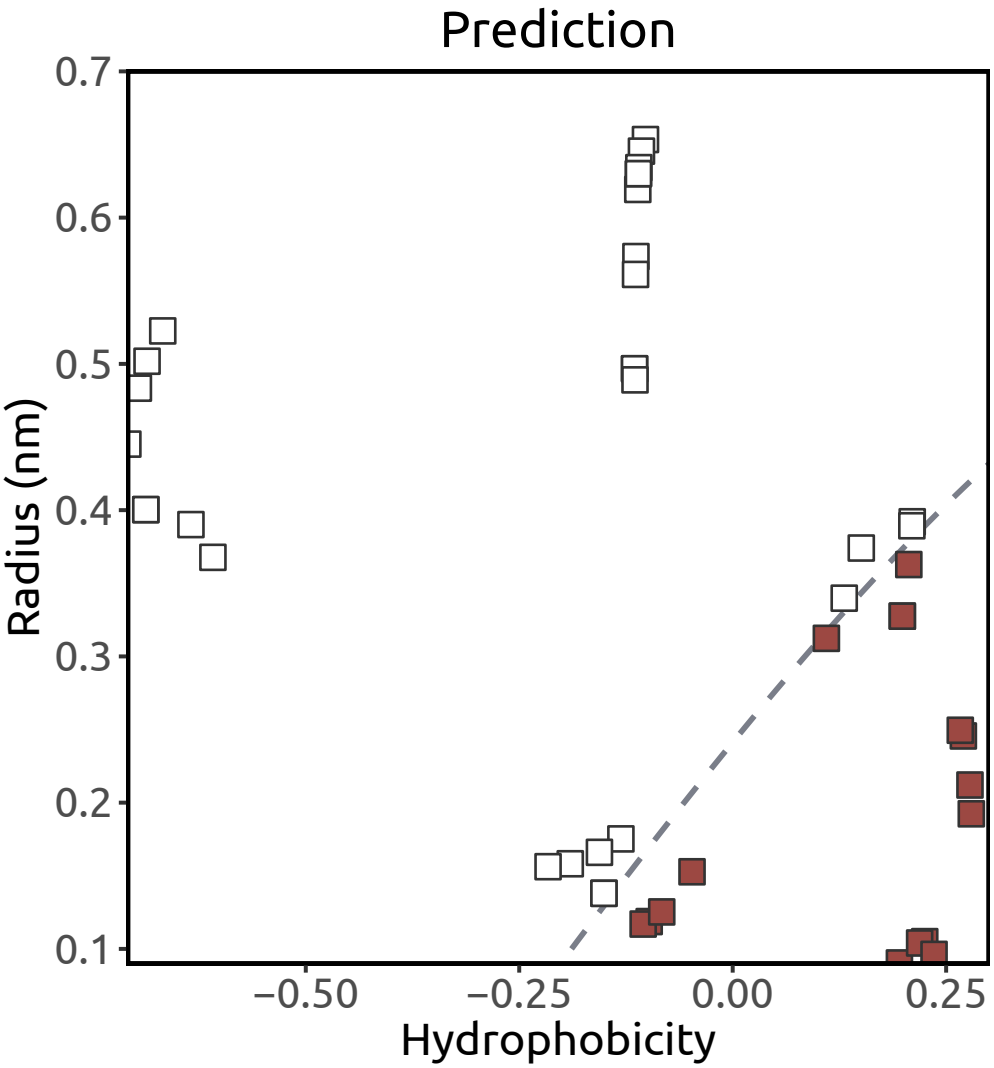
Mus musculus

cryo–EM (3.59 Å)

Chen et al., 2017







Heuristic score:

1.89 (n = 16)

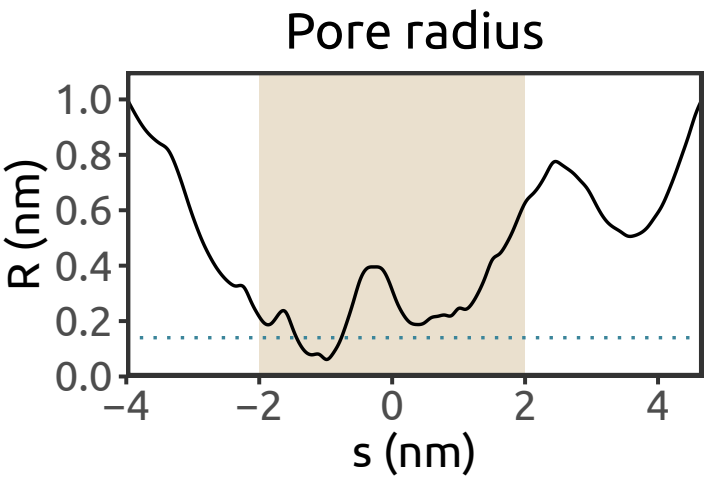
Simulation result:

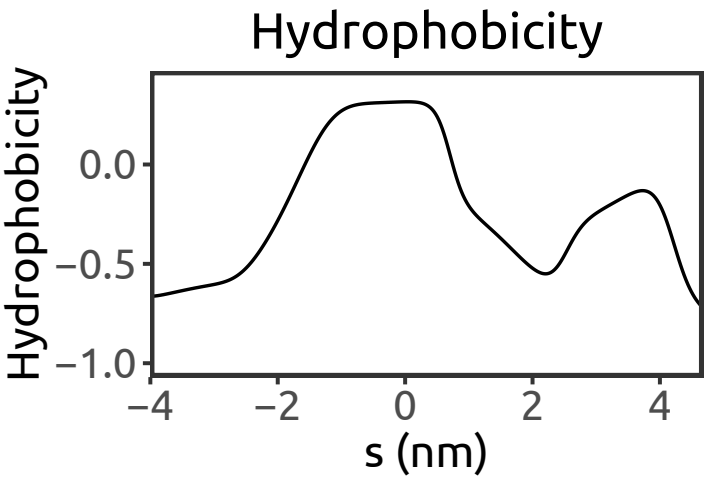
barrier to water

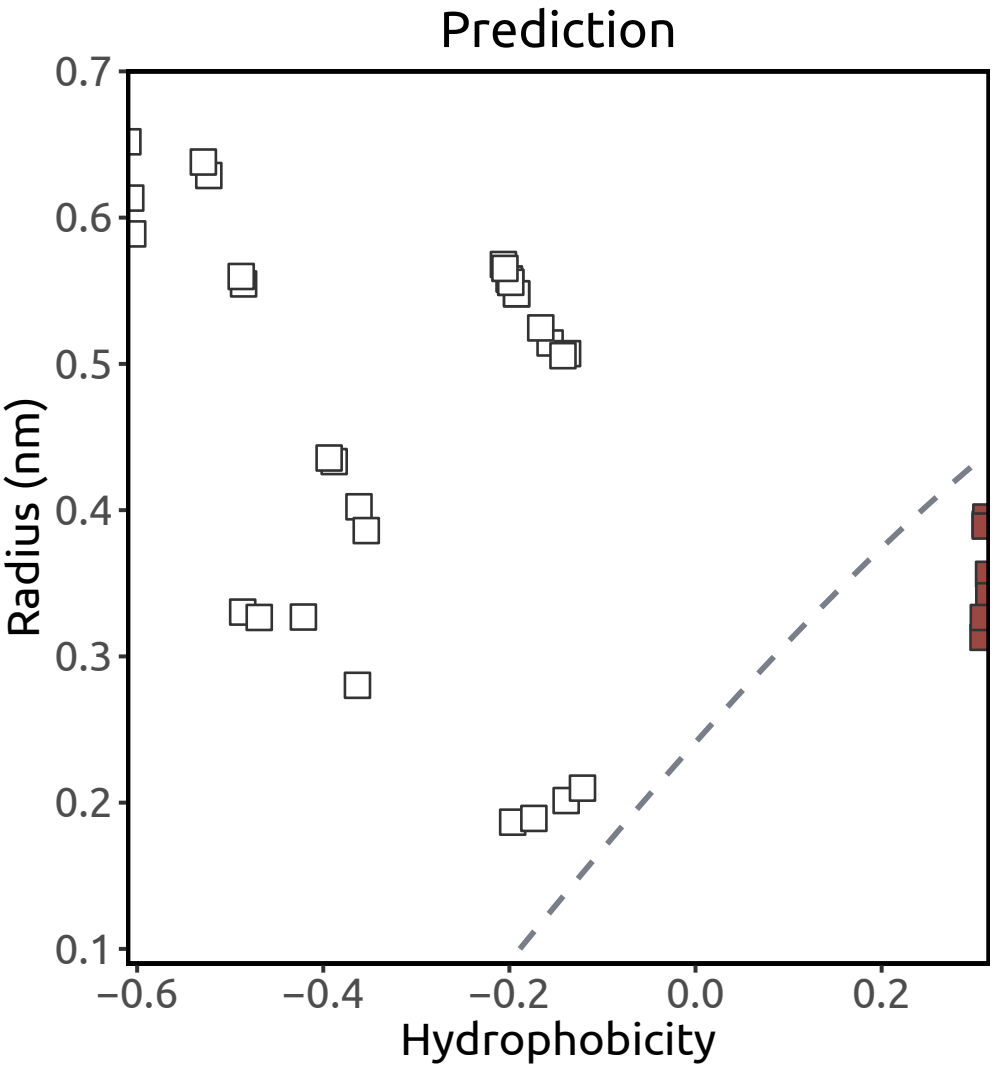
TRPML3 (PDB ID: 5W3S)

Callithrix jacchus
cryo–EM (2.94 Å)

Hirschi et al., 2017







Heuristic score:
1.56 (n = 12)

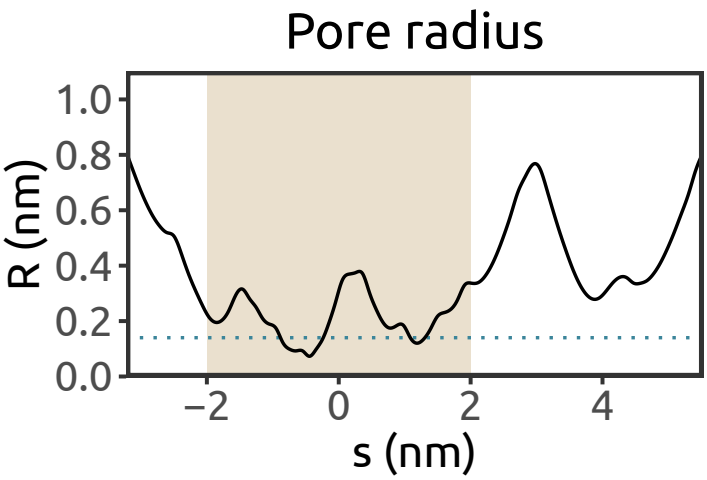
Simulation result:
barrier to water

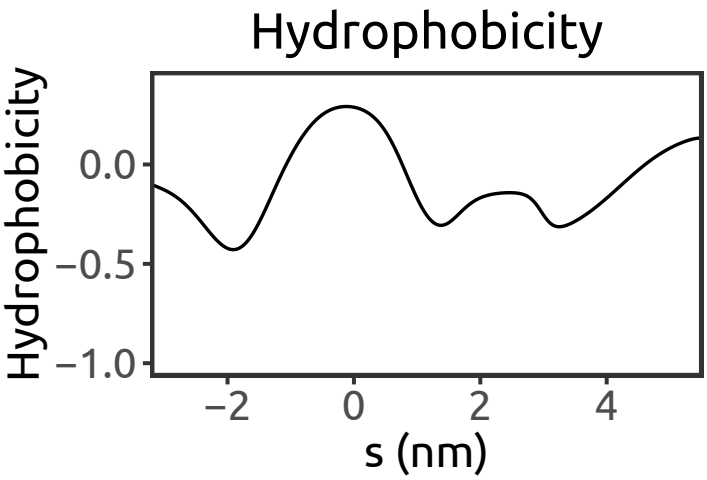
TRPML3 (PDB ID: 6AYE)

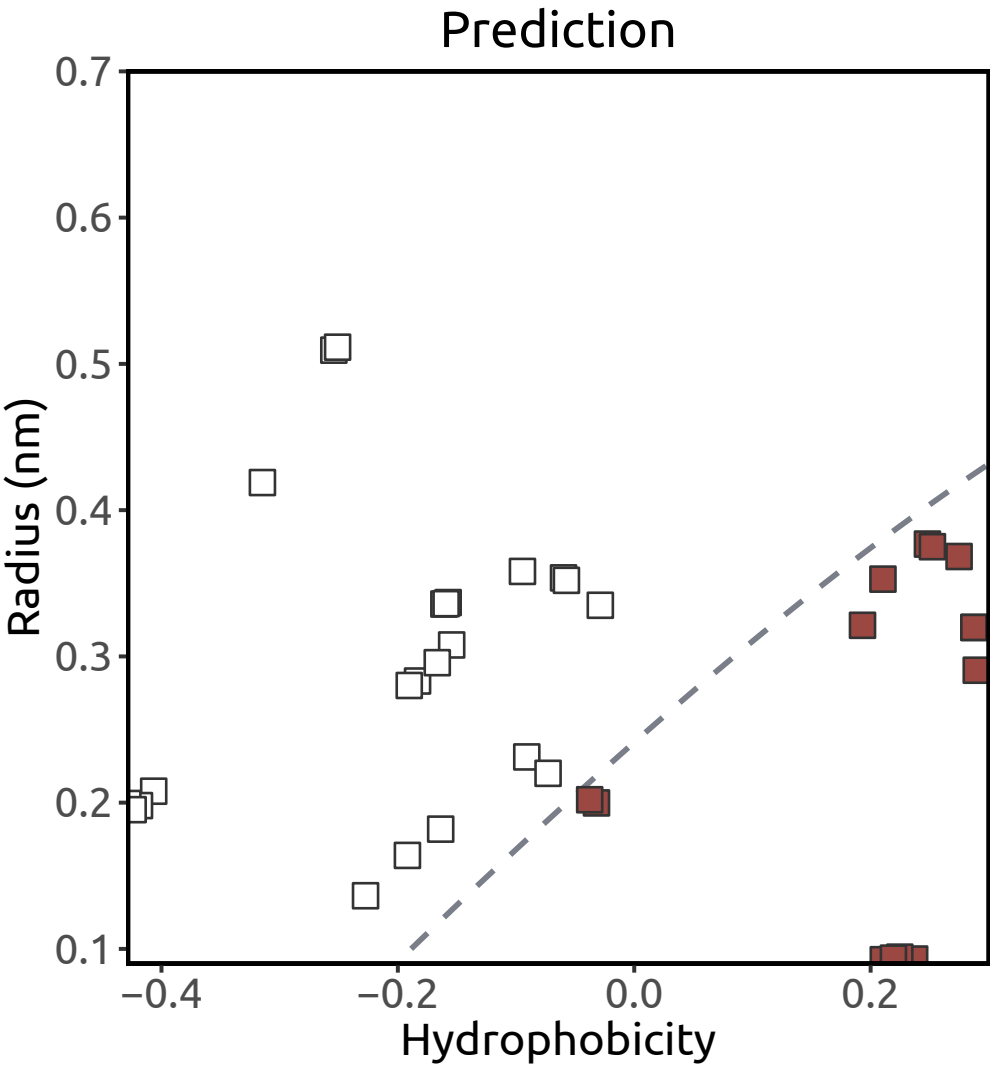
Homo sapiens

cryo–EM (4.06 Å)

Zhou et al., 2017







Heuristic score:

1.48 (n = 14)

Simulation result:

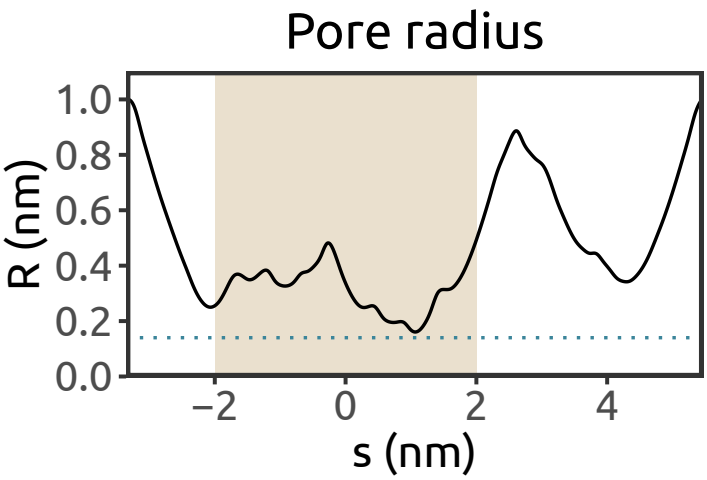
barrier to water

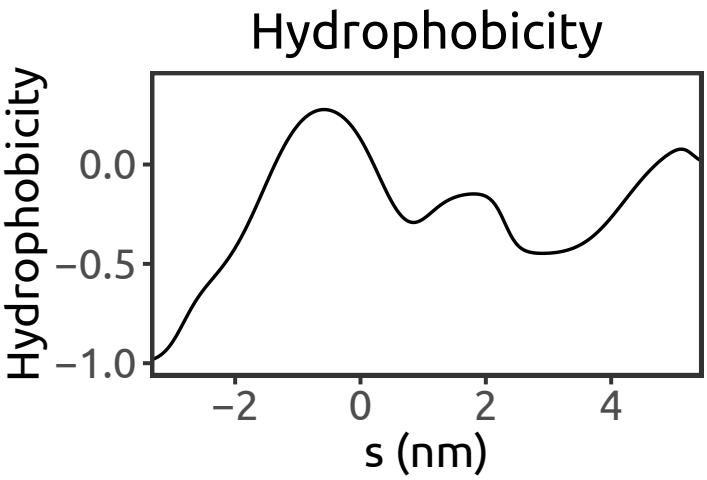
TRPML3 (PDB ID: 6AYF)

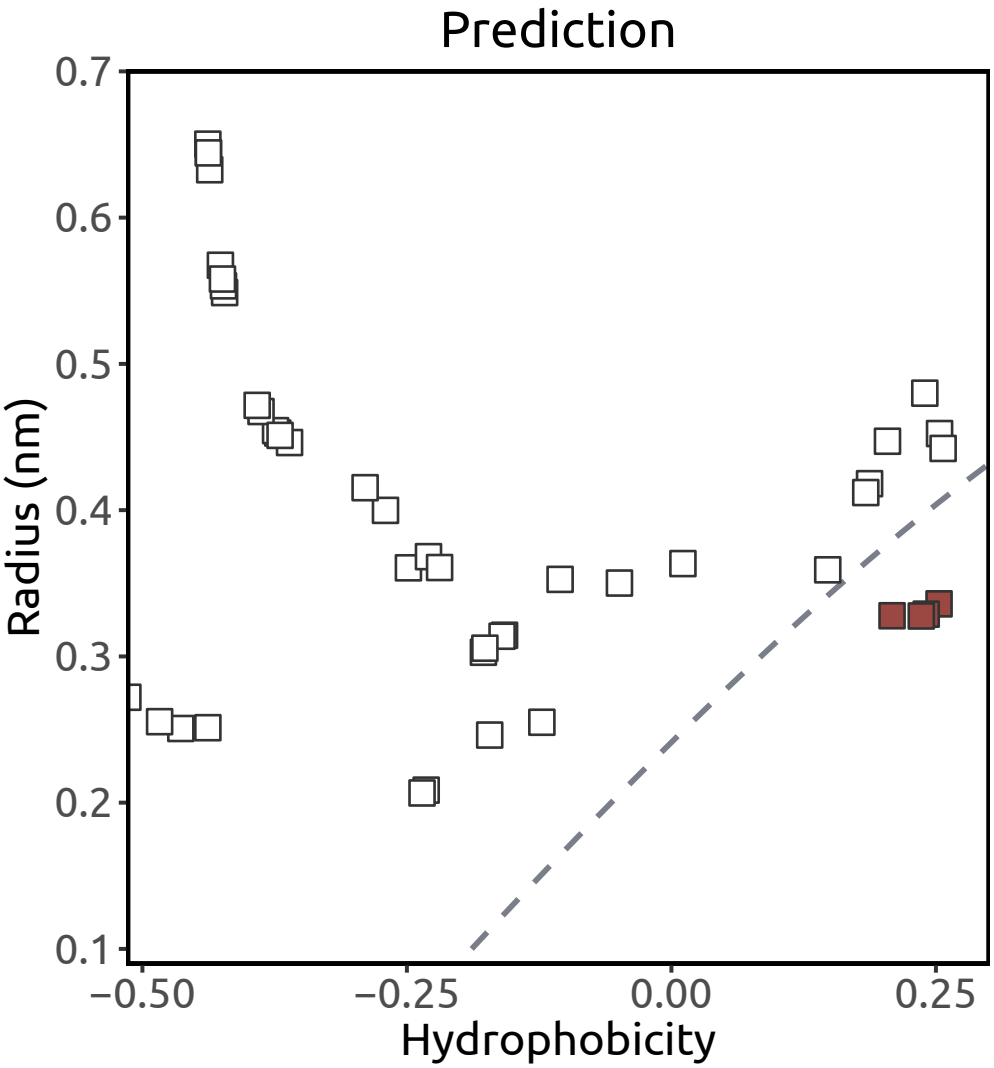
Homo sapiens

cryo–EM (3.62 Å)

Zhou et al., 2017







Heuristic score:

0.22 (n = 4)

Simulation result:

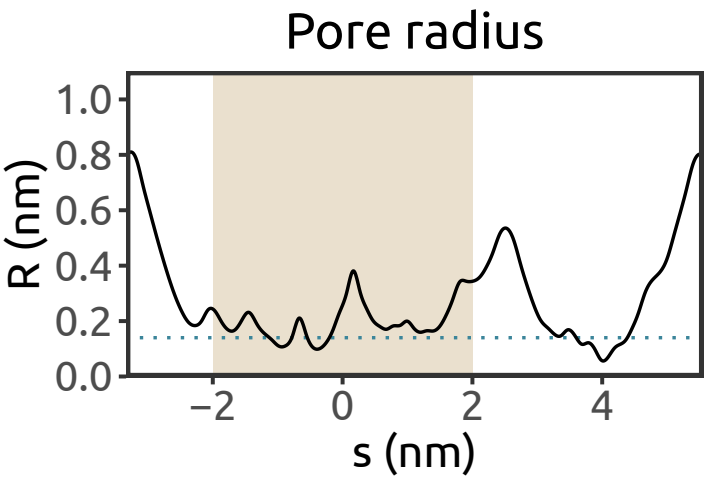
hydrated channel

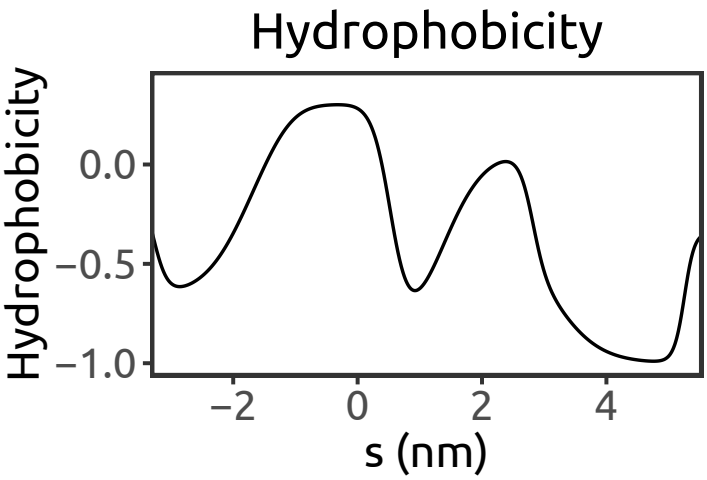
TRPML3 (PDB ID: 6AYG)

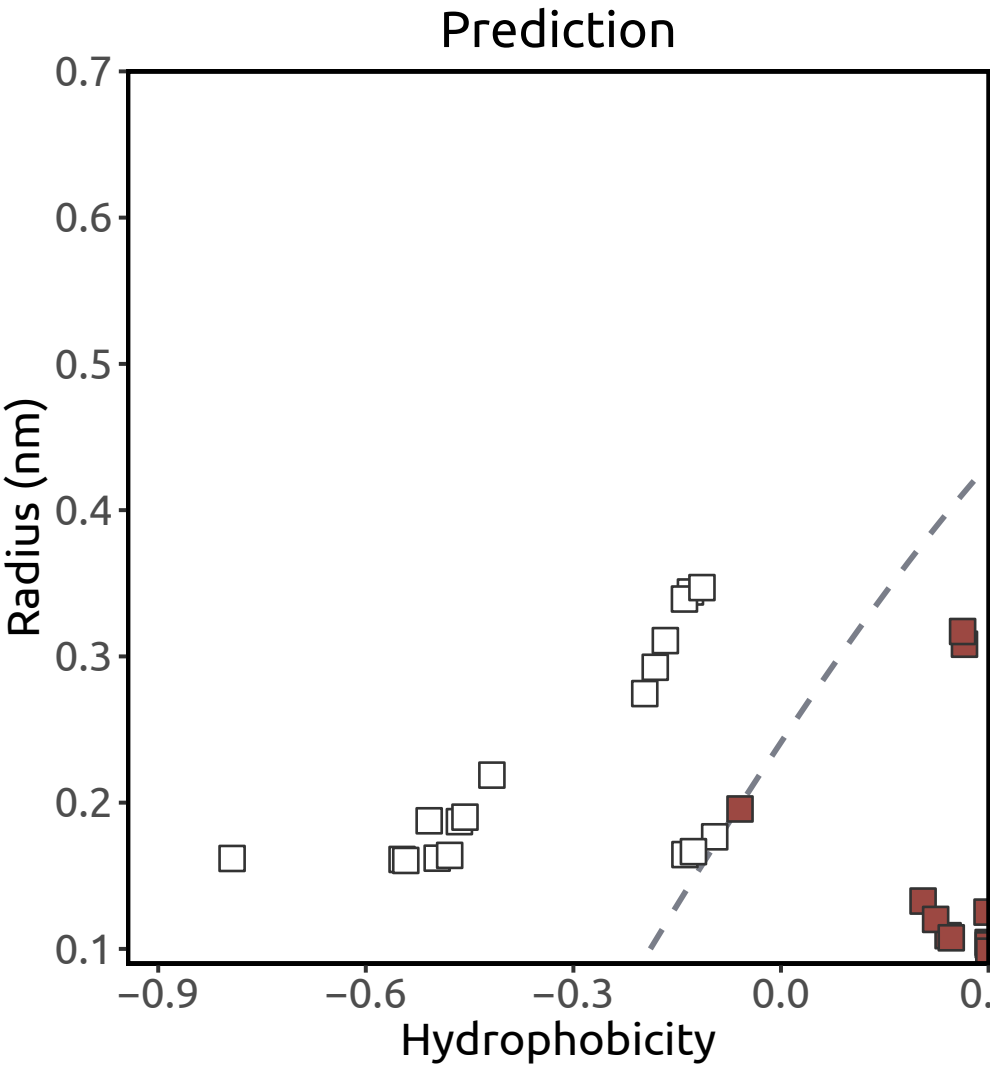
Homo sapiens

cryo–EM (4.65 Å)

Zhou et al., 2017







Heuristic score:

2.22 (n = 11)

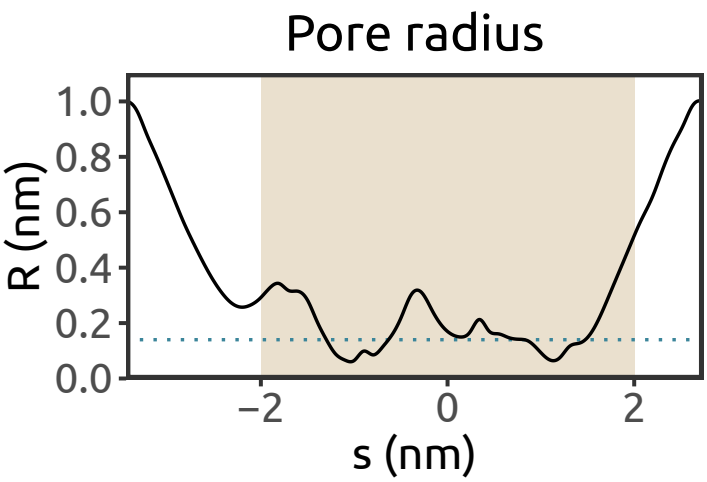
Simulation result:

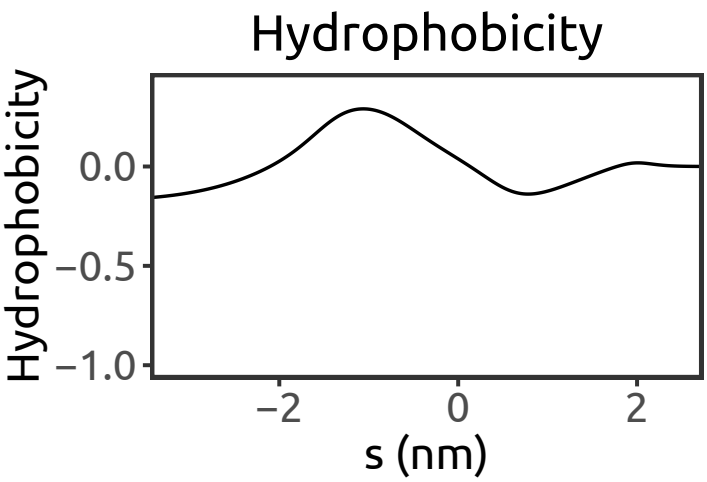
barrier to water

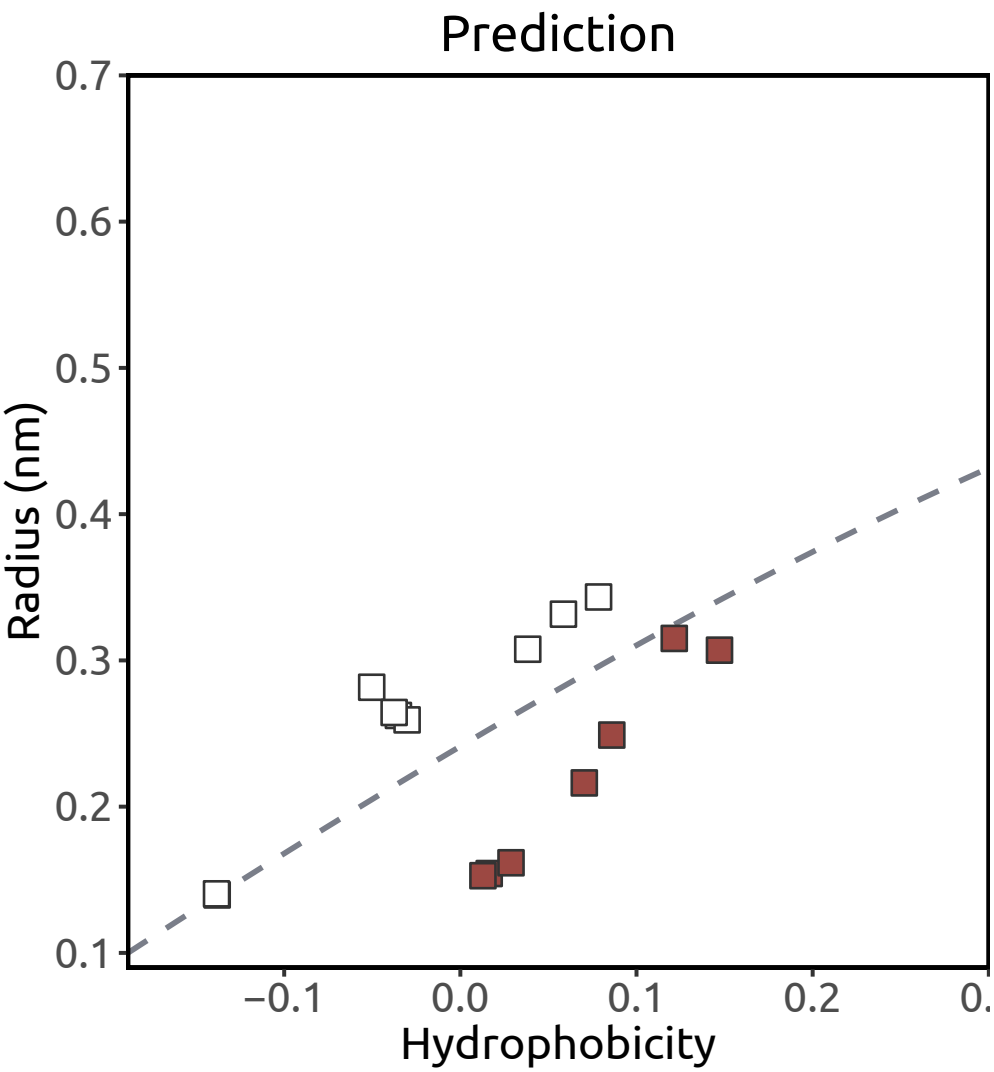
TRPV1 (PDB ID: 3J5P)

Rattus norvegicus
cryo–EM (3.28 Å)

Liao et al., 2013







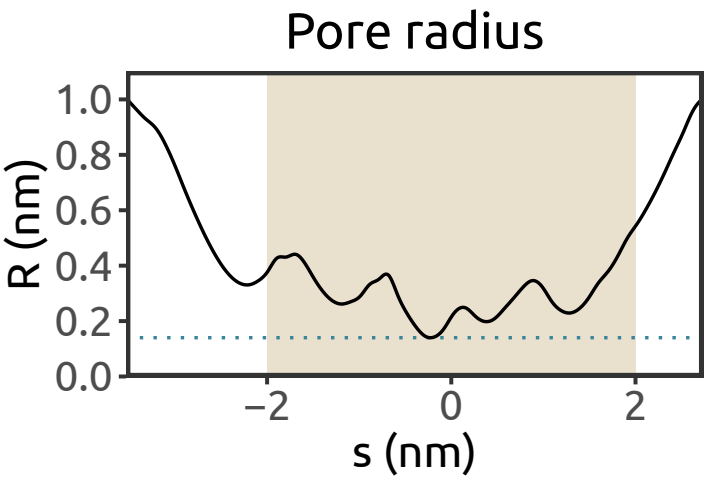
Heuristic score:
1.74 (n = 13)

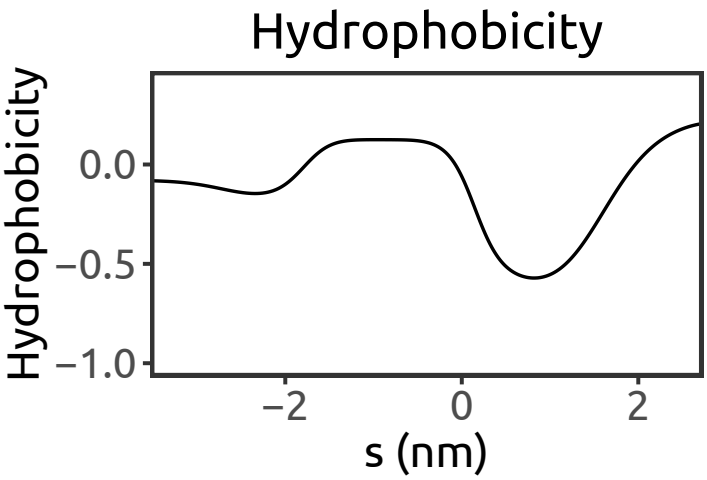
Simulation result:
barrier to water

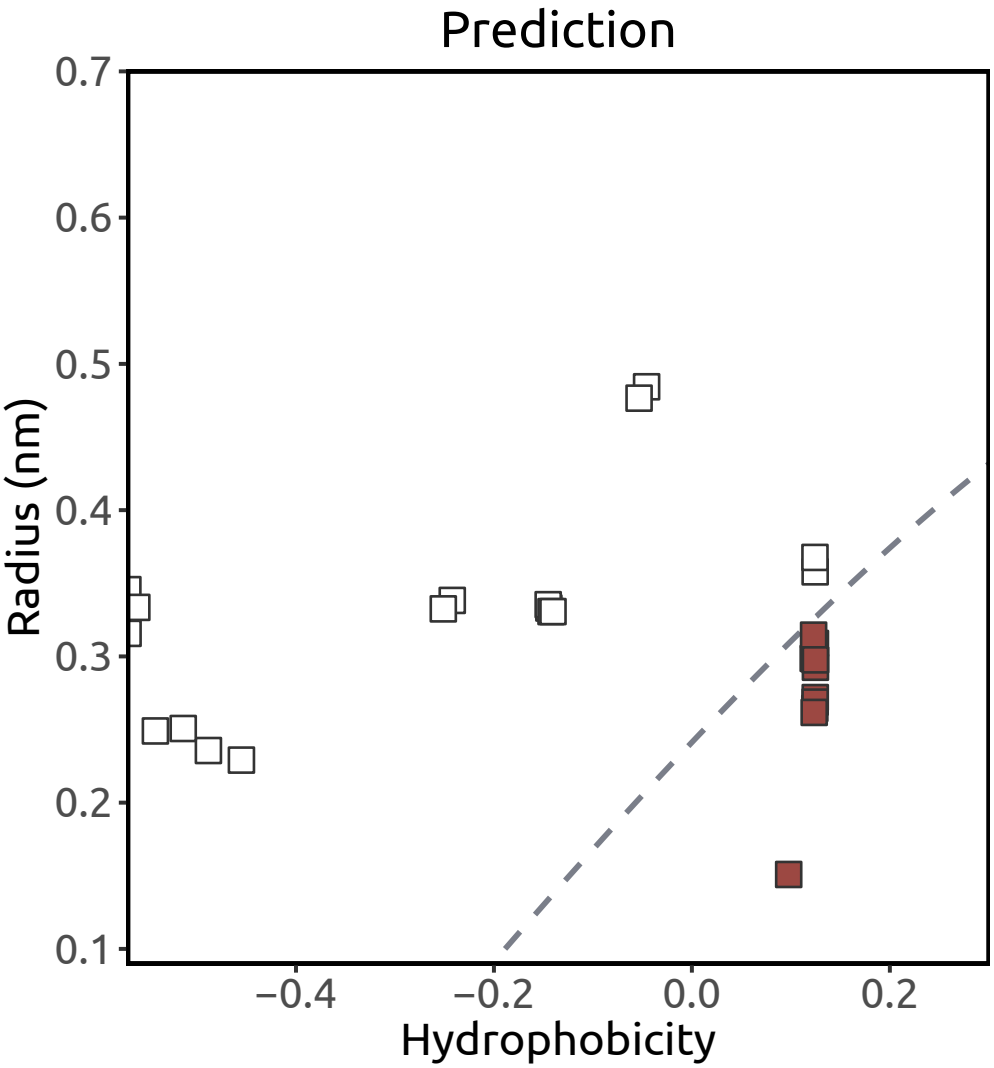
TRPV1 (PDB ID: 3J5Q)

Rattus norvegicus
cryo–EM (3.8 Å)

Cao et al., 2013







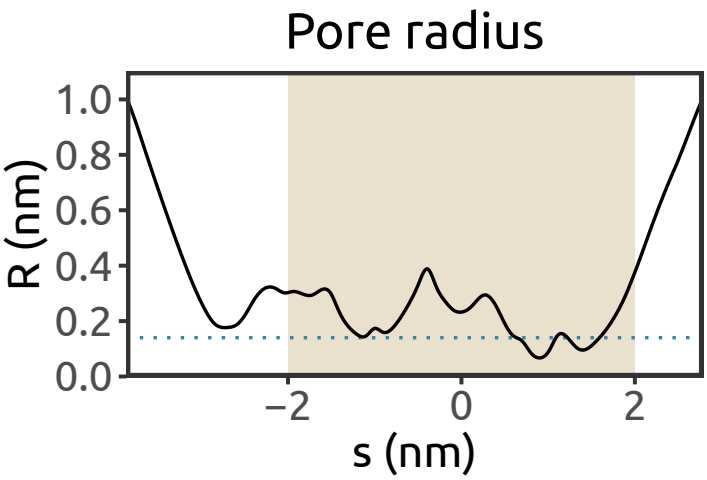
Heuristic score:
0.45 (n = 11)

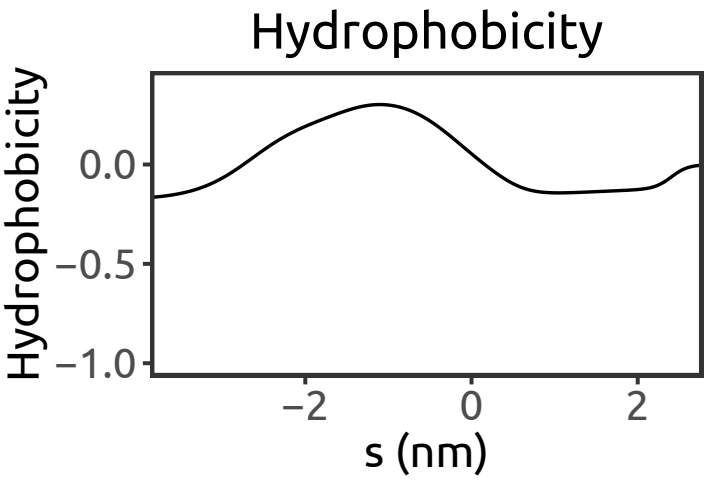
Simulation result:
barrier to water

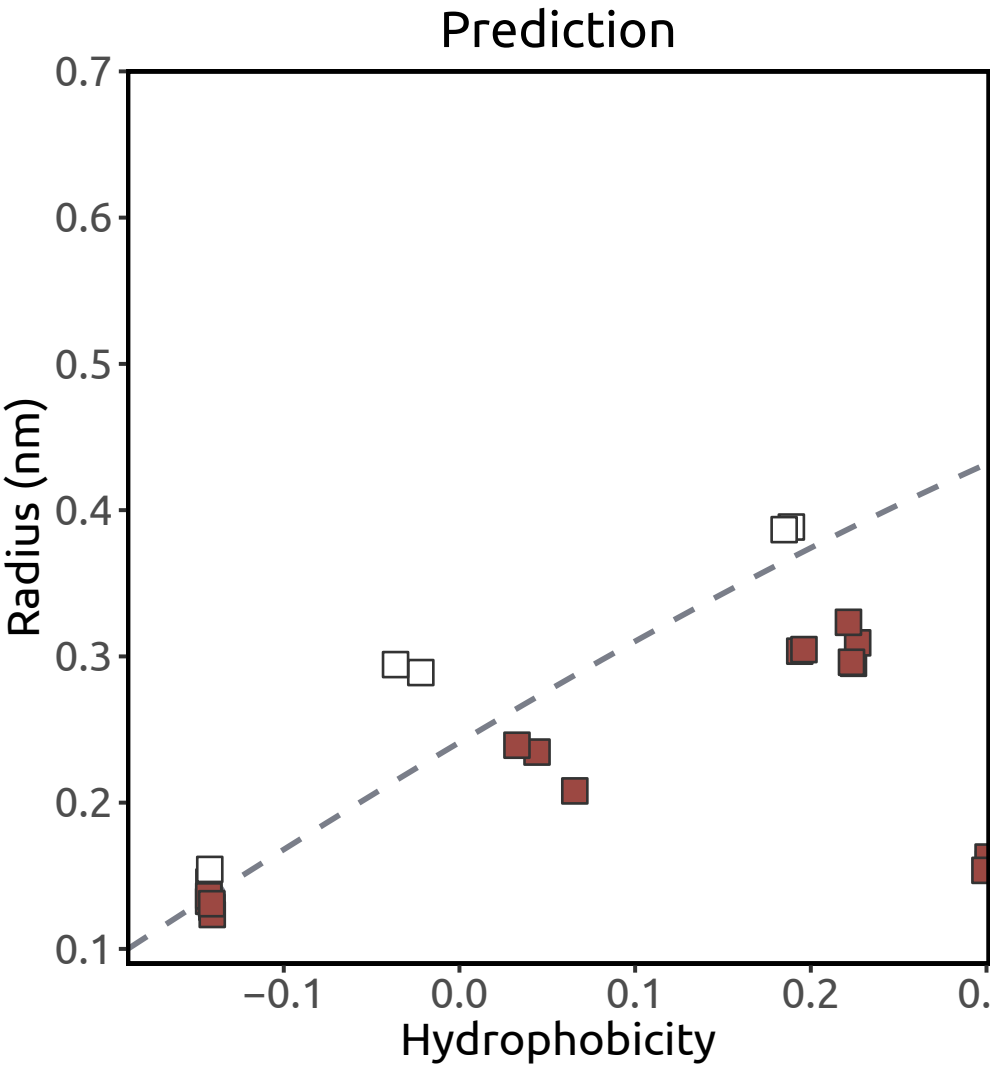
TRPV1 (PDB ID: 3J5R)

Rattus norvegicus
cryo–EM (4.2 Å)

Cao et al., 2013







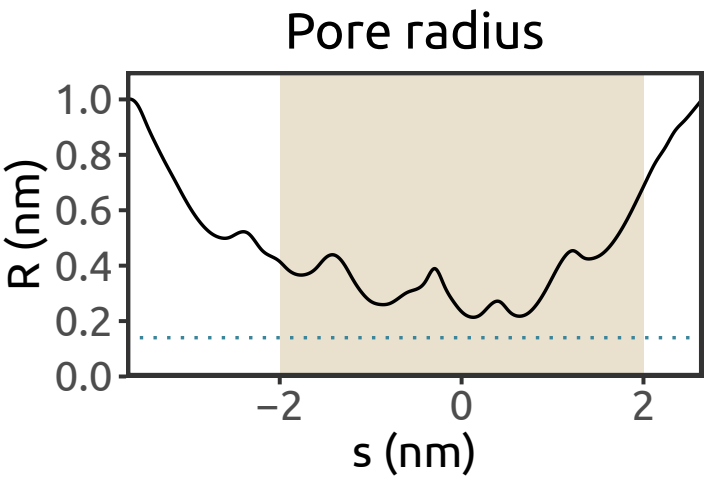
Heuristic score:
1.49 (n = 19)

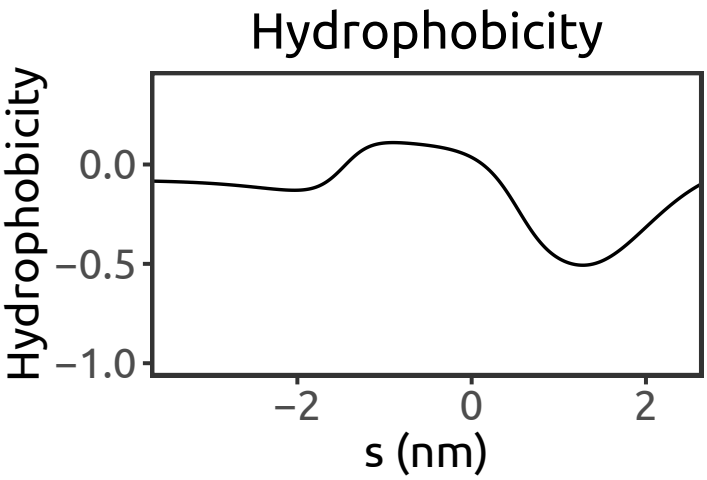
Simulation result:
barrier to water

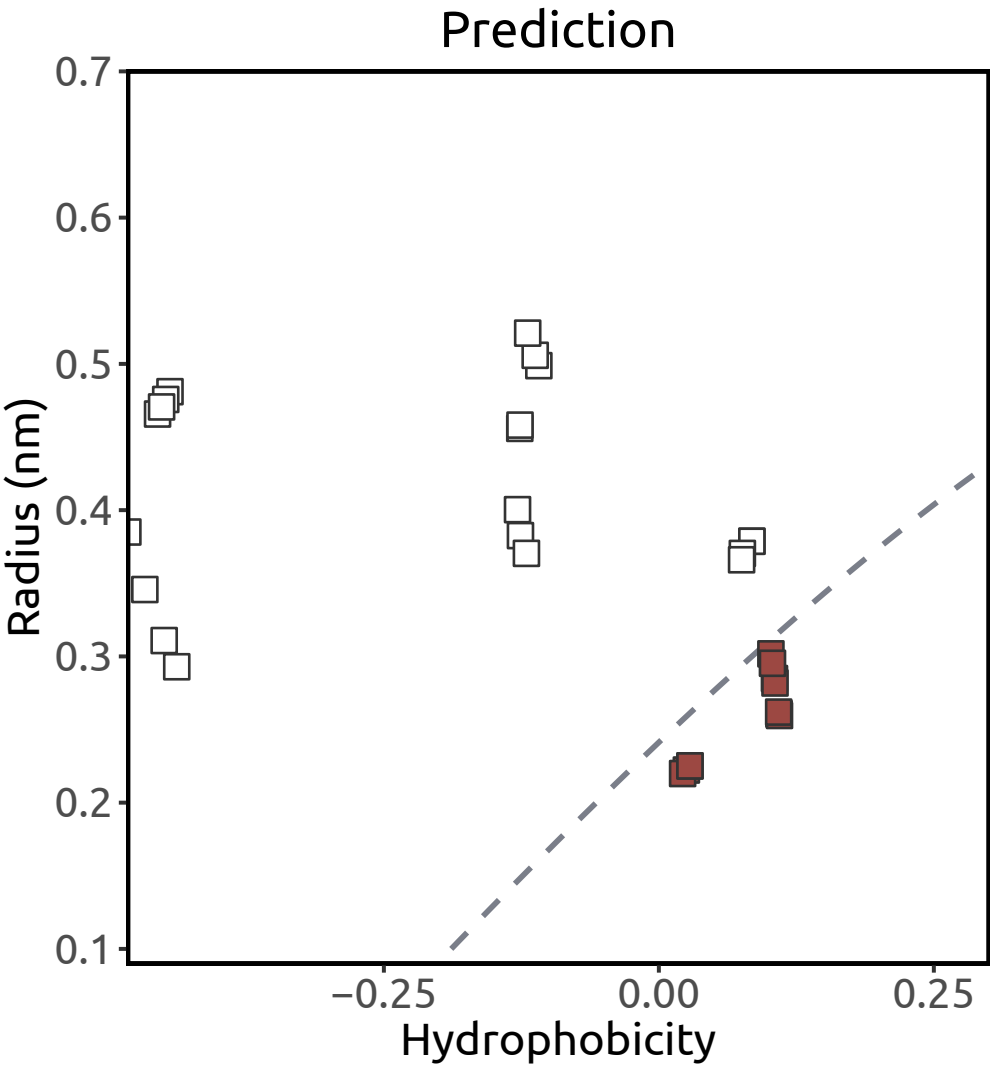
TRPV1 (PDB ID: 5IRX)

Rattus norvegicus
cryo–EM (2.95 Å)

Gao et al., 2015







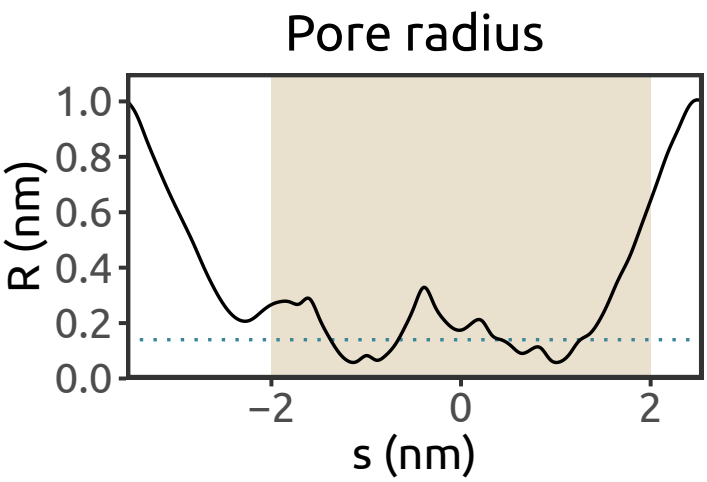
Heuristic score:
0.38 (n = 12)

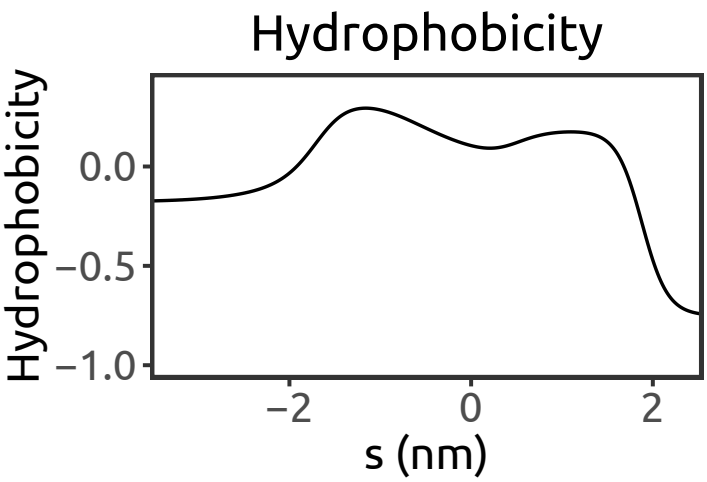
Simulation result:
hydrated channel

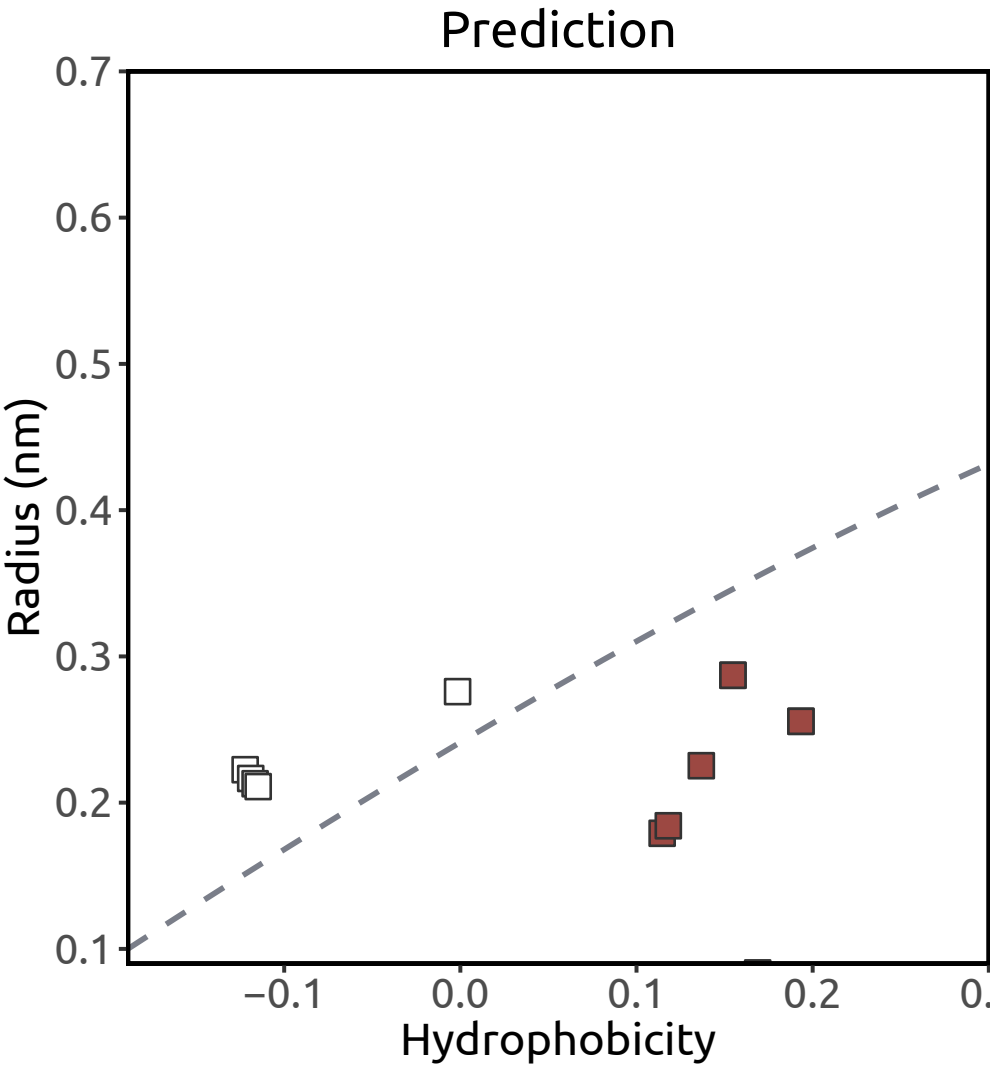
TRPV1 (PDB ID: 5IRZ)

Rattus norvegicus
cryo–EM (3.28 Å)

Gao et al., 2015







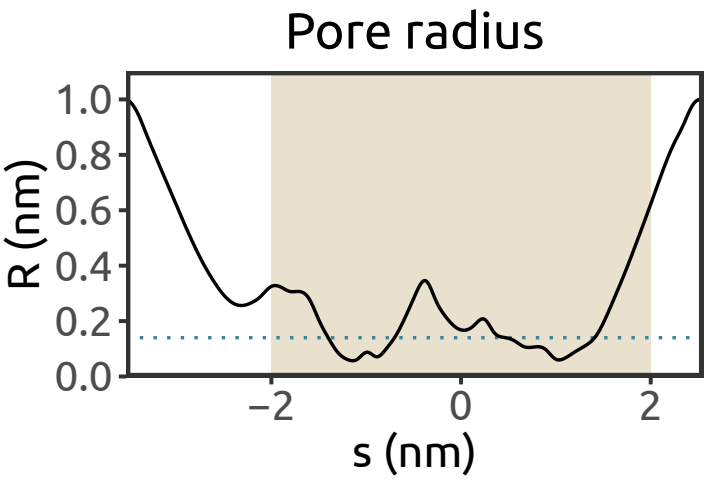
Heuristic score:
2.79 (n = 15)

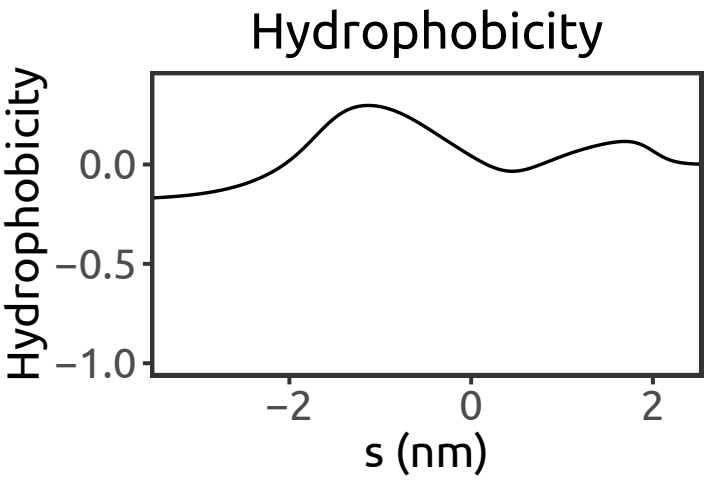
Simulation result:
barrier to water

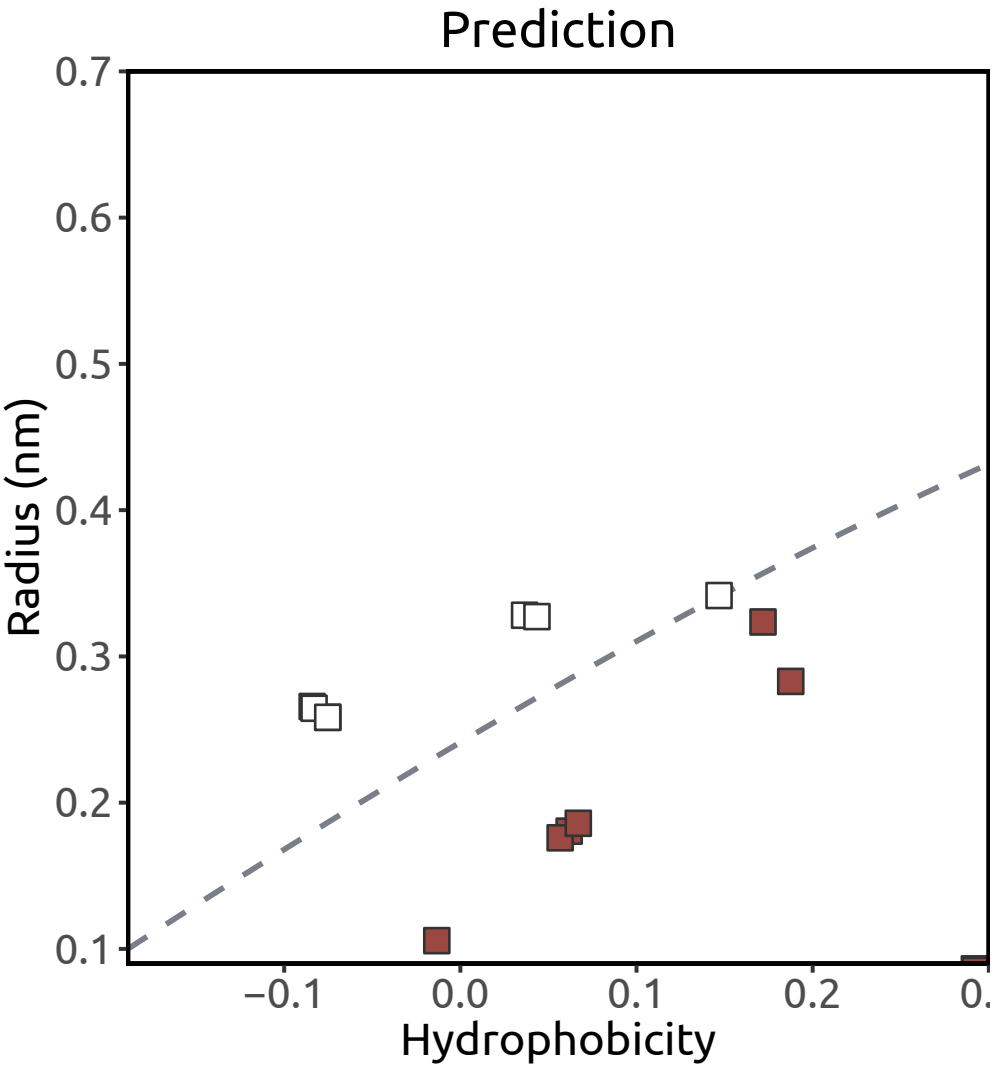
TRPV1 (PDB ID: 5IS0)

Rattus norvegicus
cryo–EM (3.43 Å)

Gao et al., 2015







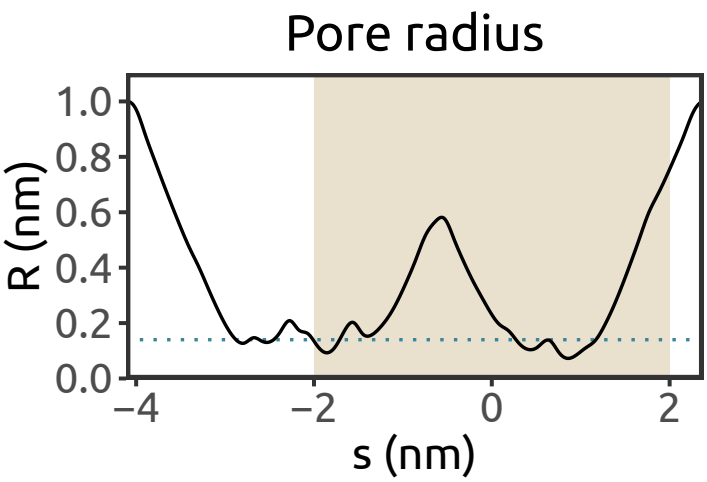
Heuristic score:
2.16 (n = 13)

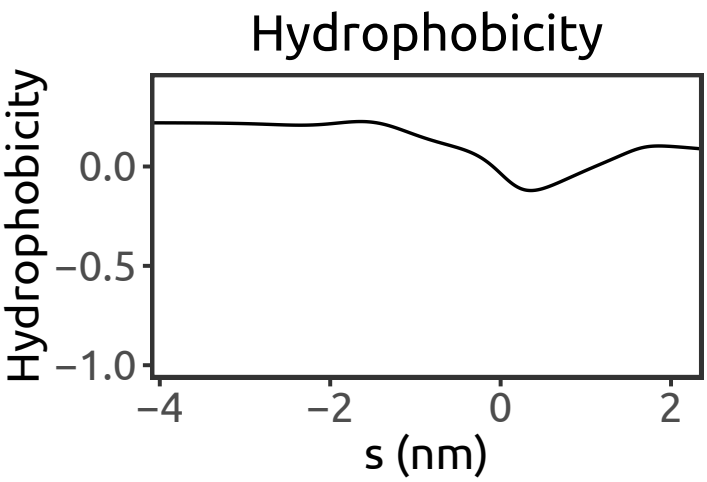
Simulation result:
barrier to water

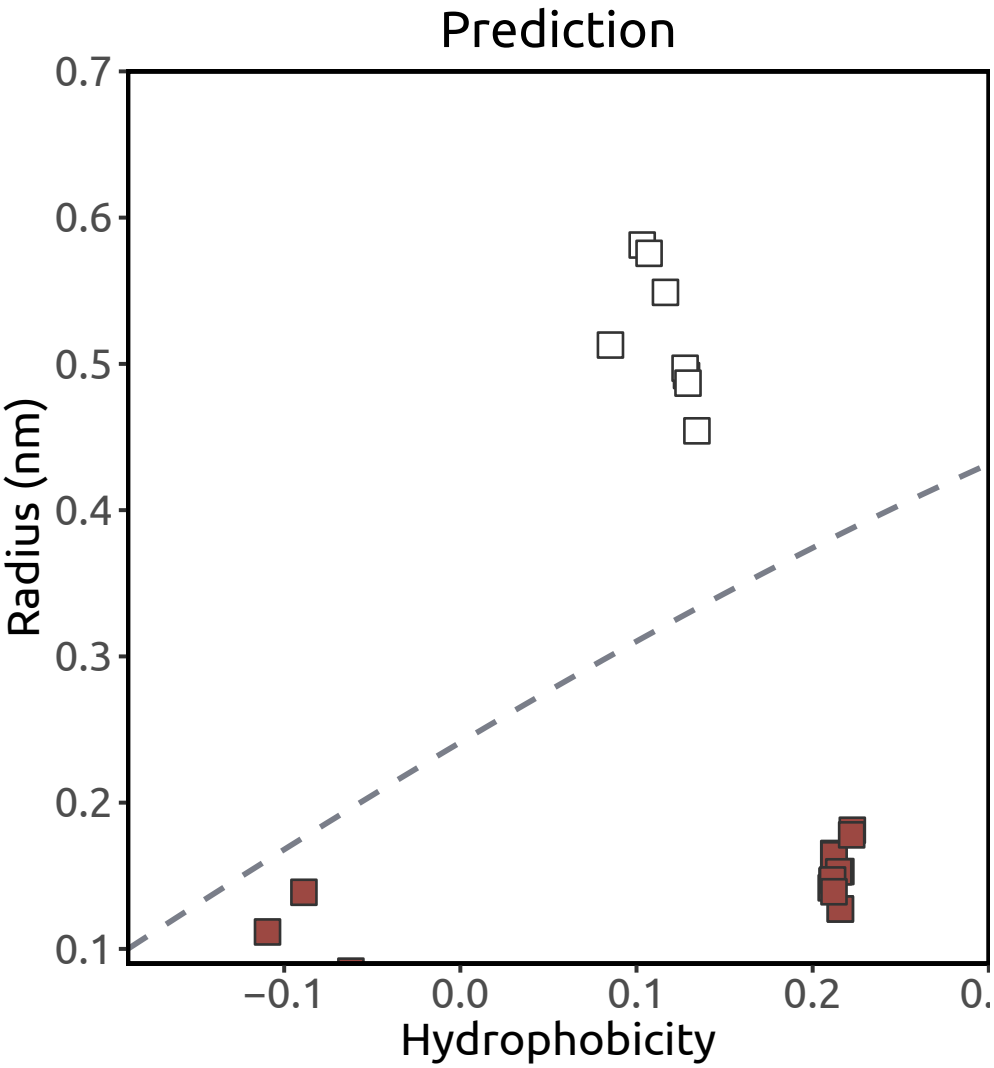
TRPV2 (PDB ID: 5AN8)

Oryctolagus cuniculus
cryo–EM (3.8 Å)

Zubcevic et al., 2016







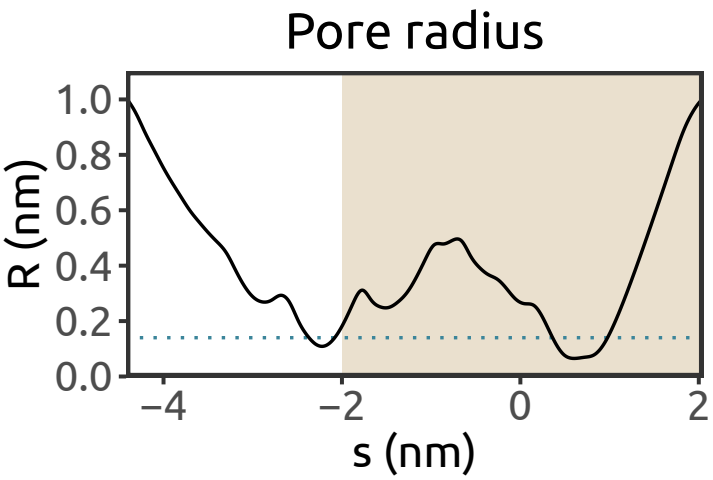
Heuristic score:
2.72 (n = 17)

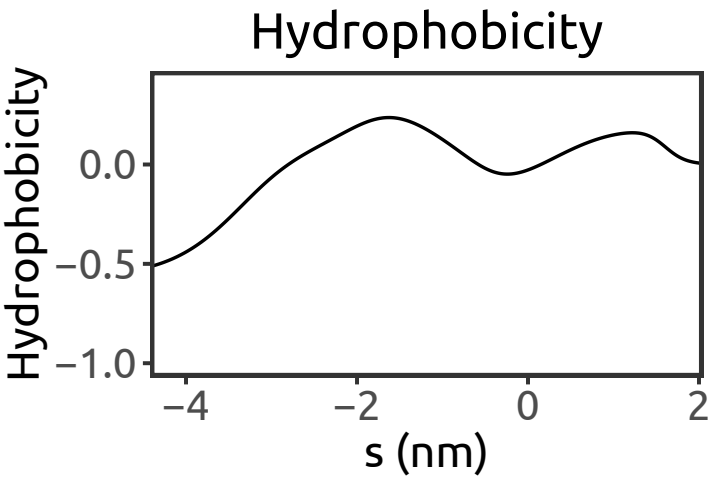
Simulation result:
barrier to water

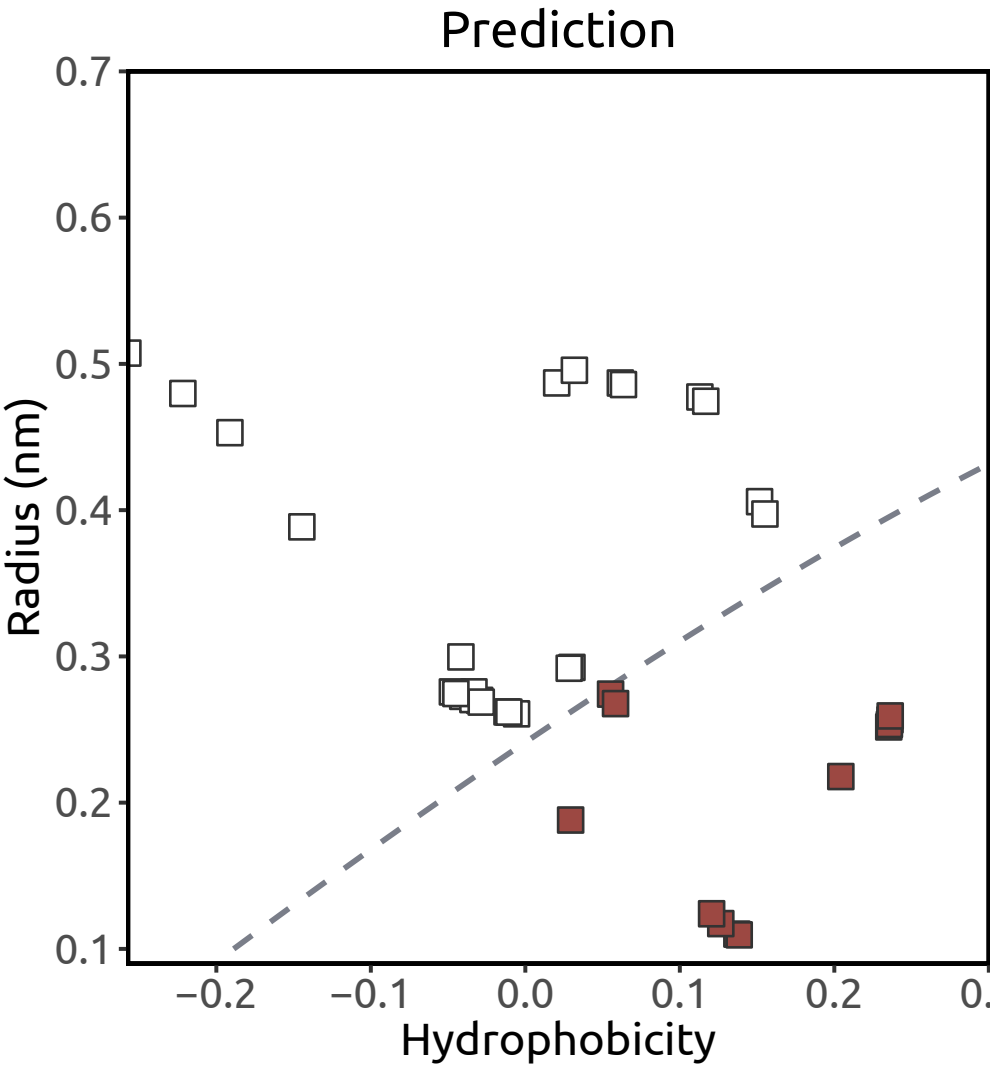
TRPV2 (PDB ID: 5HI9)

Rattus norvegicus
cryo–EM (4.4 Å)

Huynh et al., 2016







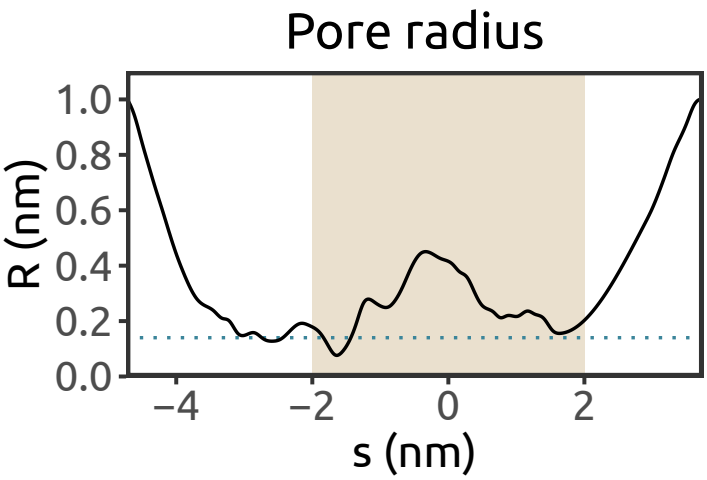
Heuristic score:
2.17 (n = 16)

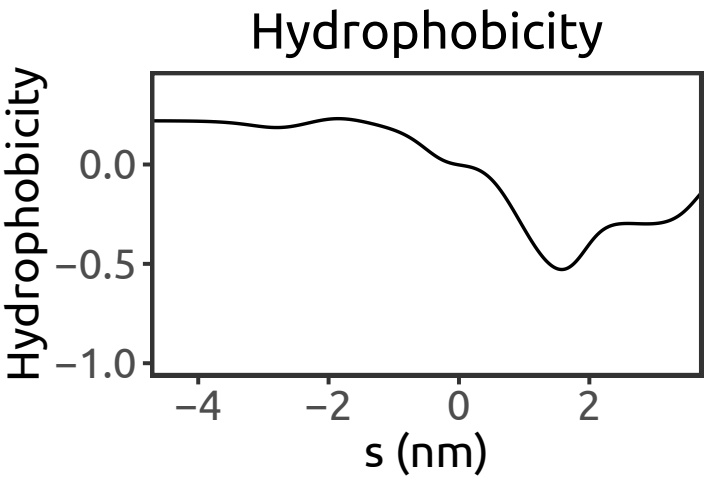
Simulation result:
barrier to water

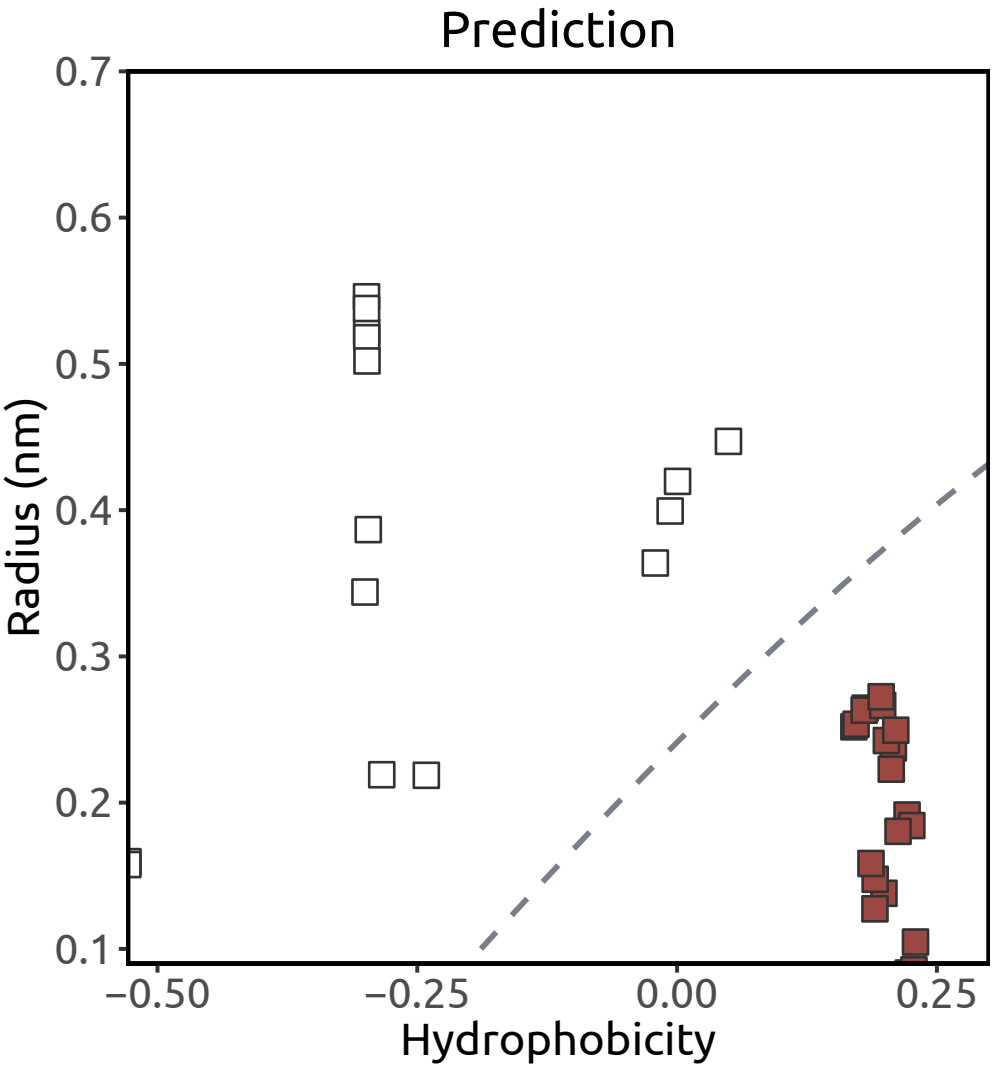
TRPV2 (PDB ID: 6BWJ)

Oryctolagus cuniculus
X–ray (3.1 Å)

Zubcevic et al., 2018







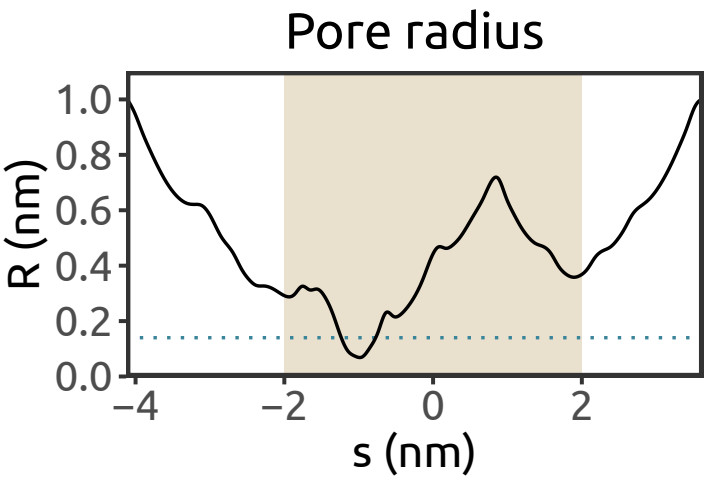
Heuristic score:
3.02 (n = 20)

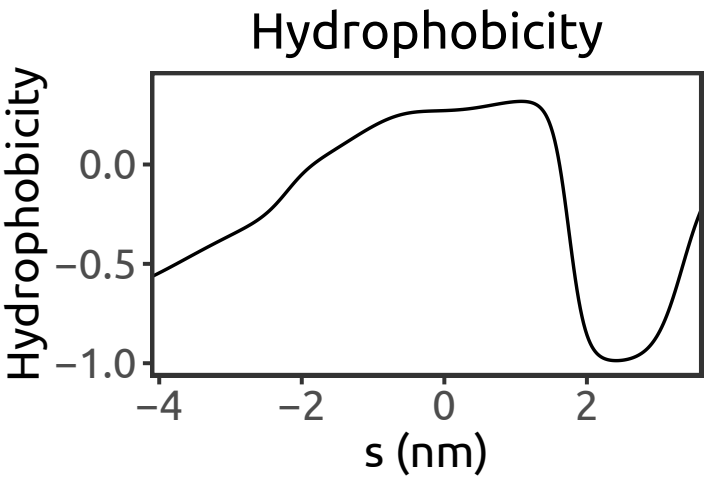
Simulation result:
barrier to water

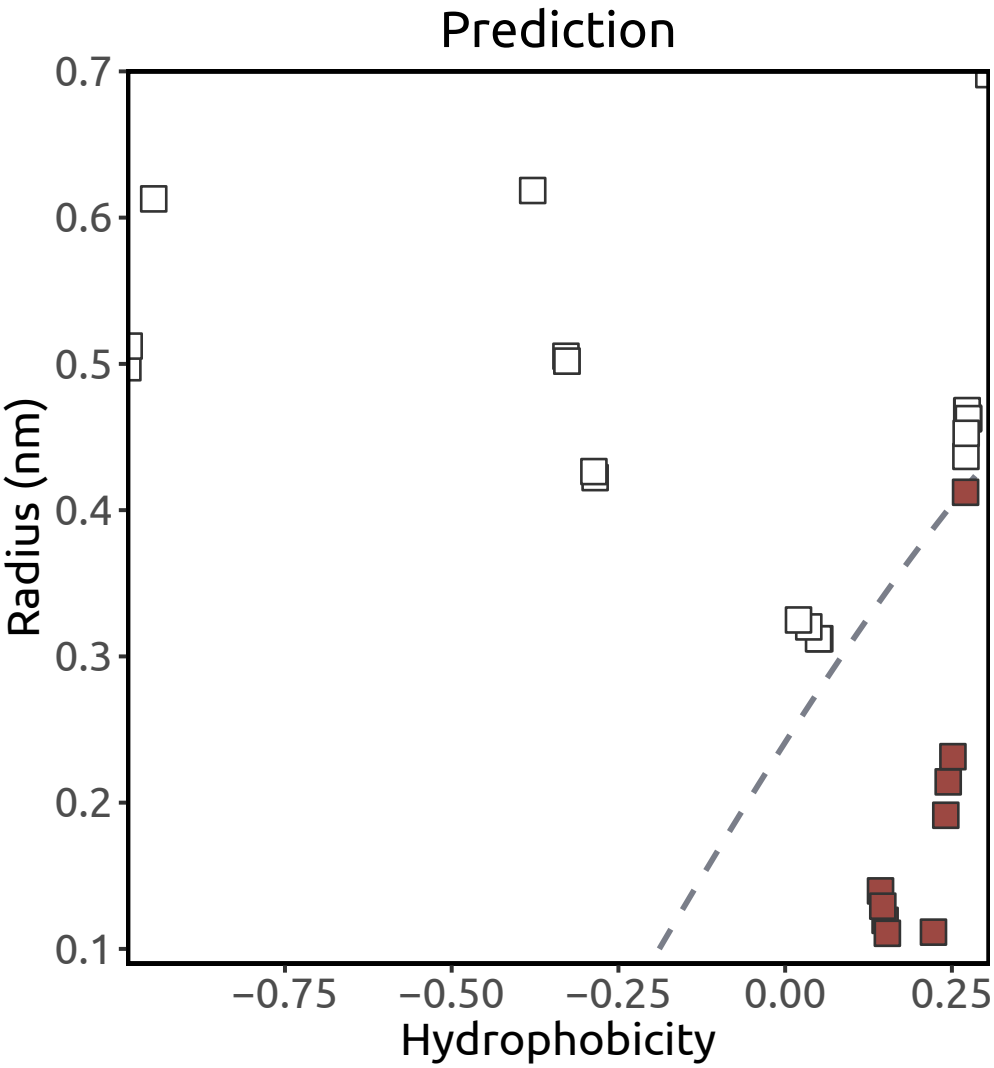
TRPV4 (PDB ID: 6BBJ)

Xenopus tropicalis
cryo–EM (3.8 Å)

Deng et al., 2018







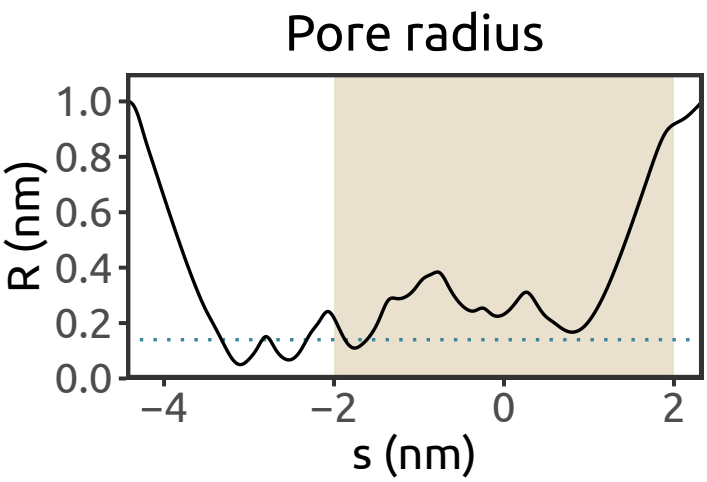
Heuristic score:
1.44 (n = 9)

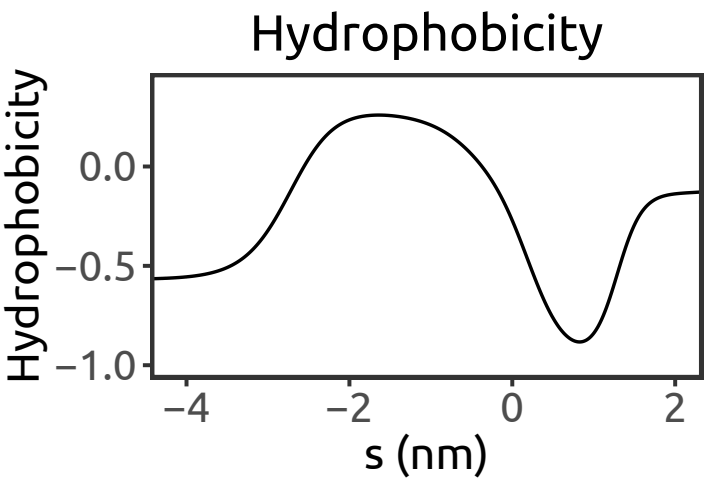
Simulation result:
barrier to water

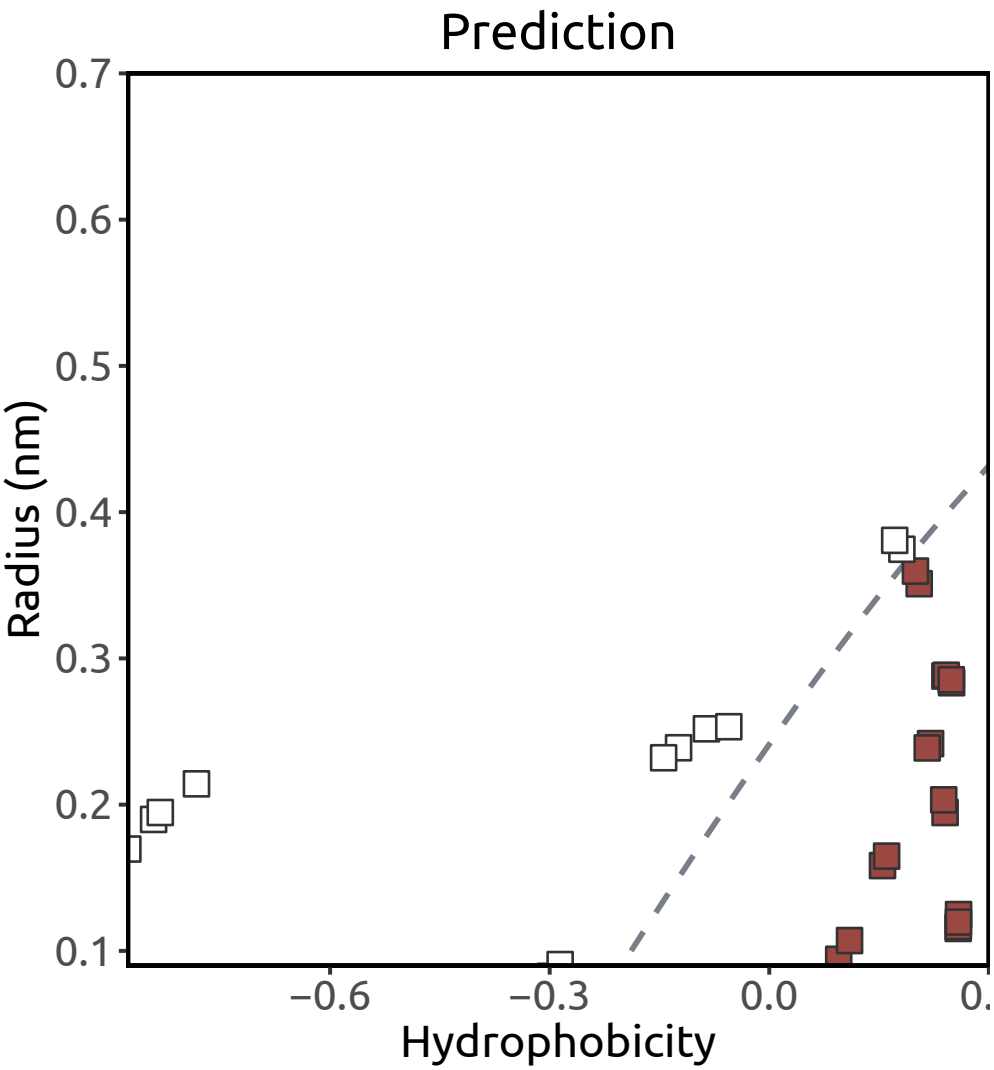
TRPV5 (PDB ID: 6B5V)

Oryctolagus cuniculus
cryo–EM (4.8 Å)

Hughes et al., 2018







Heuristic score:
2.66 (n = 18)

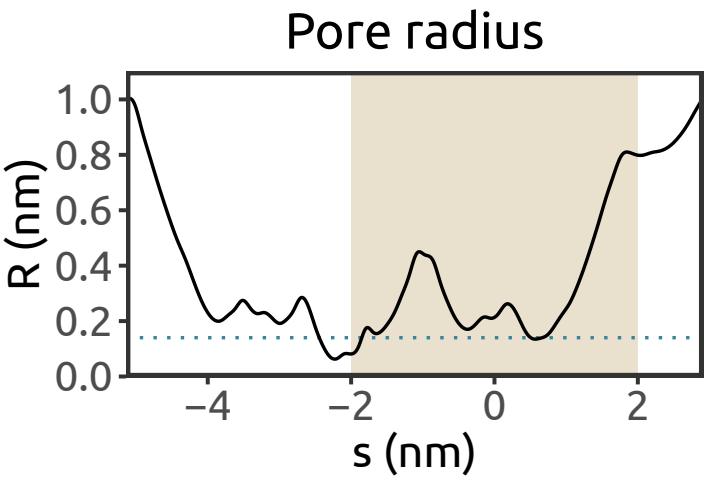
Simulation result:
barrier to water

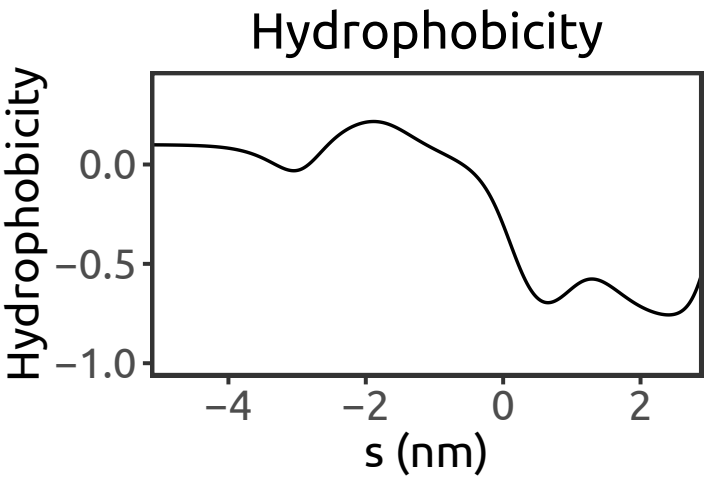
TRPV6 (PDB ID: 5IWK)

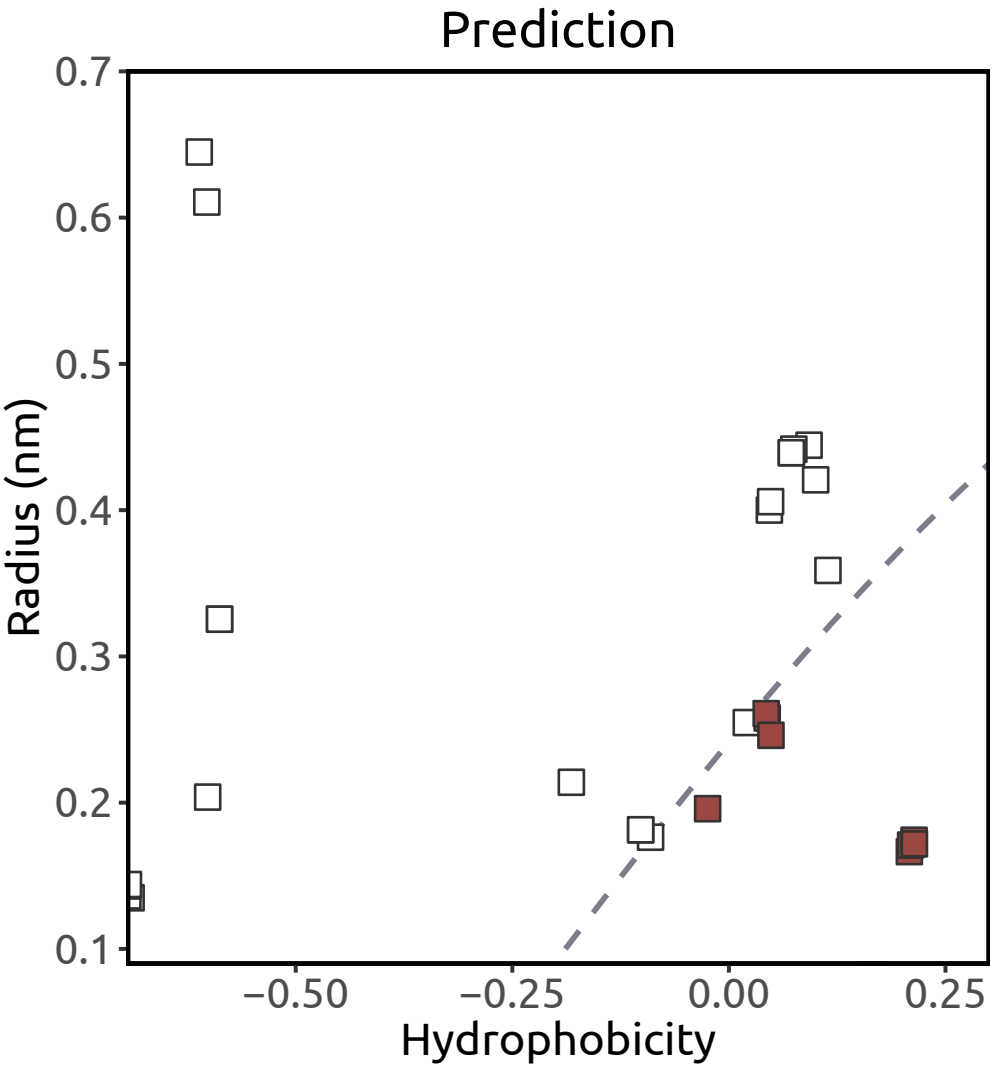
Rattus norvegicus

X–ray (3.25 Å)

Saotome et al., 2016







Heuristic score:

1.71 (n = 12)

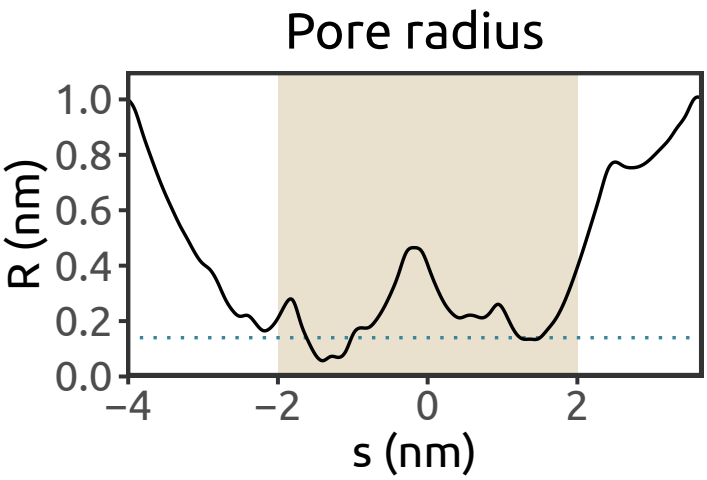
Simulation result:

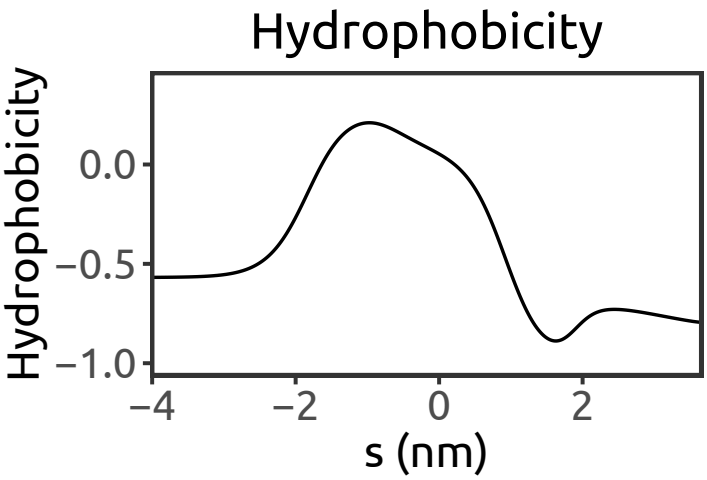
barrier to water

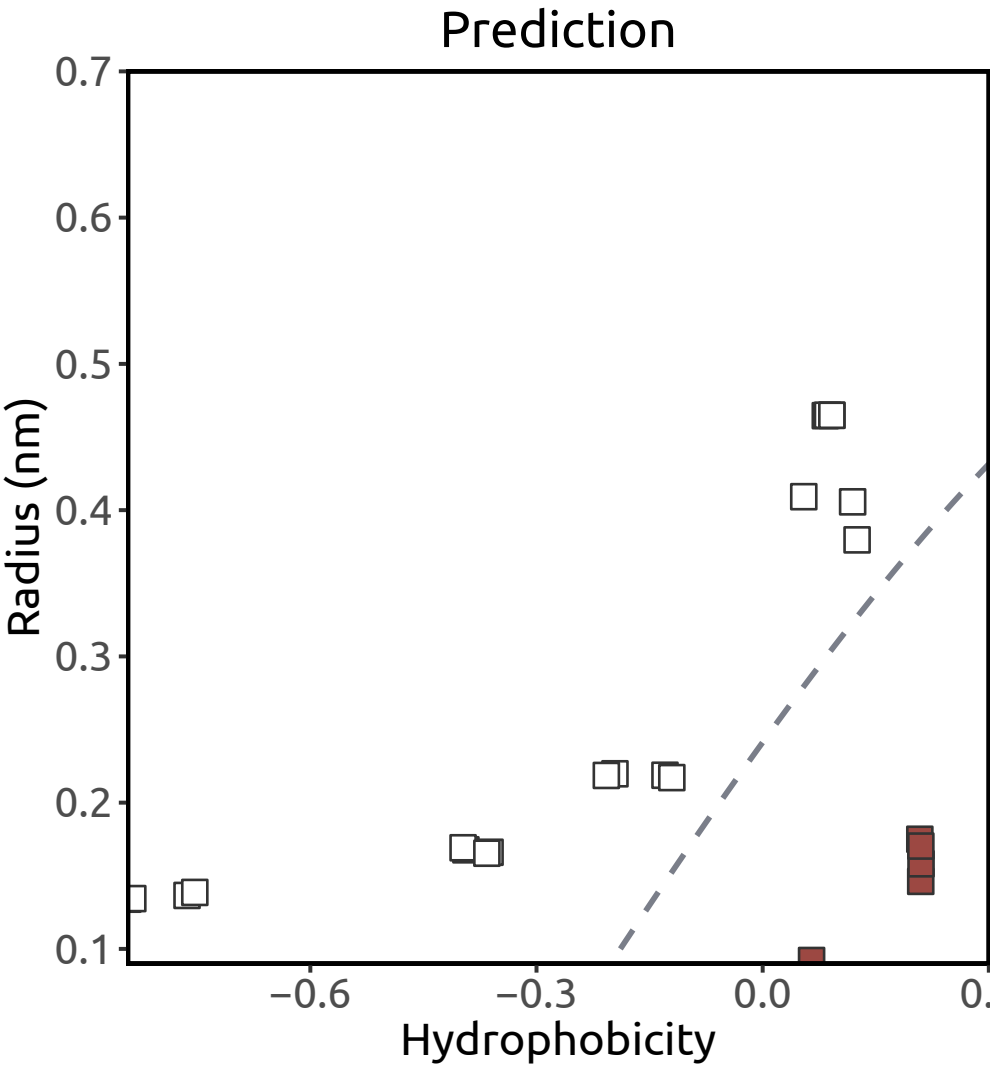
TRPV6 (PDB ID: 5IWP)

Rattus norvegicus
X–ray (3.65 Å)

Saotome et al., 2016







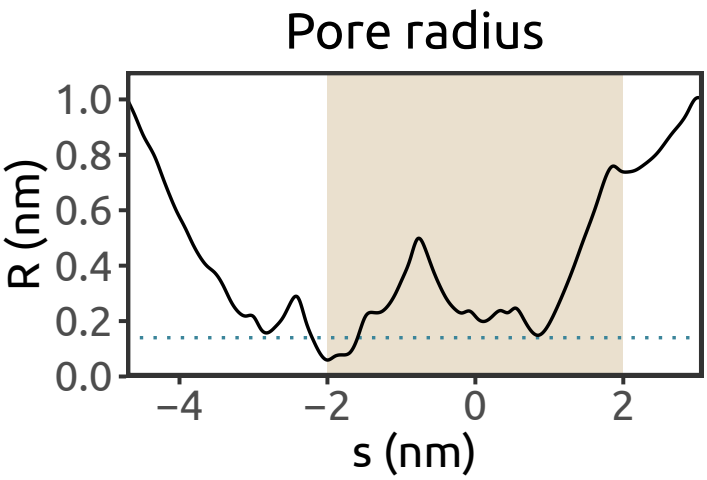
Heuristic score:
1.47 (n = 8)

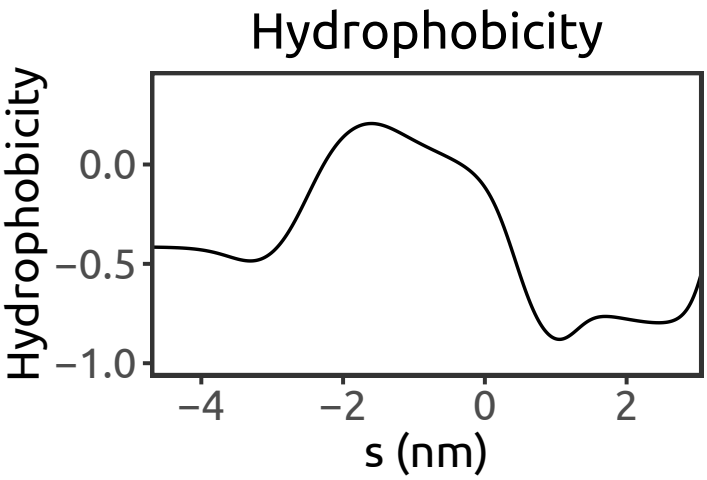
Simulation result:
barrier to water

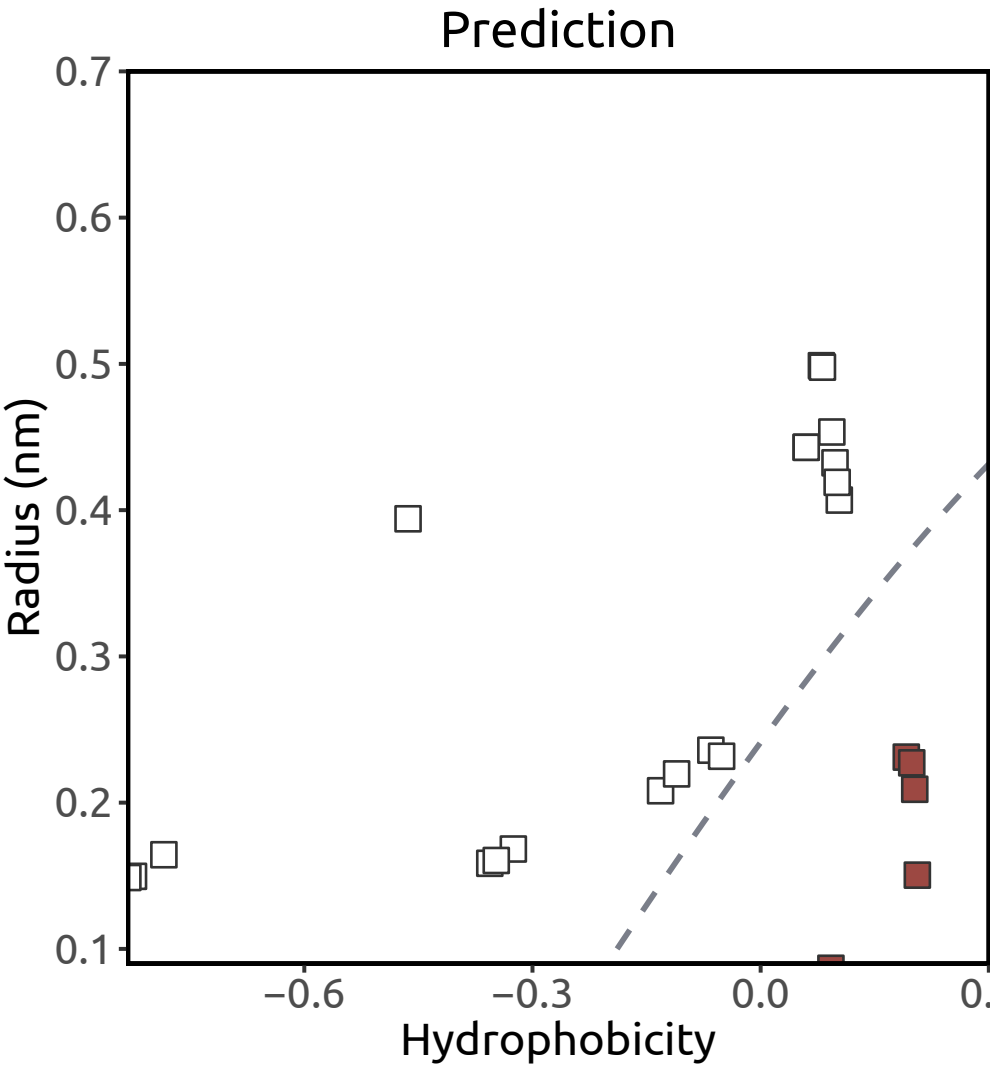
TRPV6 (PDB ID: 5WO6)

Rattus norvegicus
X–ray (3.31 Å)

Singh et al., 2017







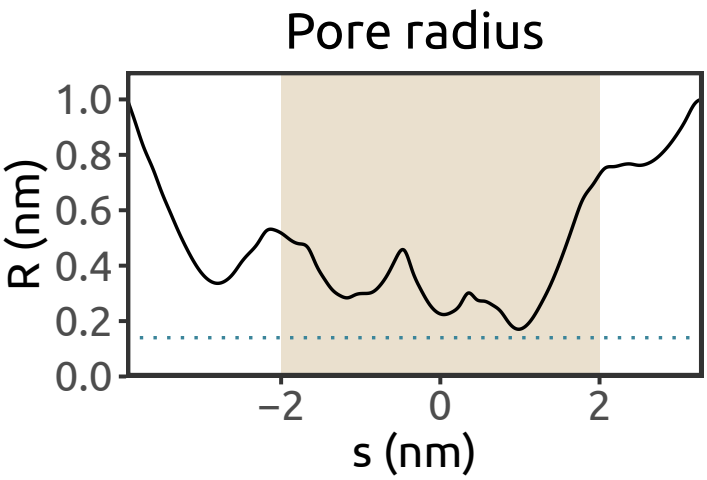
Heuristic score:
1.34 (n = 8)

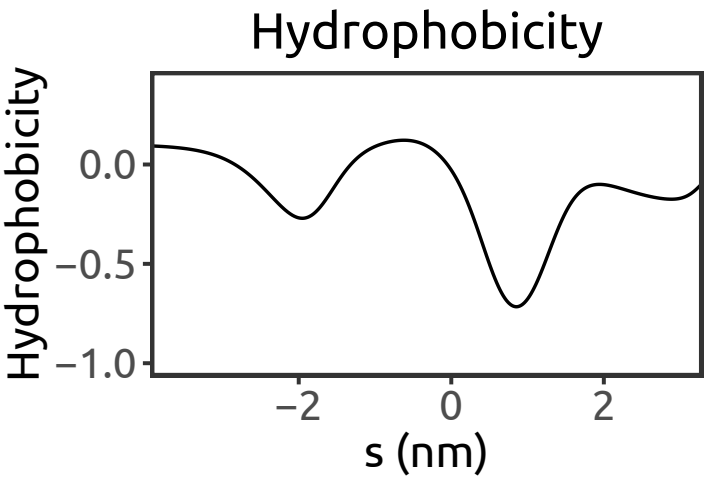
Simulation result:
barrier to water

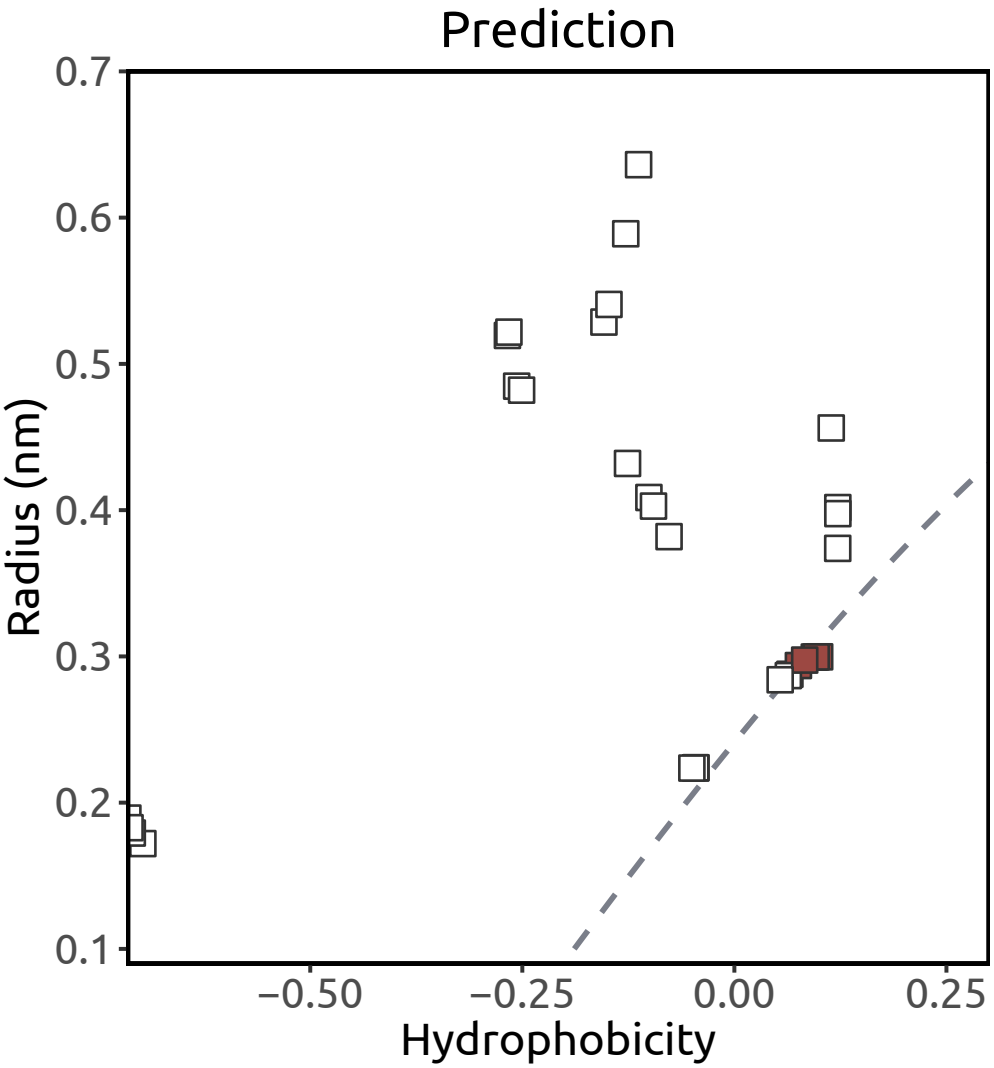
TRPV6 (PDB ID: 6BO8)

Homo sapiens
cryo–EM (3.6 Å)

McGoldrick et al., 2018







Heuristic score:
0.03 (n = 5)

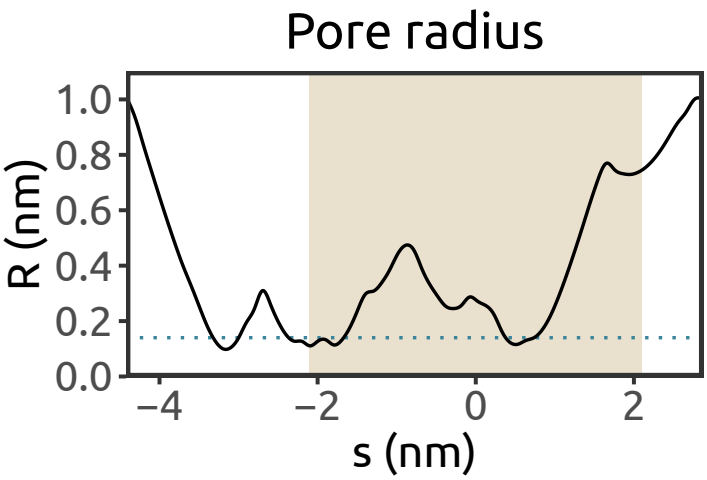
Simulation result:
hydrated channel

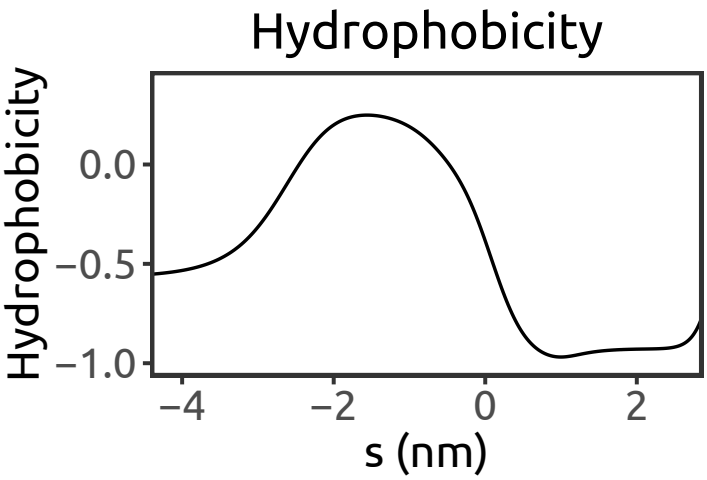
TRPV6 (PDB ID: 6BOB)

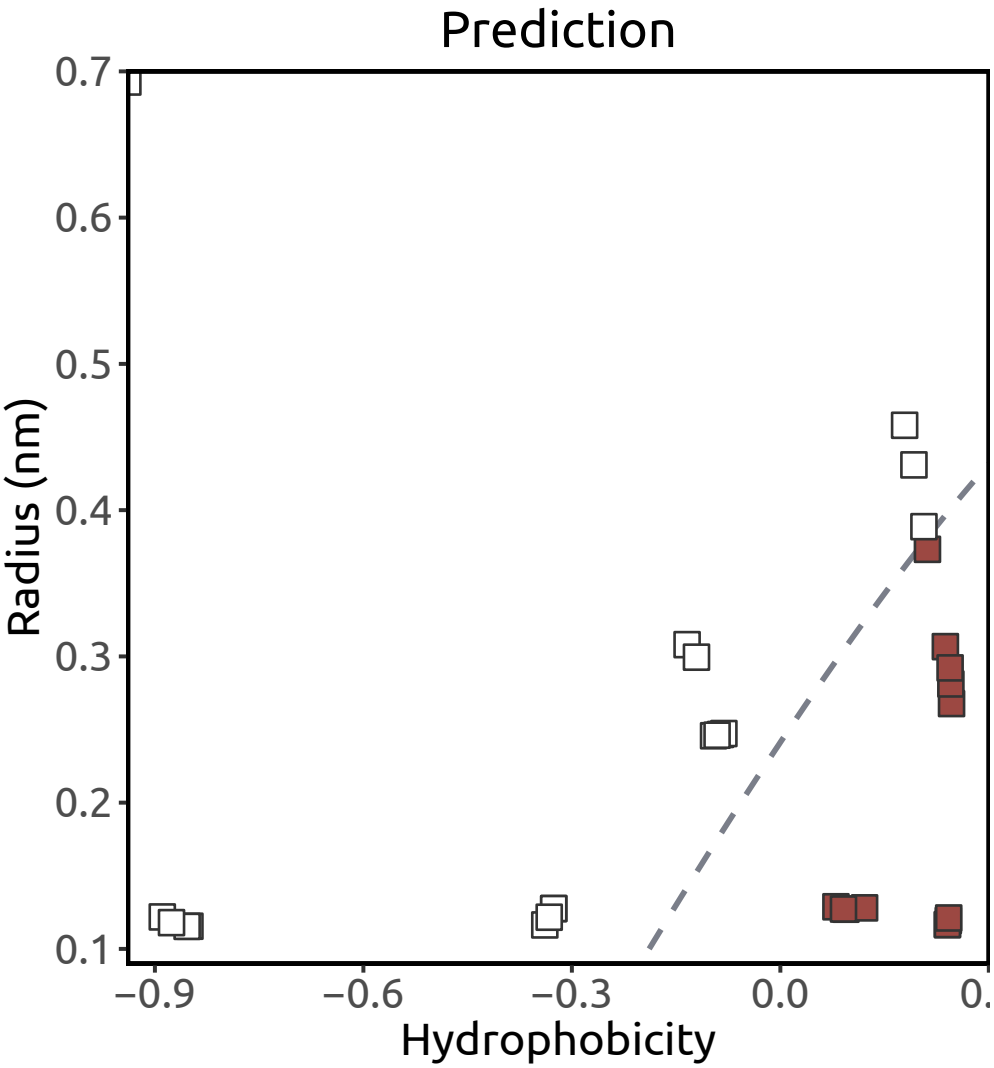
Homo sapiens

cryo–EM (3.9 Å)

McGoldrick et al., 2018







Heuristic score:

1.94 (n = 13)

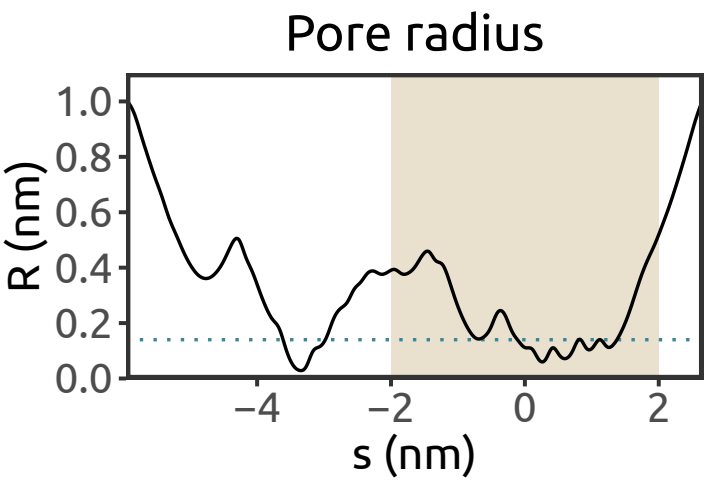
Simulation result:

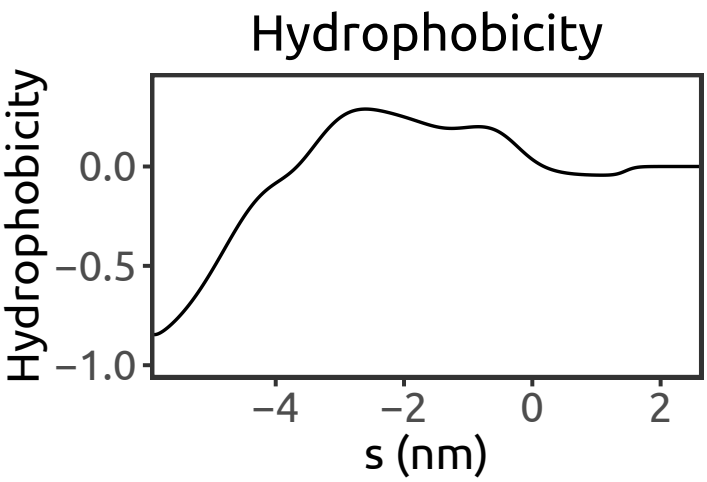
barrier to water

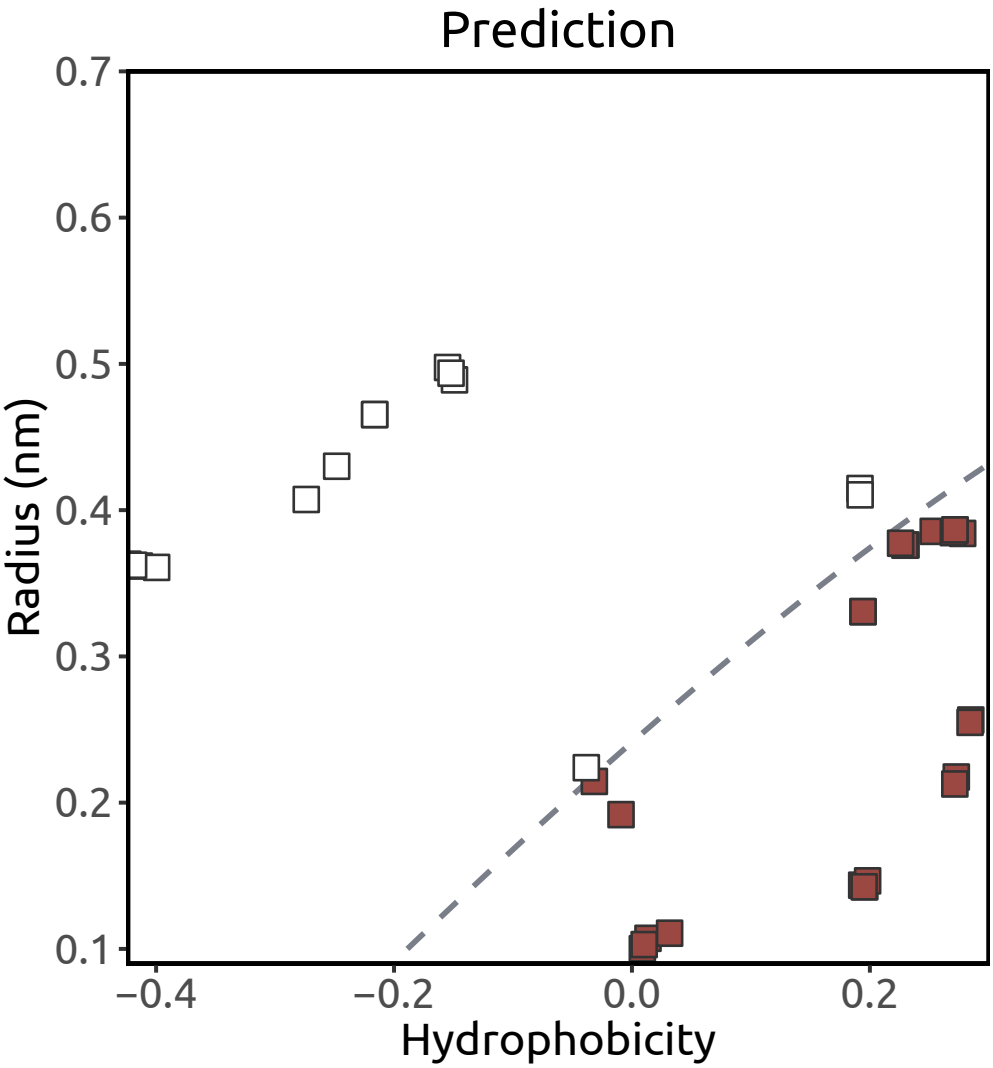
GsuK (PDB ID: 4GX5)

Geobacter sulfurreducens
X–ray (3.7 Å)

Kong et al., 2012







Heuristic score:
3.15 (n = 28)

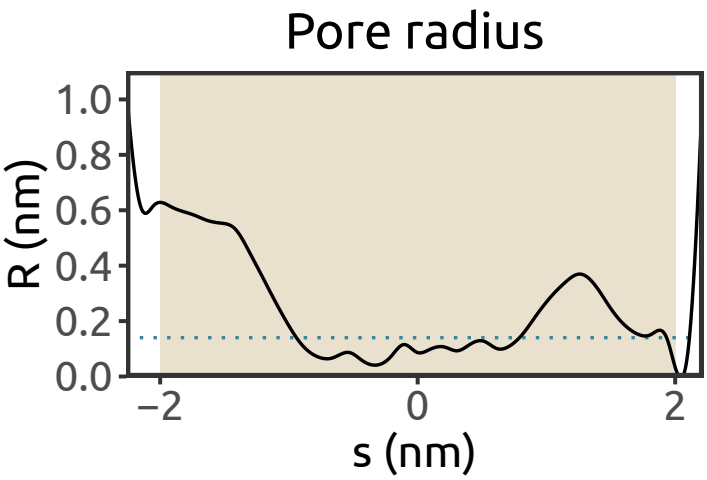
Simulation result:
barrier to water

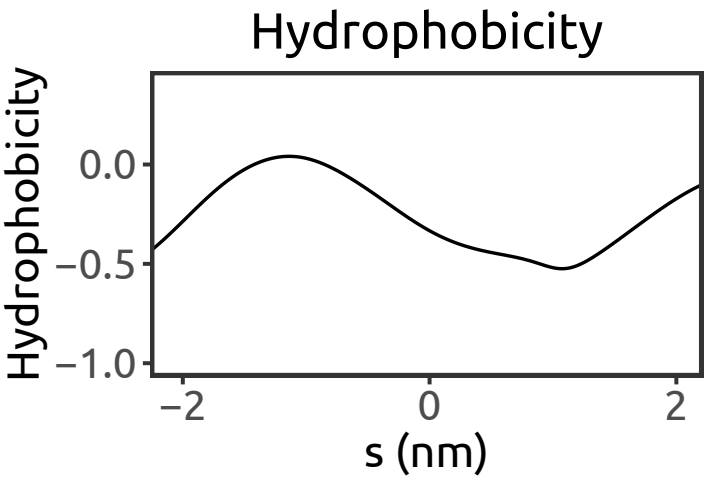
K2P10.1 (PDB ID: 4BW5)

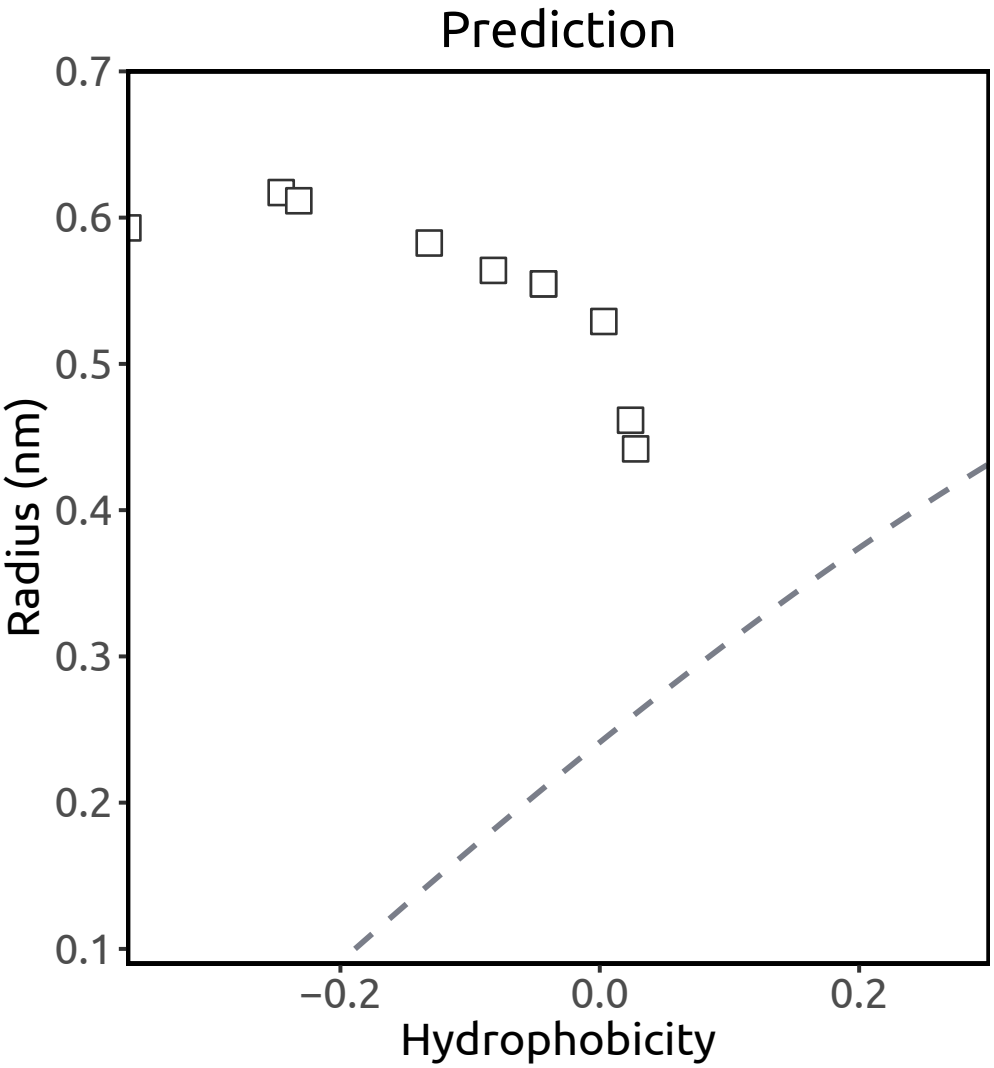
Homo sapiens

X–ray (3.2 Å)

Dong et al., 2015







Heuristic score:

0 (n = 0)

Simulation result:

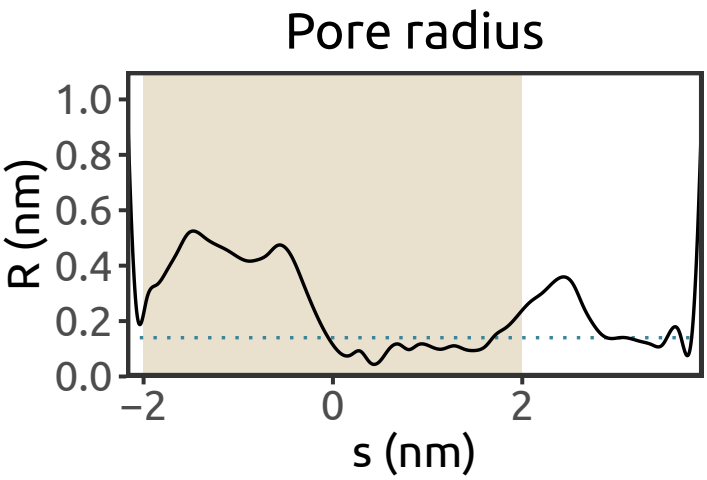
hydrated channel

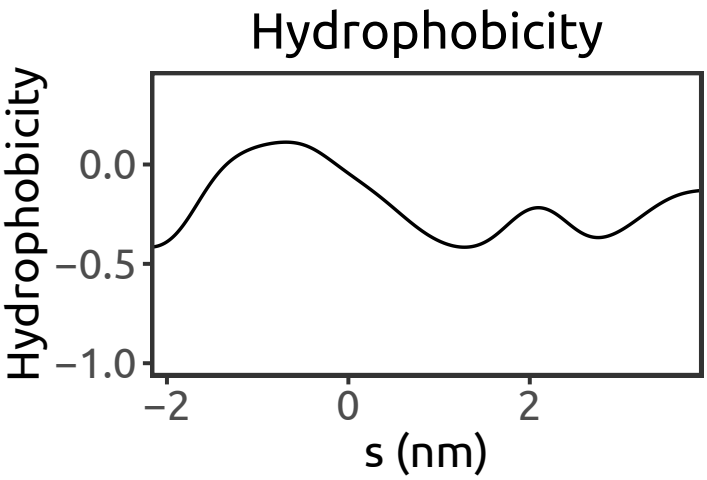
K2P10.1 (PDB ID: 4XDL)

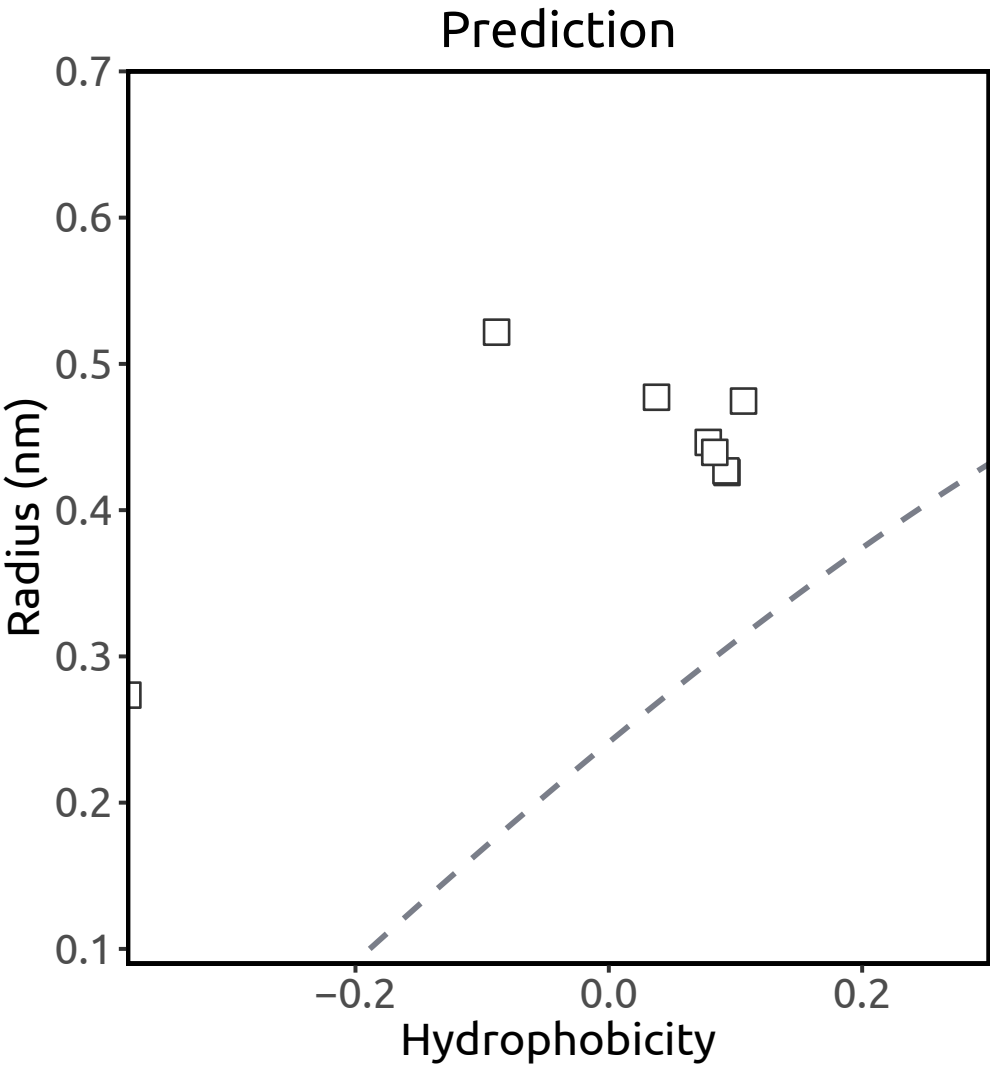
Homo sapiens

X–ray (3.5 Å)

Dong et al., 2015







Heuristic score:

0 (n = 0)

Simulation result:

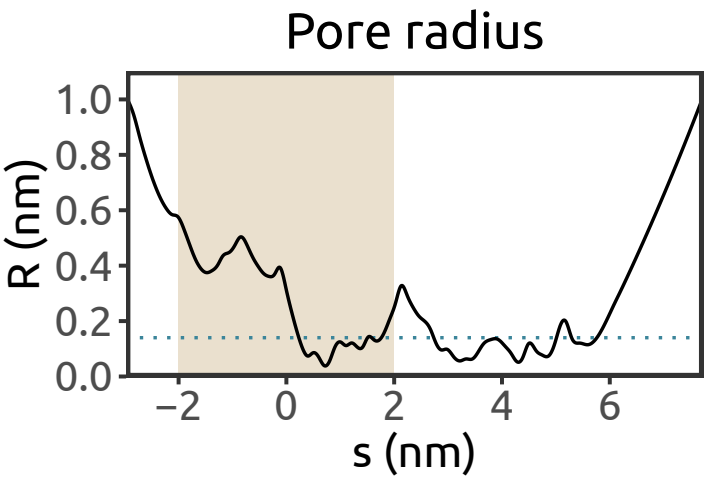
hydrated channel

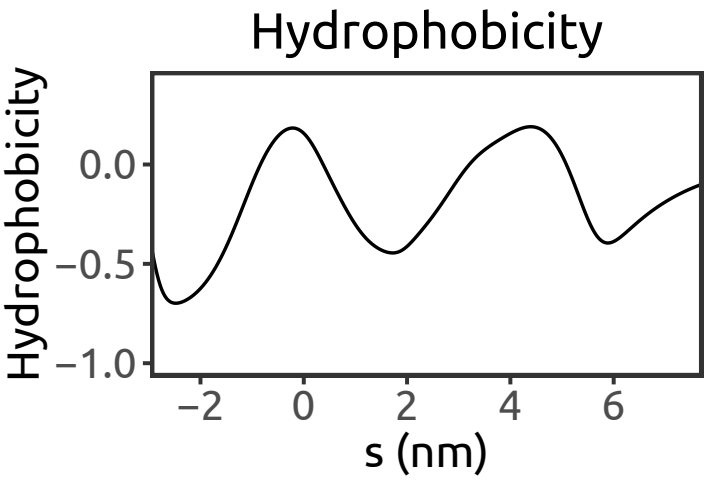
K2P1.1 (PDB ID: 3UKM)

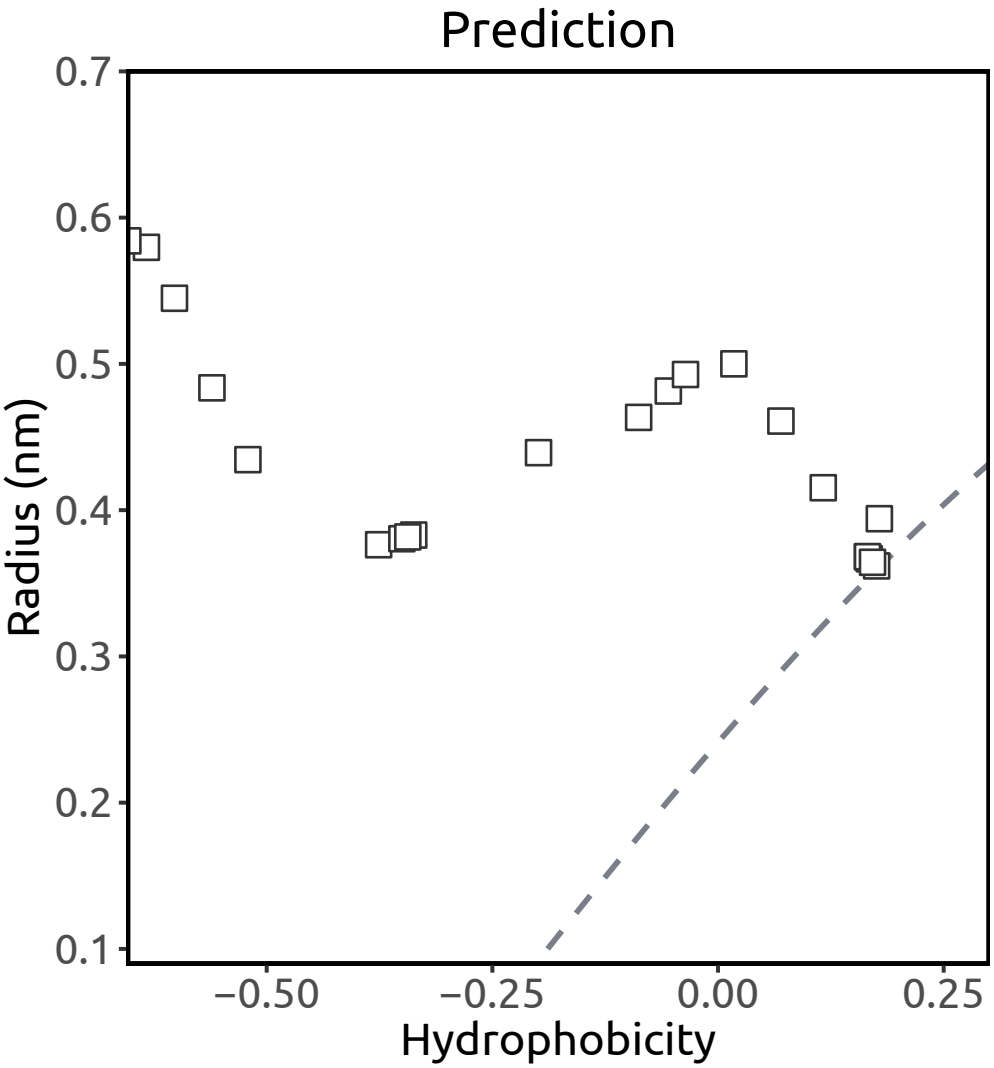
Homo sapiens

X–ray (3.4 Å)

Miller & Long, 2012







Heuristic score:

0 (n = 0)

Simulation result:

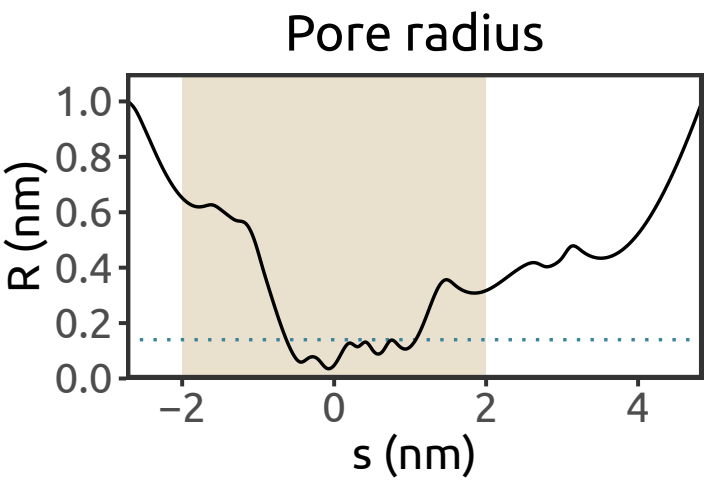
hydrated channel

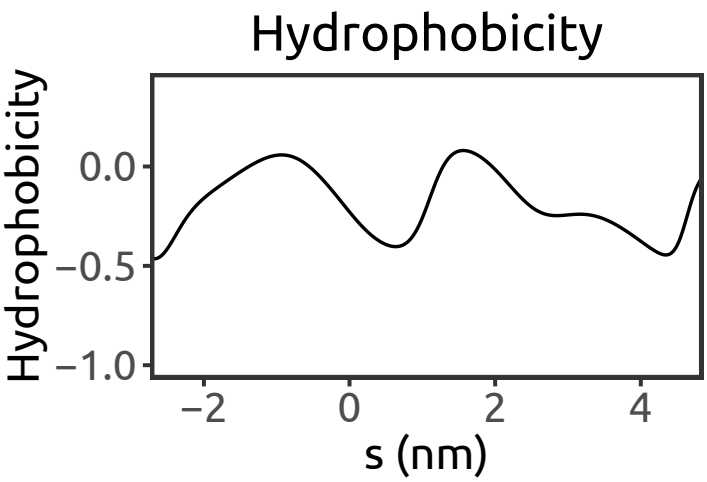
K2P2.1 (PDB ID: 5VKP)

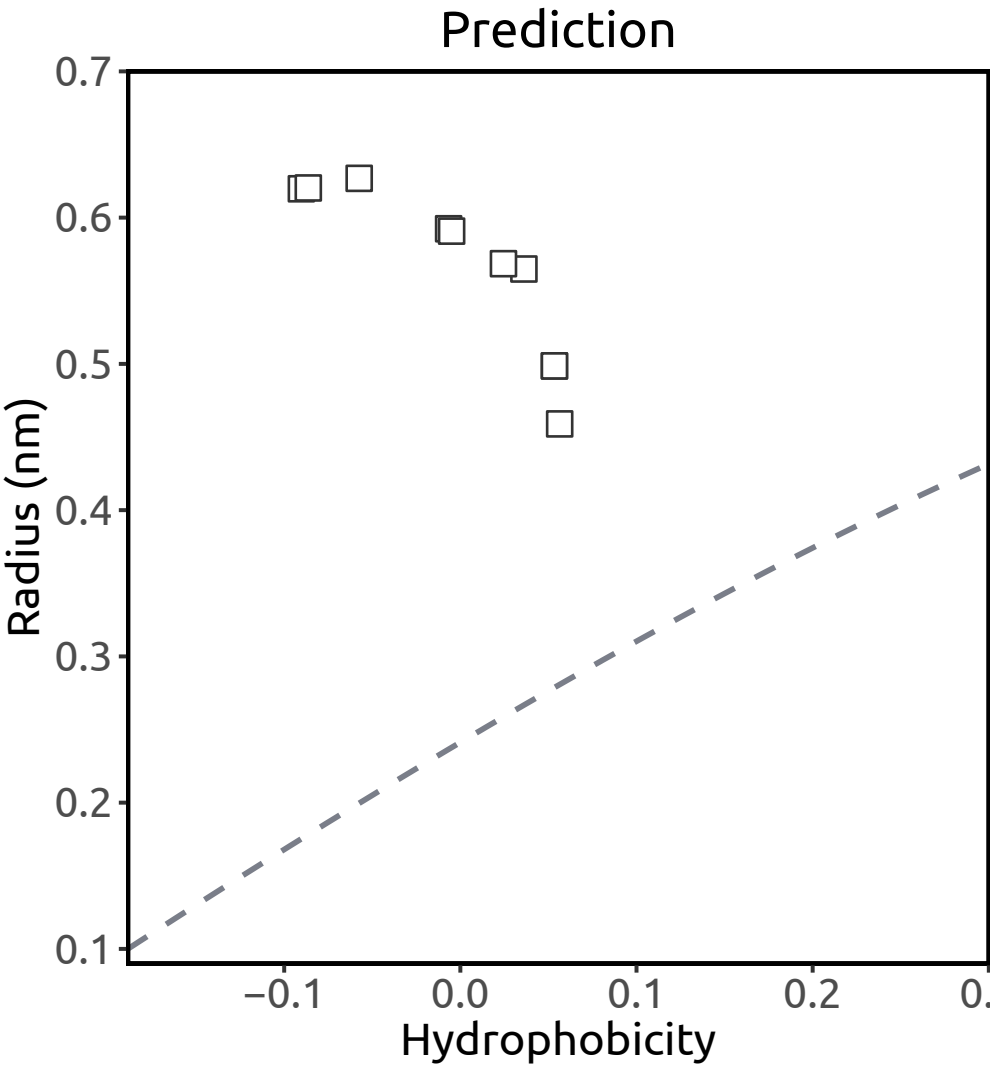
Mus musculus

X–ray (2.8 Å)

Lolicato et al., 2017







Heuristic score:

0 (n = 0)

Simulation result:

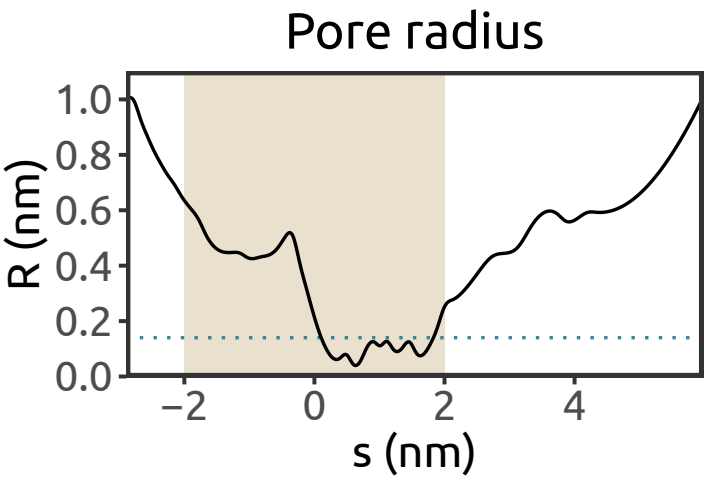
hydrated channel

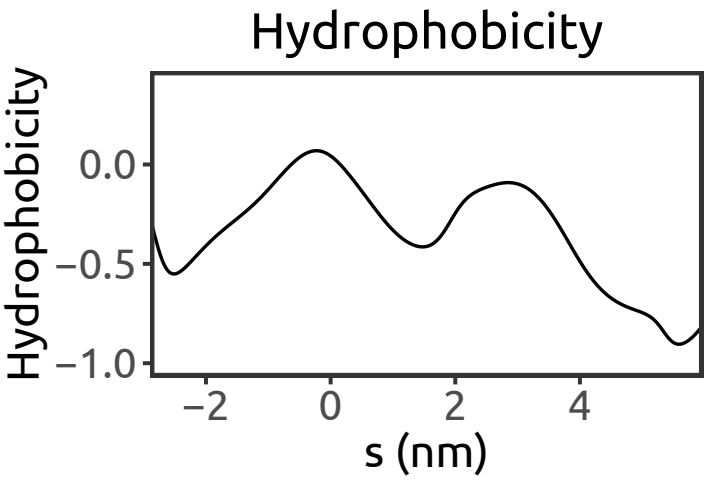
K2P4.1 (PDB ID: 4WFE)

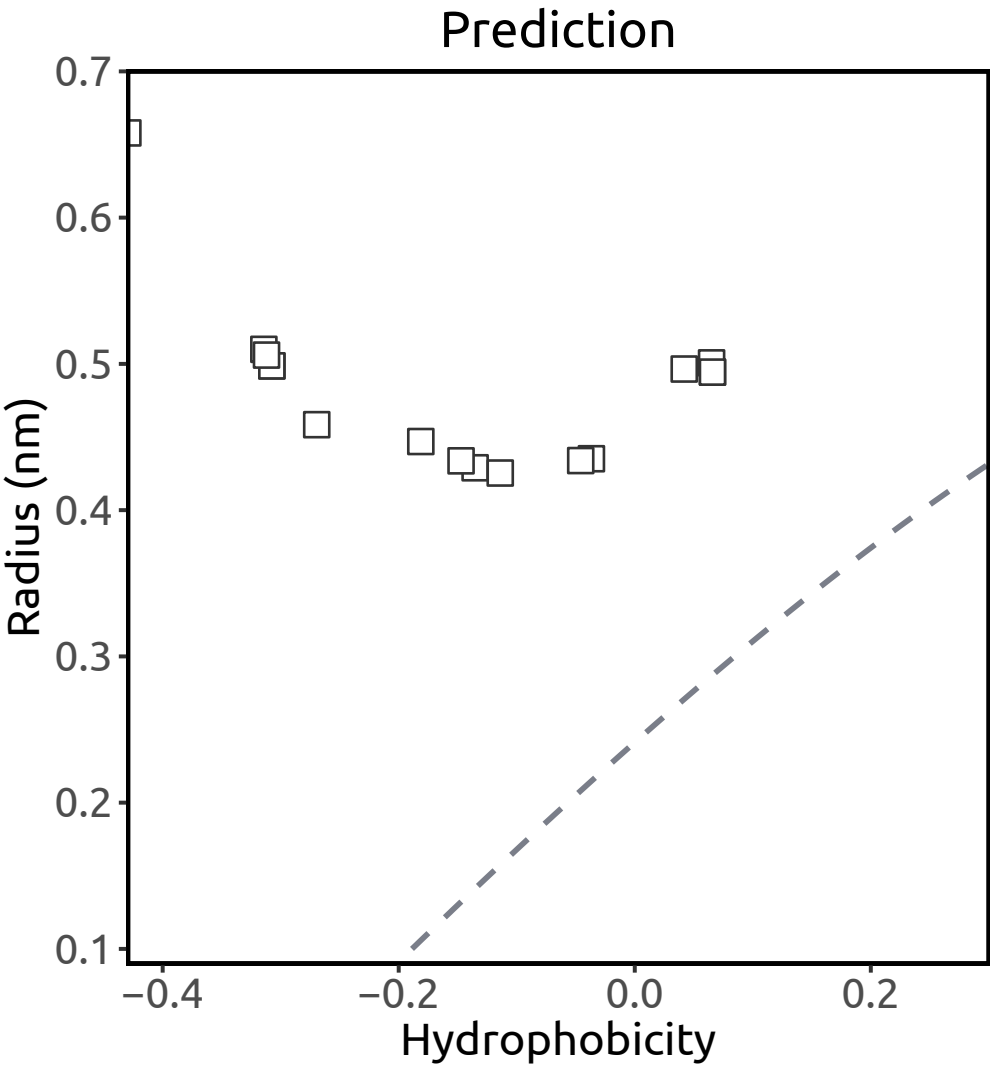
Homo sapiens

X–ray (2.5 Å)

Brohawn et al., 2014







Heuristic score:

0 (n = 0)

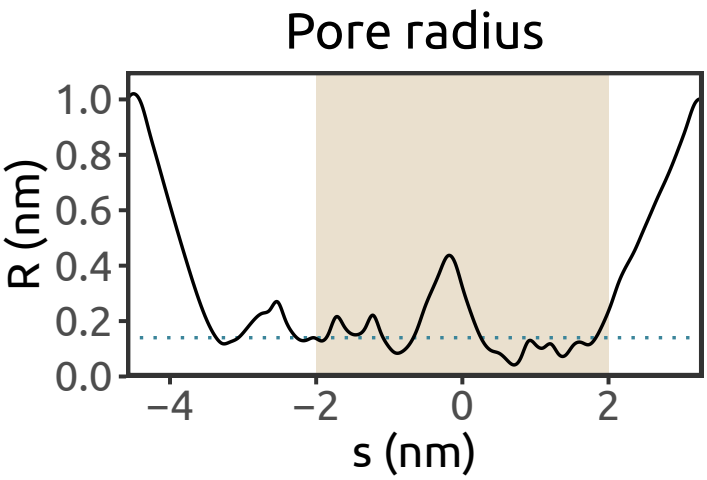
Simulation result:

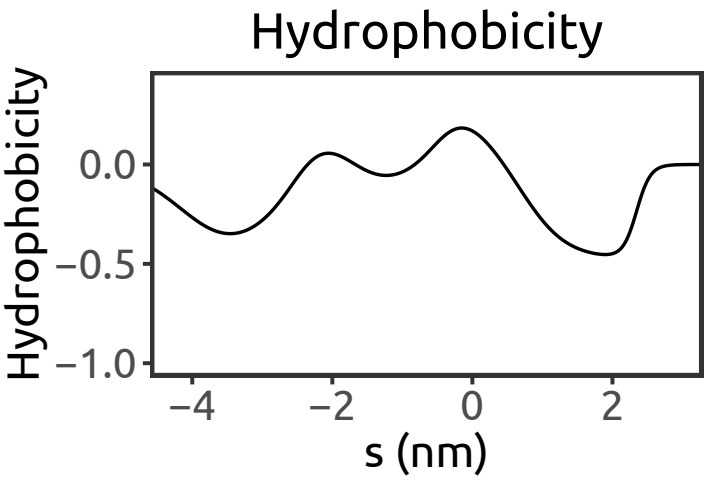
hydrated channel

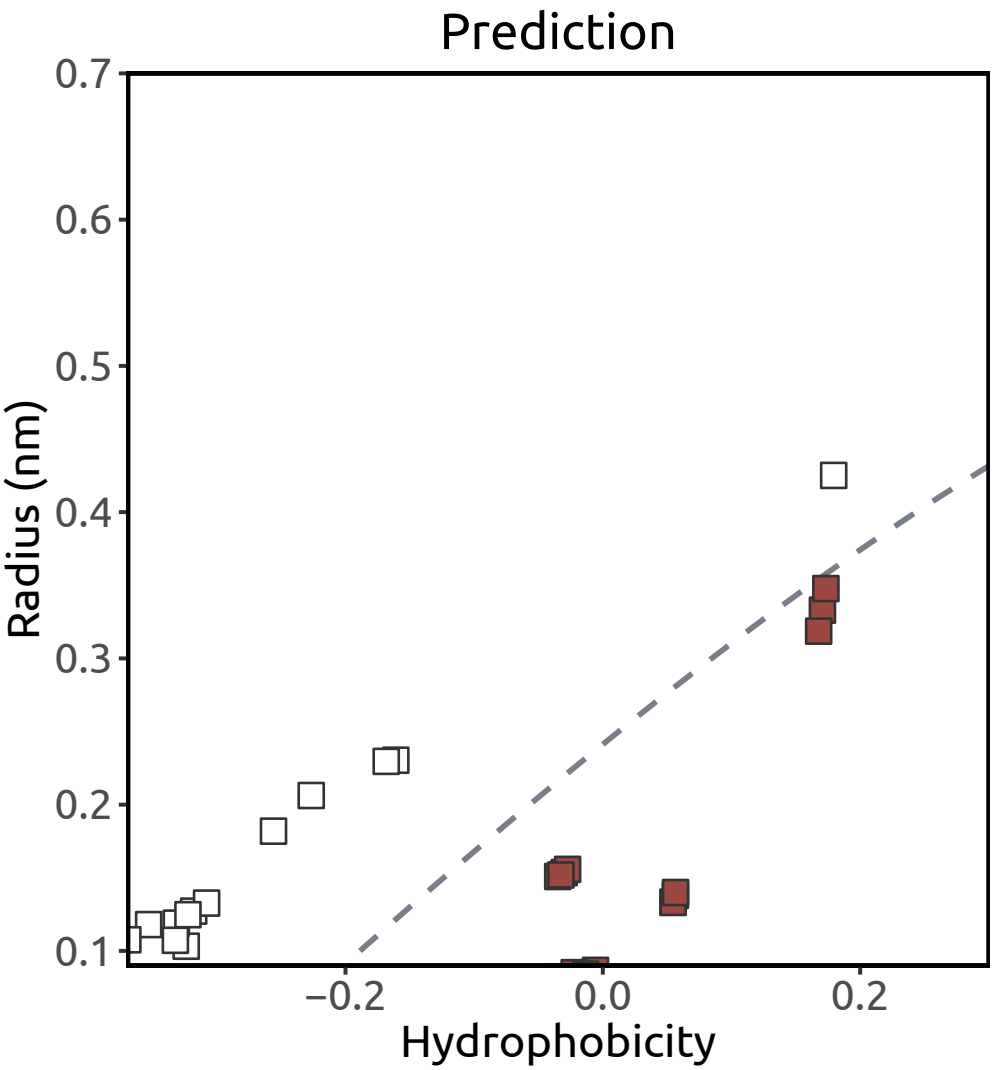
KcsA (PDB ID: 1K4C)

Streptomyces lividans
X–ray (2 Å)

Zhou et al., 2001







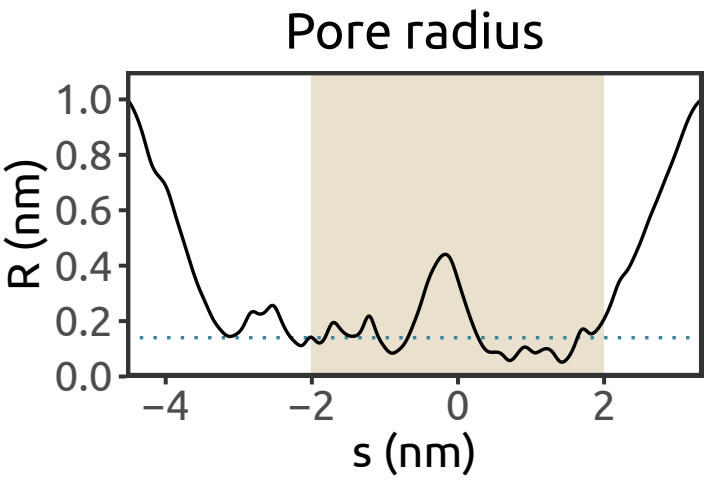
Heuristic score:
1.63 (n = 19)

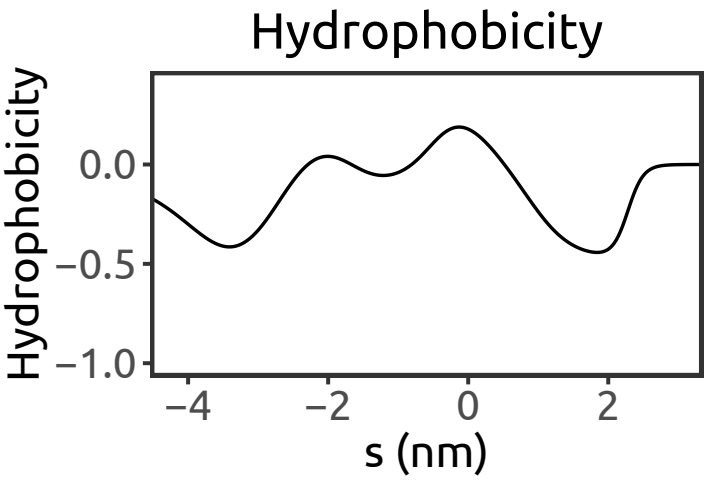
Simulation result:
barrier to water

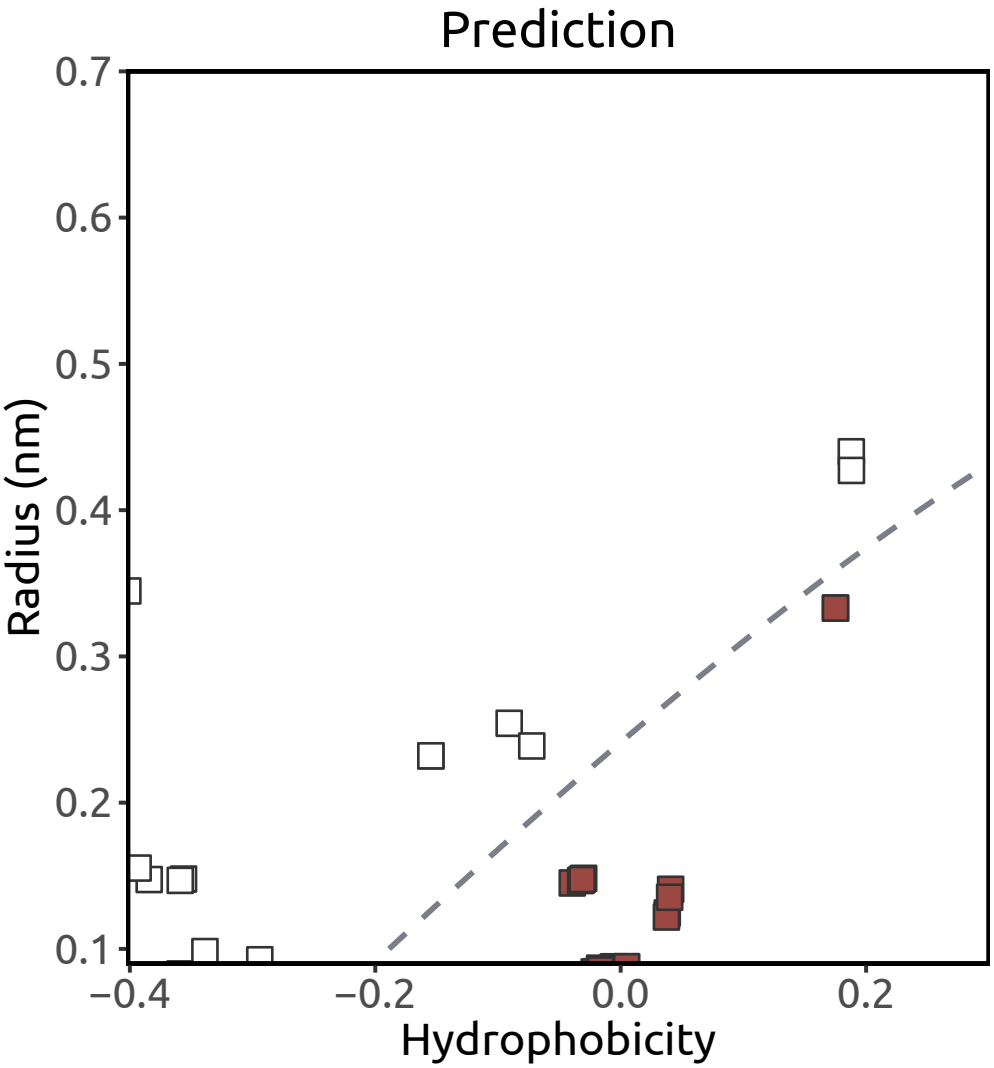
KcsA (PDB ID: 2ITD)

Streptomyces lividans
X–ray (2.7 Å)

Lockless et al., 2007







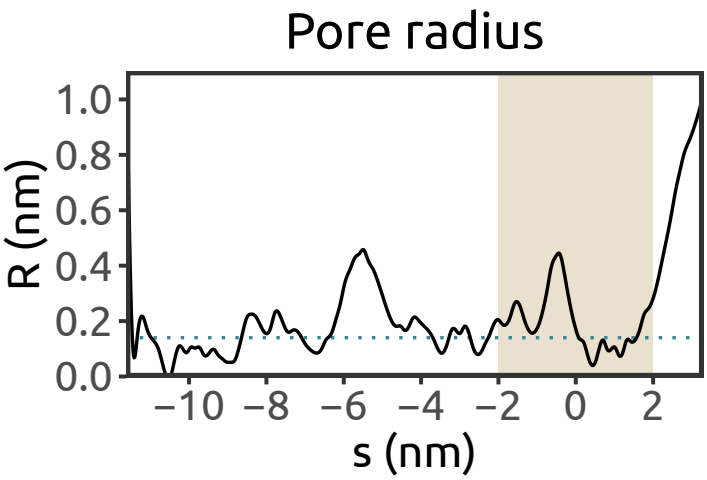
Heuristic score:
1.65 (n = 18)

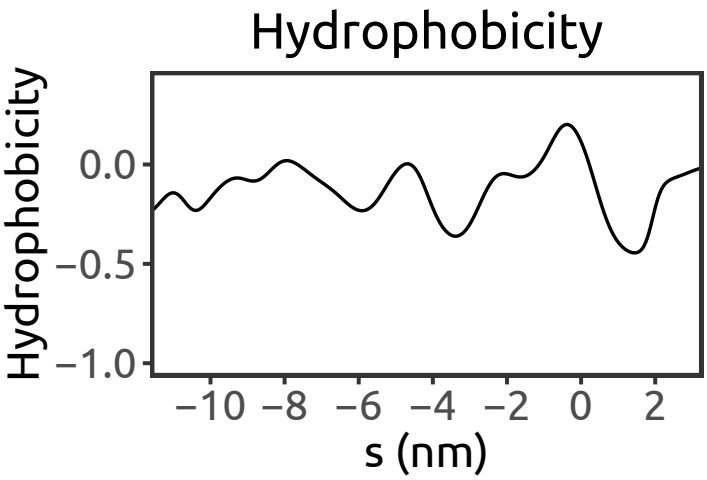
Simulation result:
barrier to water

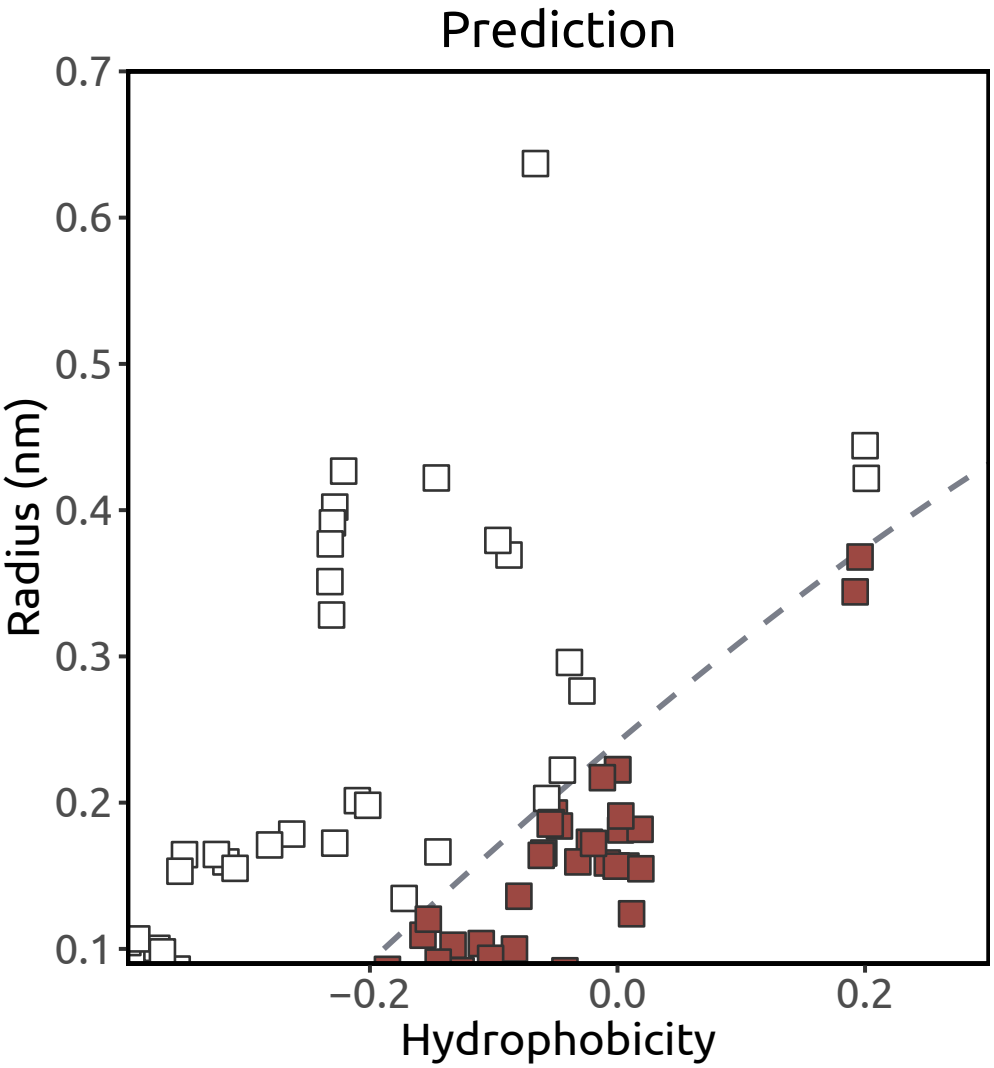
KcsA (PDB ID: 3EFF)

Streptomyces lividans
X–ray (3.8 Å)

Uysal et al., 2009







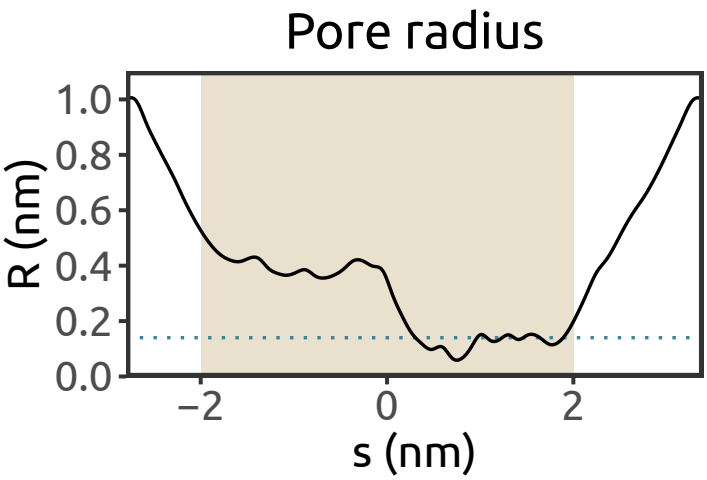
Heuristic score:
1.95 (n = 41)

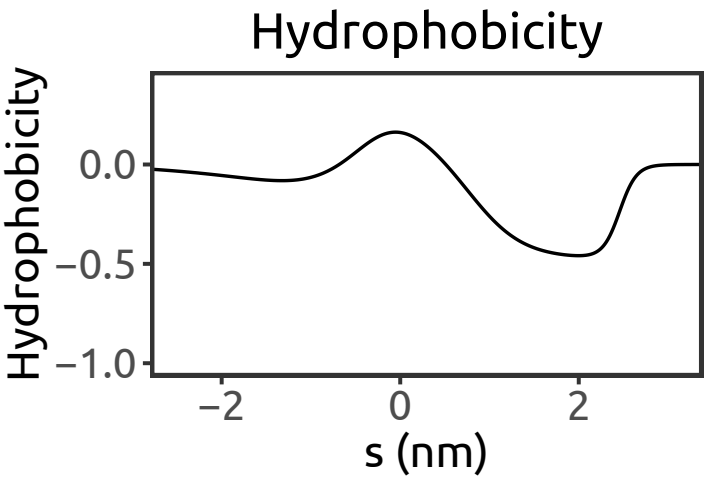
Simulation result:
barrier to water

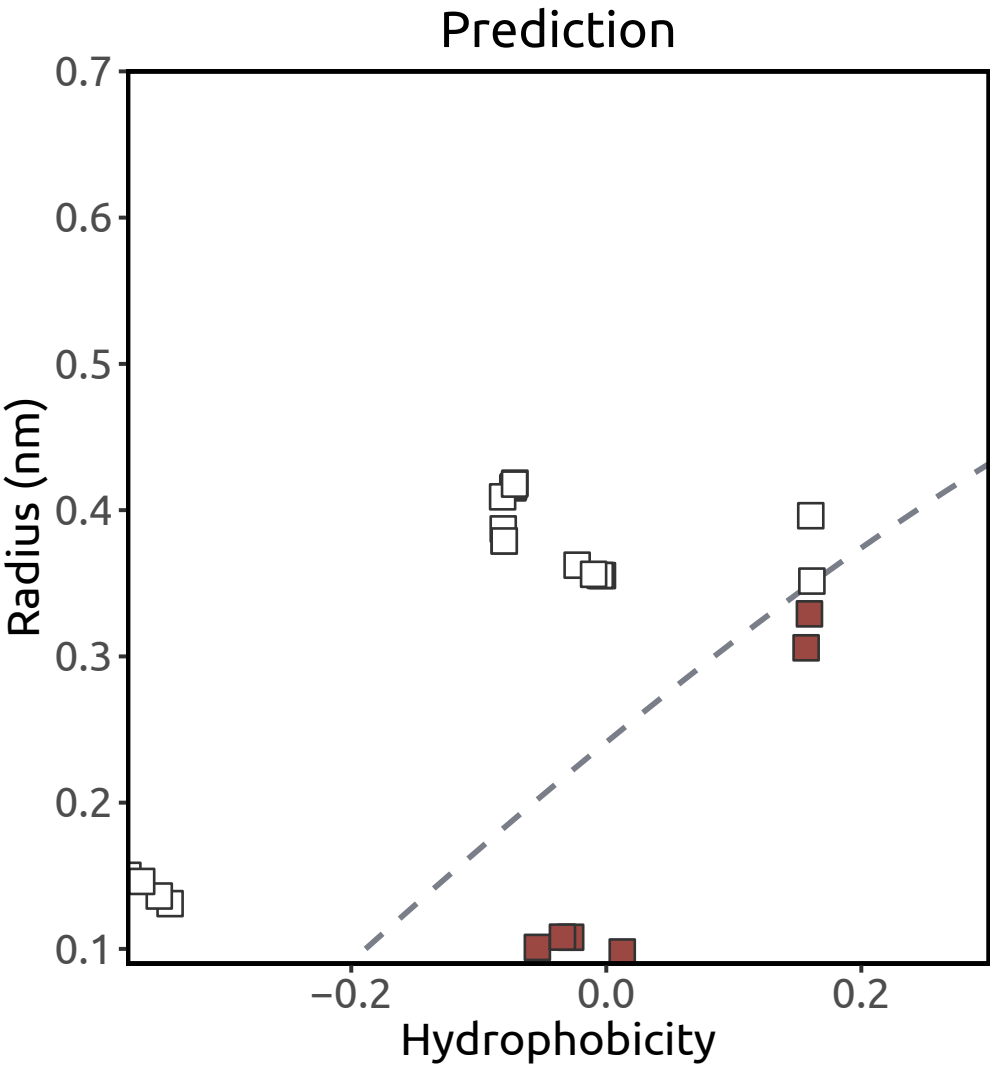
KcsA (PDB ID: 3FB5)

Streptomyces lividans
X–ray (2.8 Å)

Cuello et al., 2010







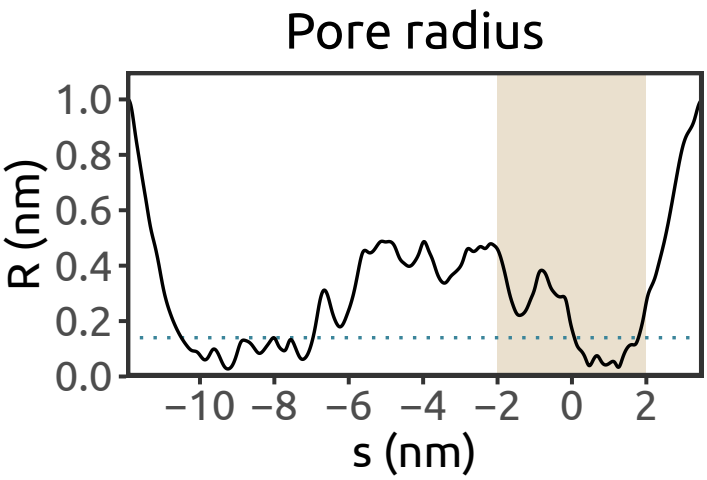
Heuristic score:
0.43 (n = 6)

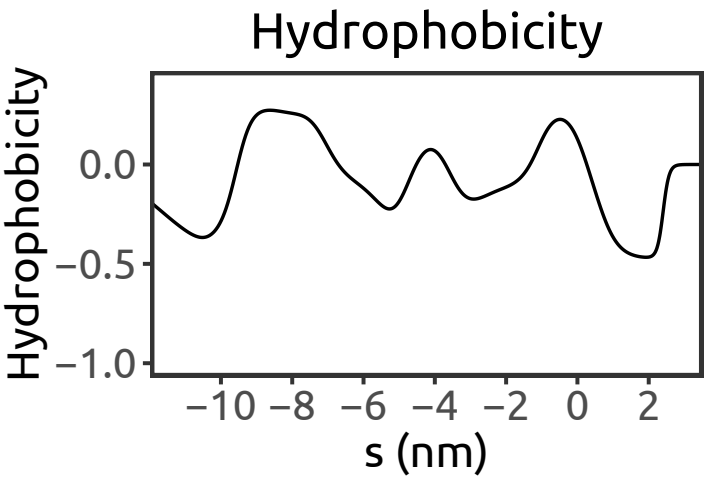
Simulation result:
hydrated channel

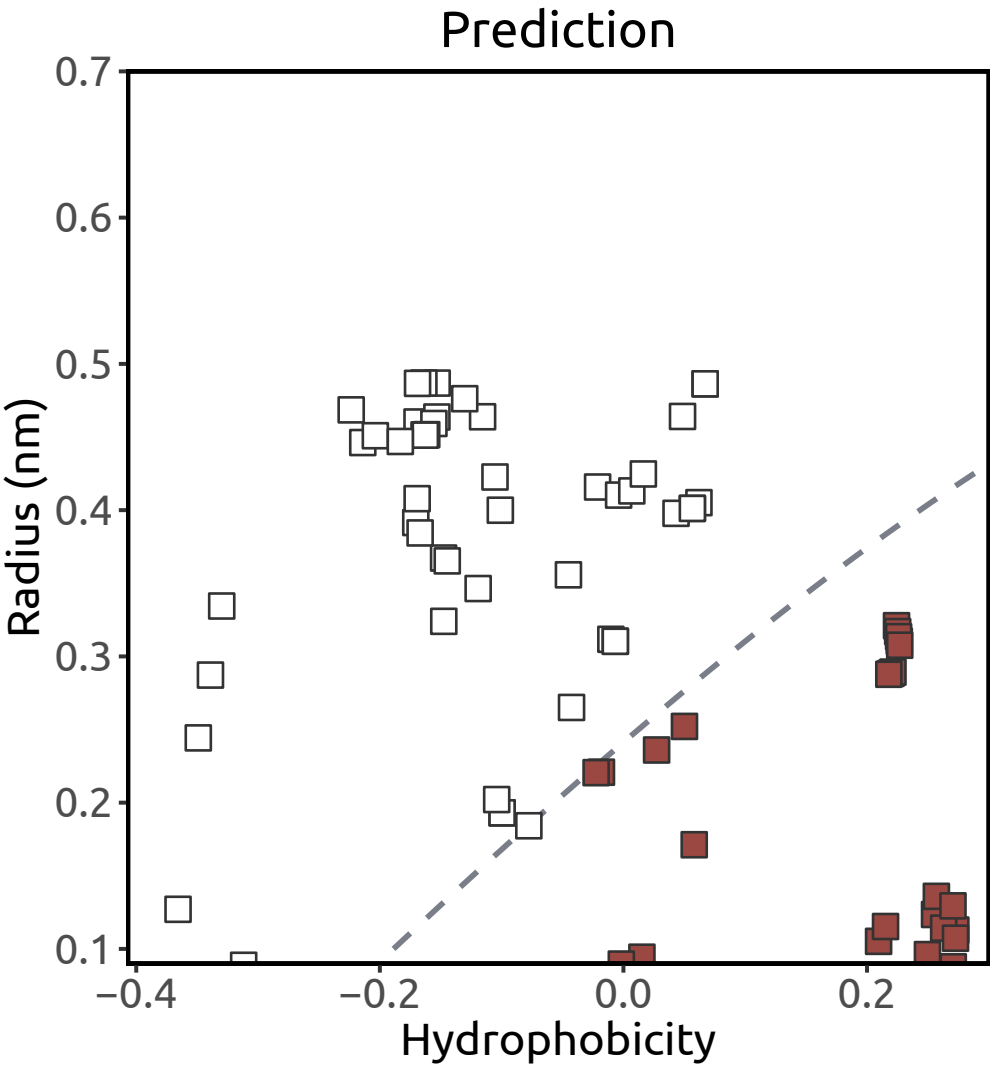
KcsA (PDB ID: 3PJS)

Streptomyces lividans
X–ray (3.8 Å)

Uysal et al., 2011







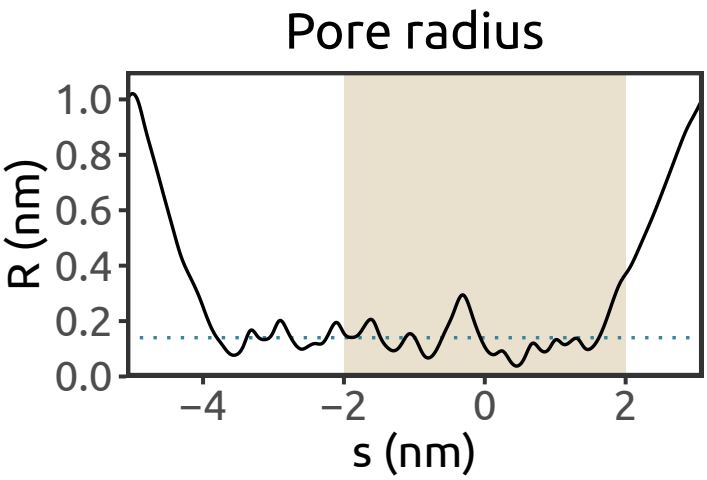
Heuristic score:
5 (n = 32)

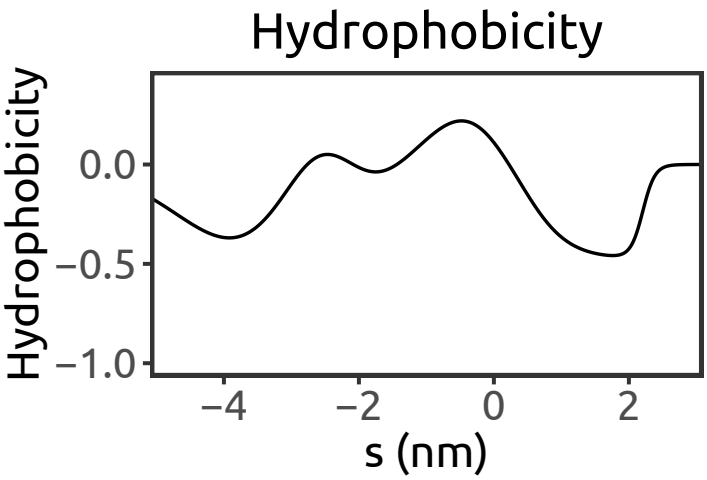
Simulation result:
barrier to water

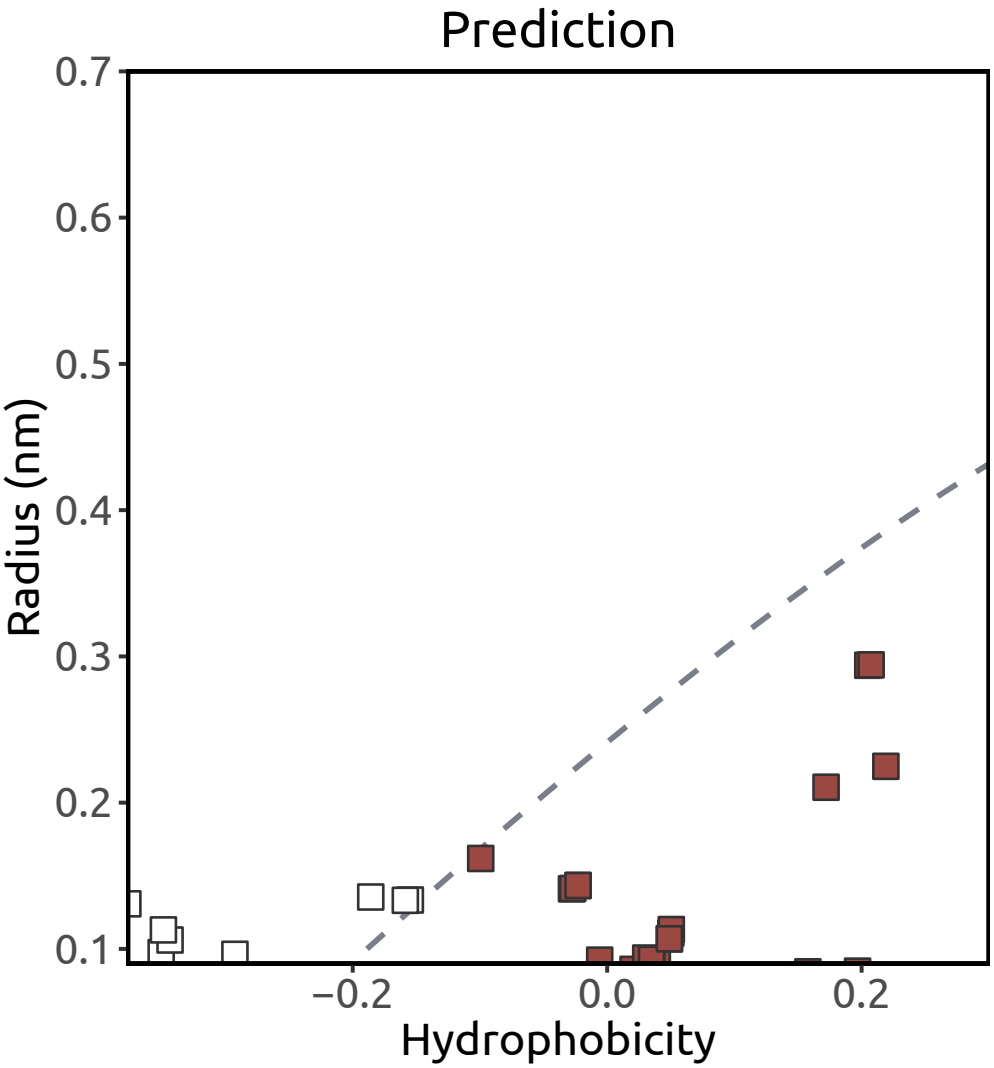
KcsA (PDB ID: 4UUJ)

Streptomyces lividans
X–ray (2.4 Å)

Lenaeus et al., 2014







Heuristic score:
3.17 (n = 25)

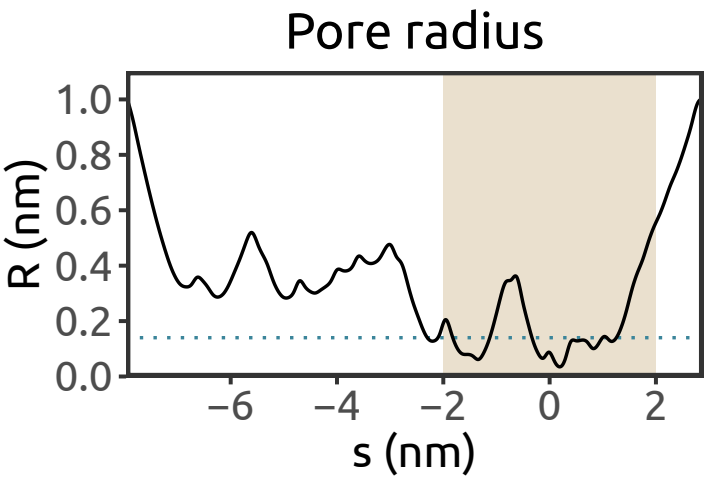
Simulation result:
barrier to water

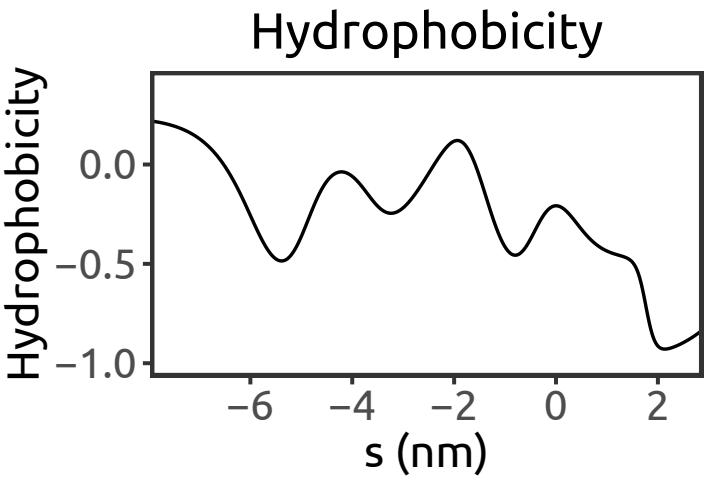
Kir2.2 (PDB ID: 3JYC)

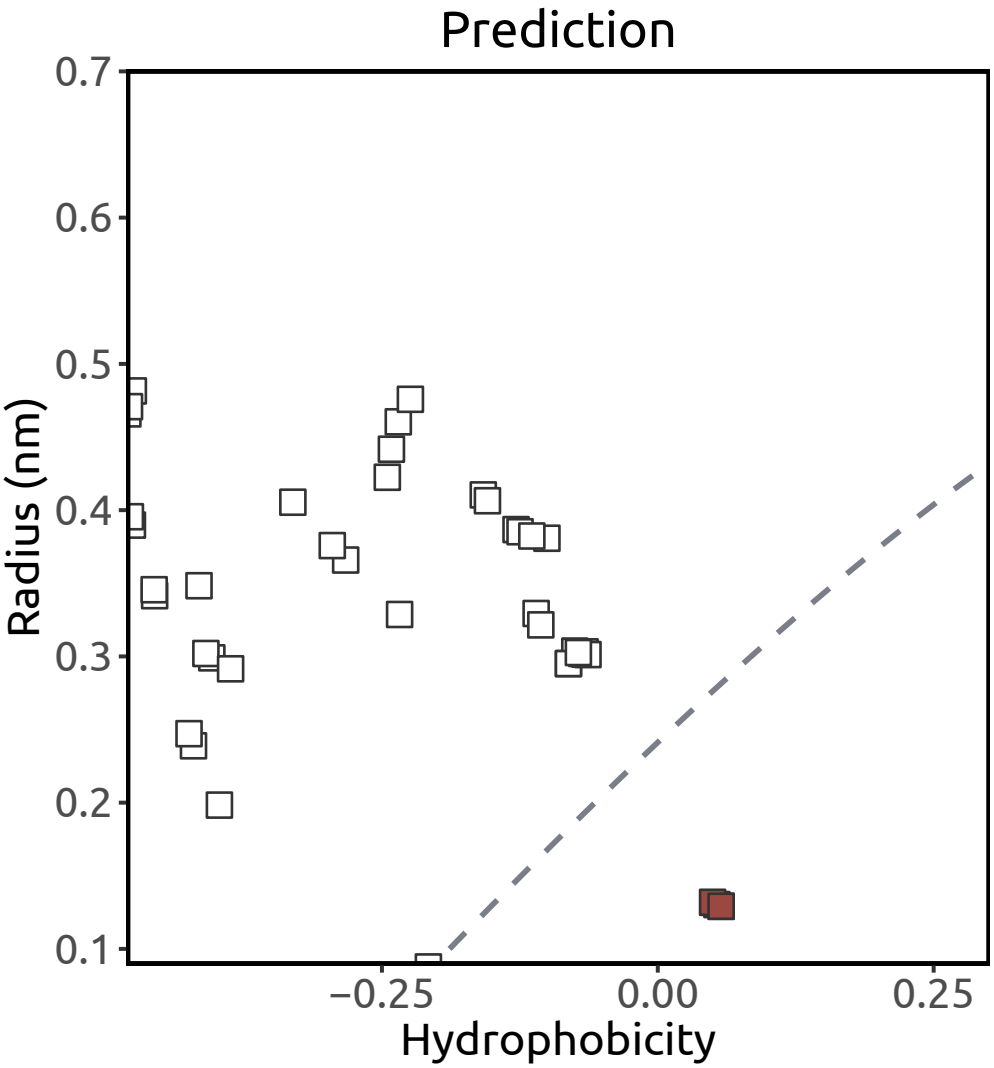
Gallus gallus

X–ray (3.11 Å)

Tao et al., 2009







Heuristic score:

0.88 (n = 8)

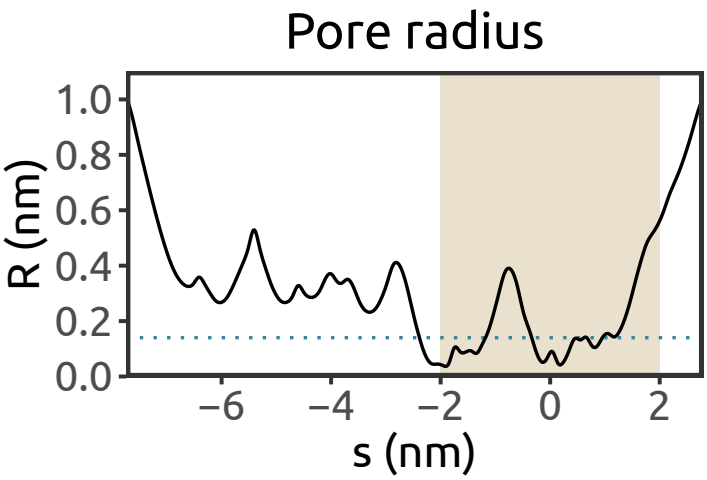
Simulation result:

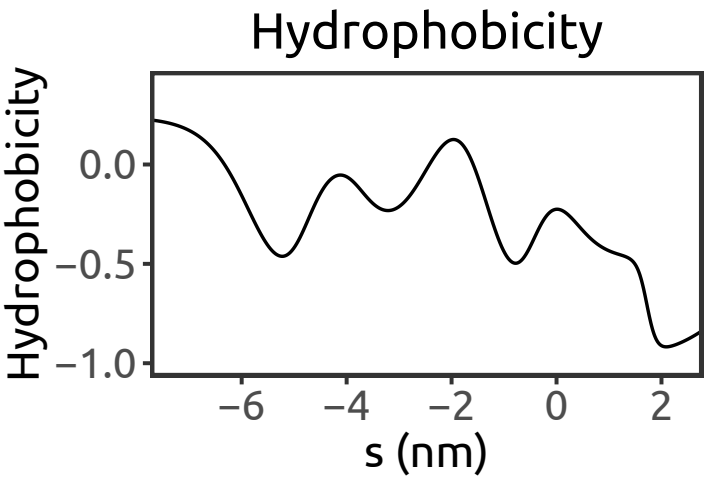
barrier to water

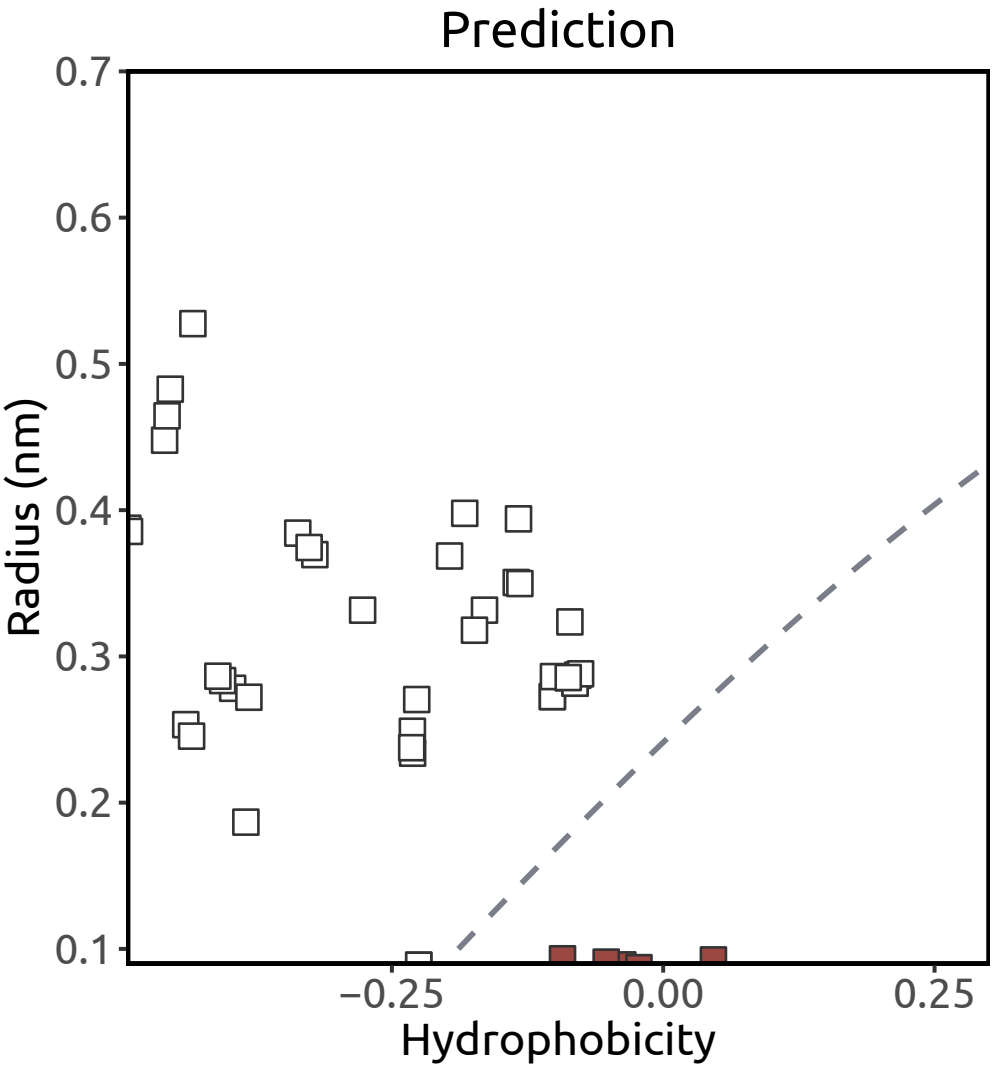
Kir2.2 (PDB ID: 3SPC)

Gallus gallus
X–ray (2.45 Å)

Hansen et al., 2011







Heuristic score:
1.15 (n = 8)

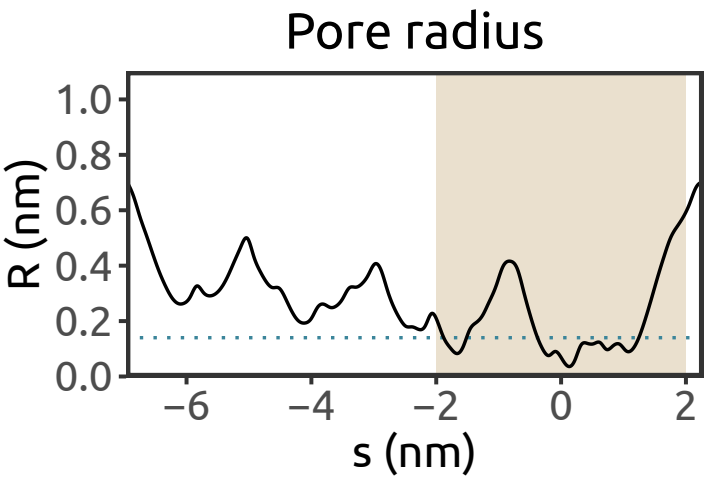
Simulation result:
barrier to water

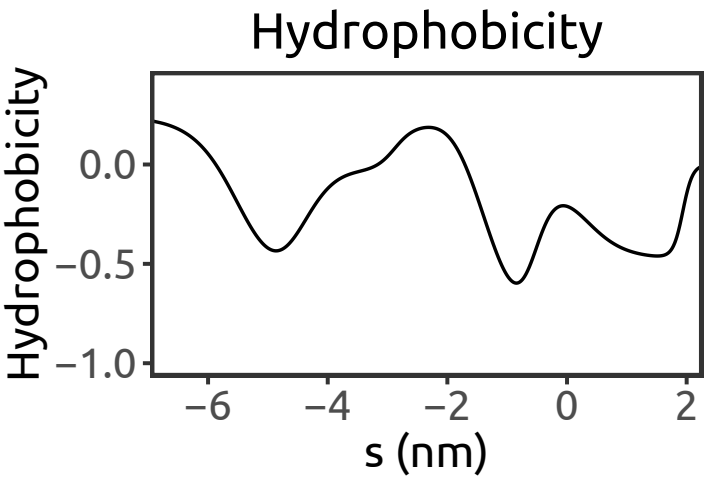
Kir2.2 (PDB ID: 3SPI)

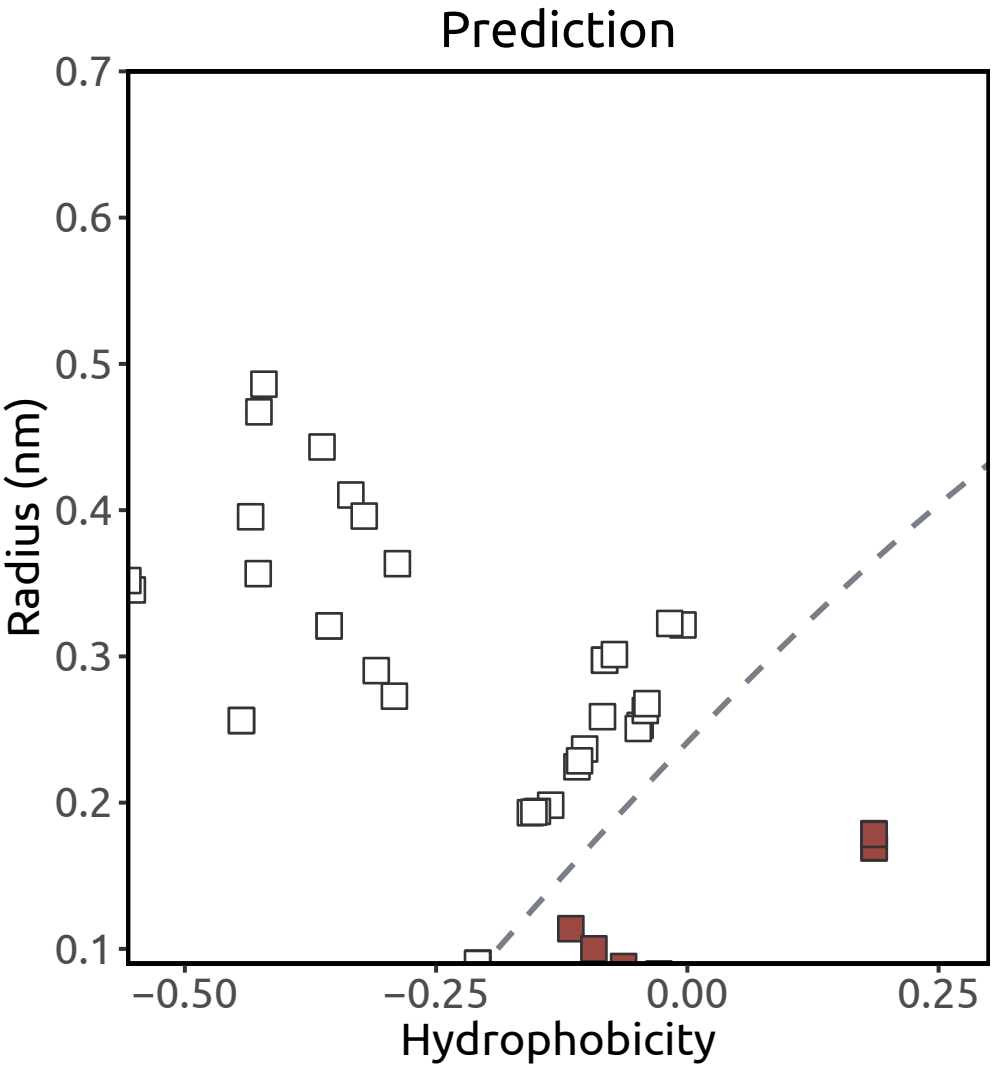
Gallus gallus

X–ray (3.31 Å)

Hansen et al., 2011







Heuristic score:

0.93 (n = 8)

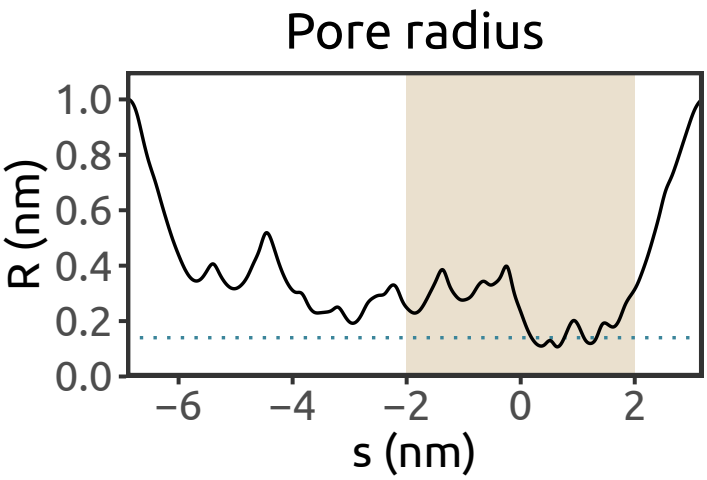
Simulation result:

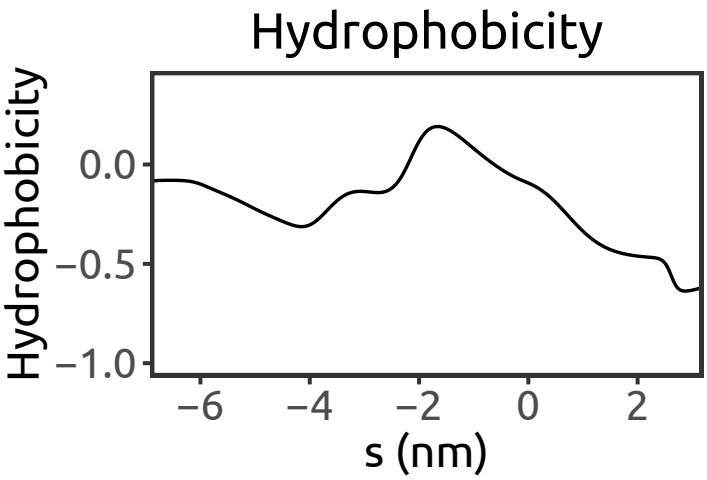
barrier to water

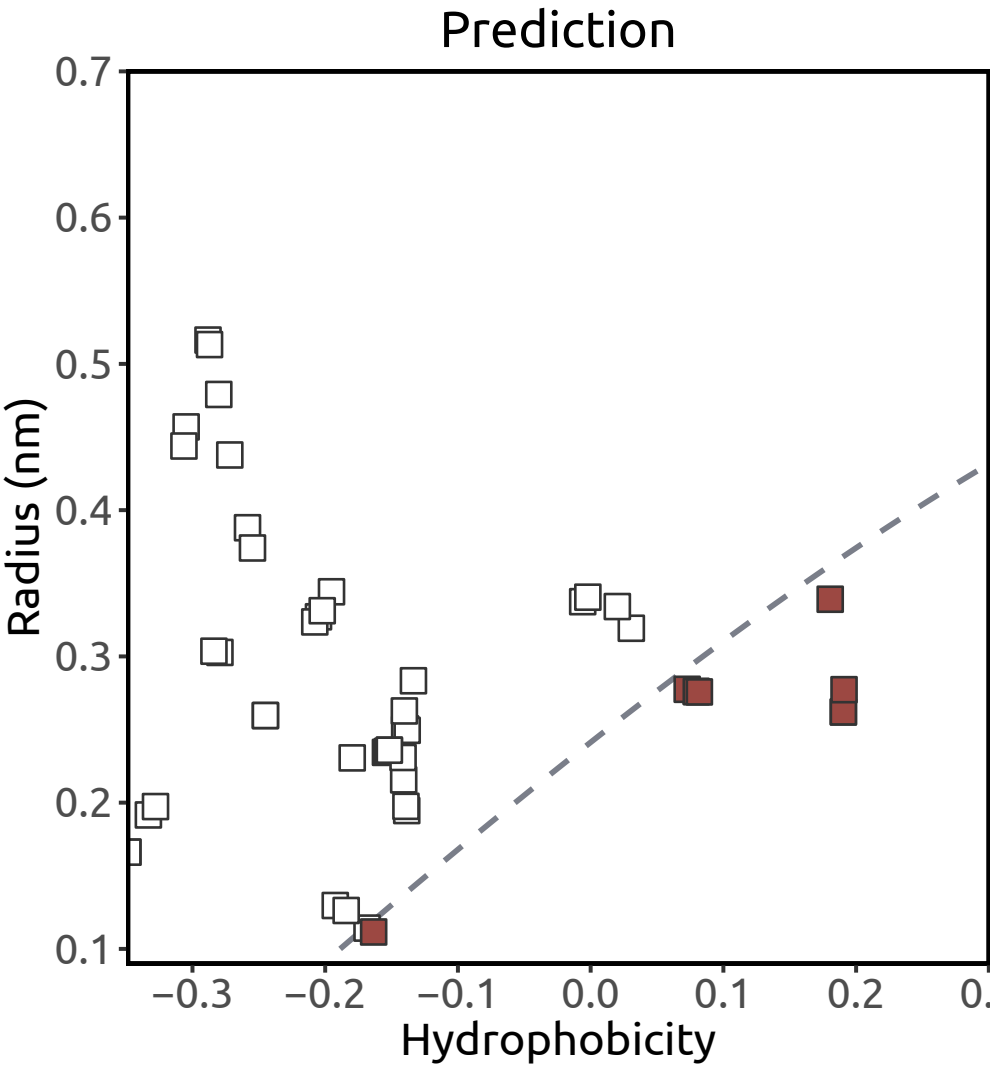
Kir3.2 (PDB ID: 3SYA)

Mus musculus
X–ray (2.98 Å)

Whorton & Mackinnon, 2011







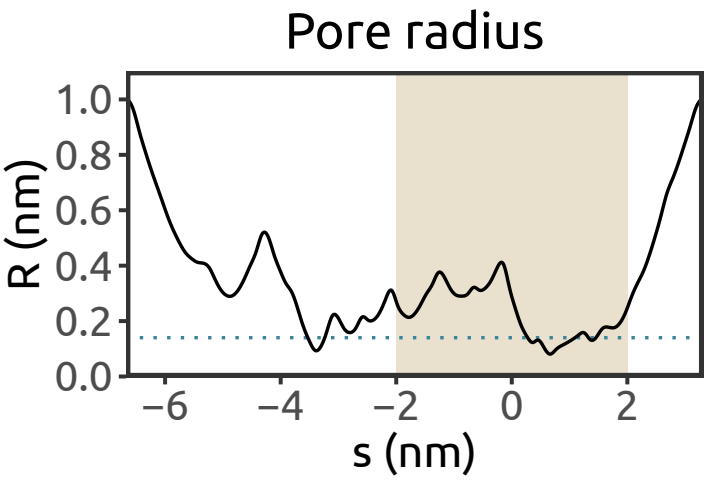
Heuristic score:
0.35 (n = 9)

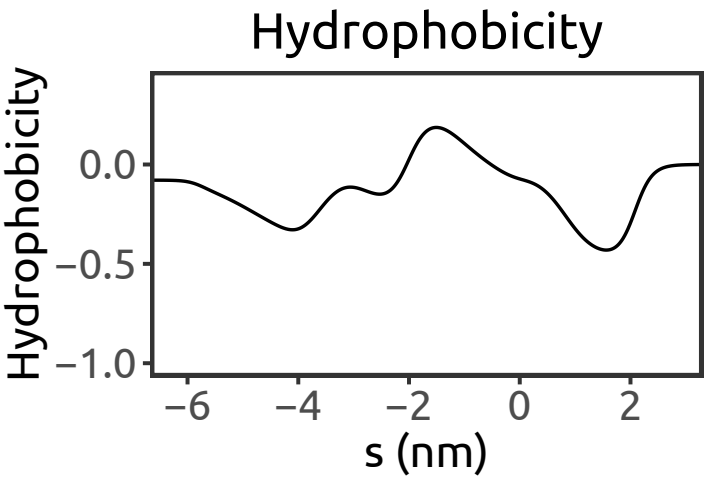
Simulation result:
barrier to water

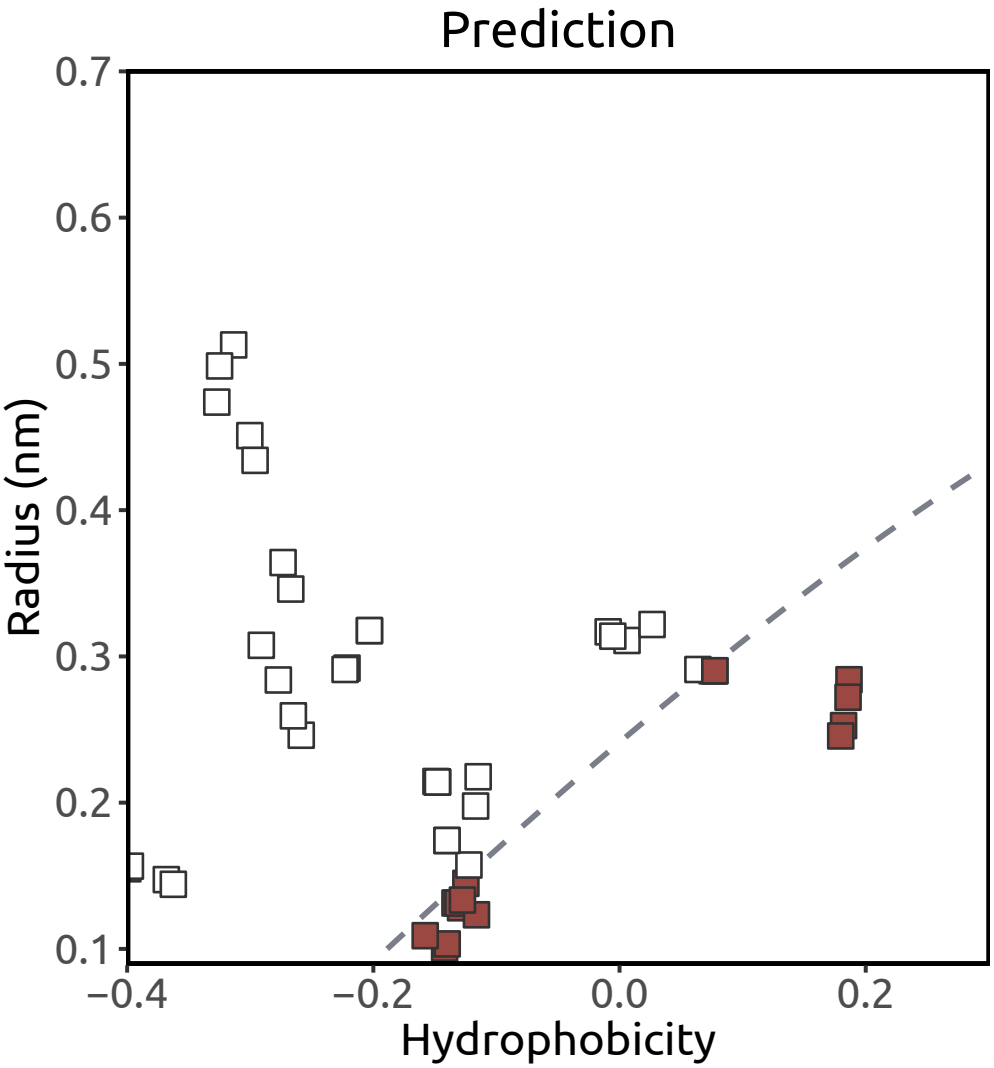
Kir3.2 (PDB ID: 3SYO)

Mus musculus
X–ray (3.54 Å)

Whorton & Mackinnon, 2011







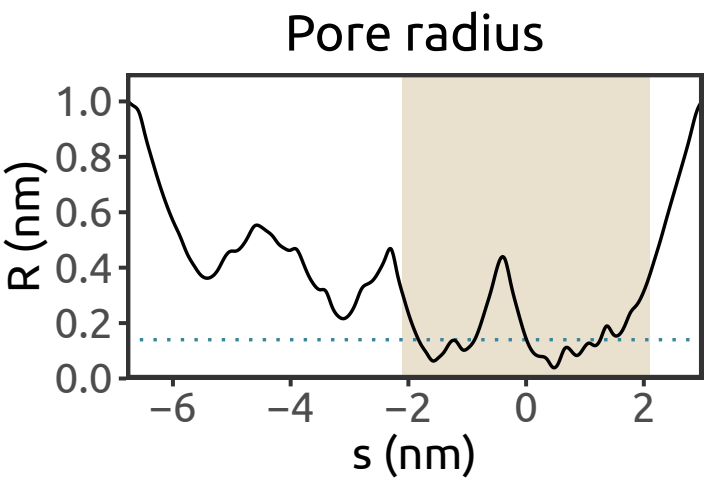
Heuristic score:
0.5 (n = 16)

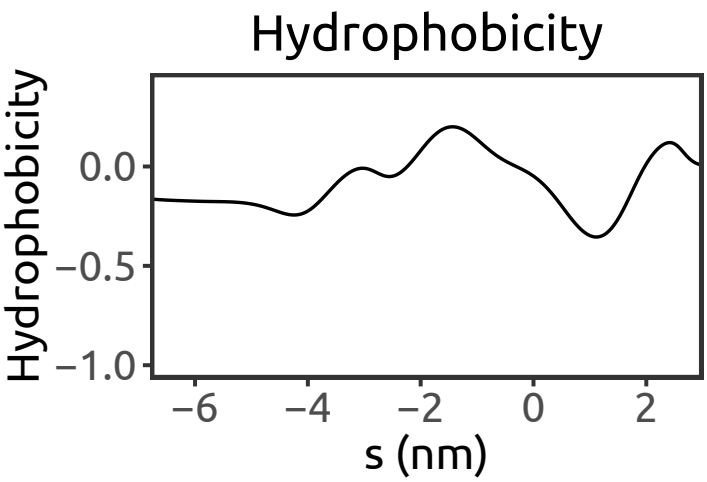
Simulation result:
hydrated channel

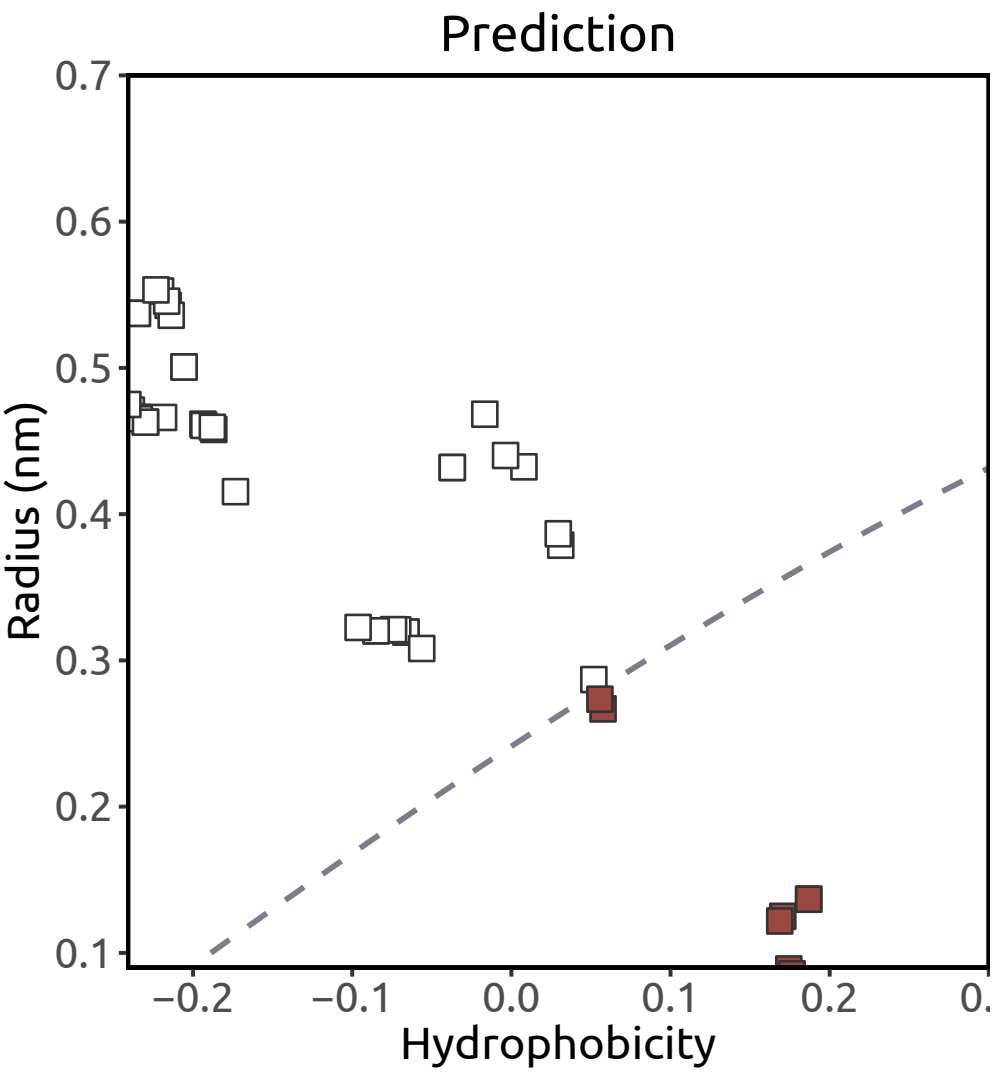
Kir6.2 (PDB ID: 6BAA)

Rattus norvegicus
cryo–EM (3.63 Å)

Martin et al., 2017







Heuristic score:
1.71 (n = 10)

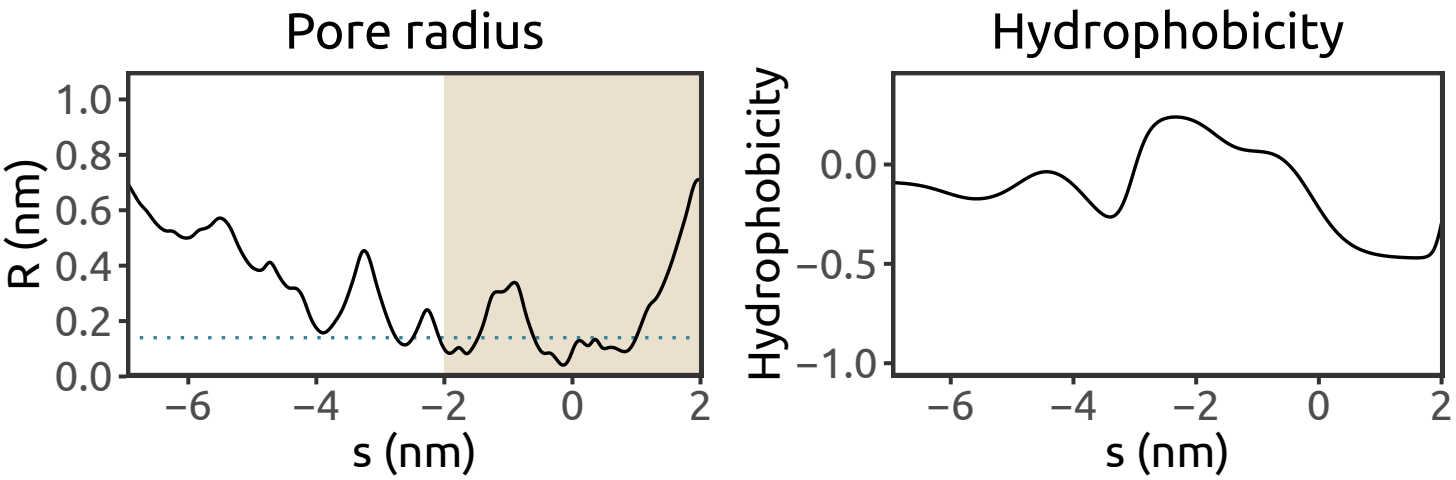
Simulation result:
barrier to water

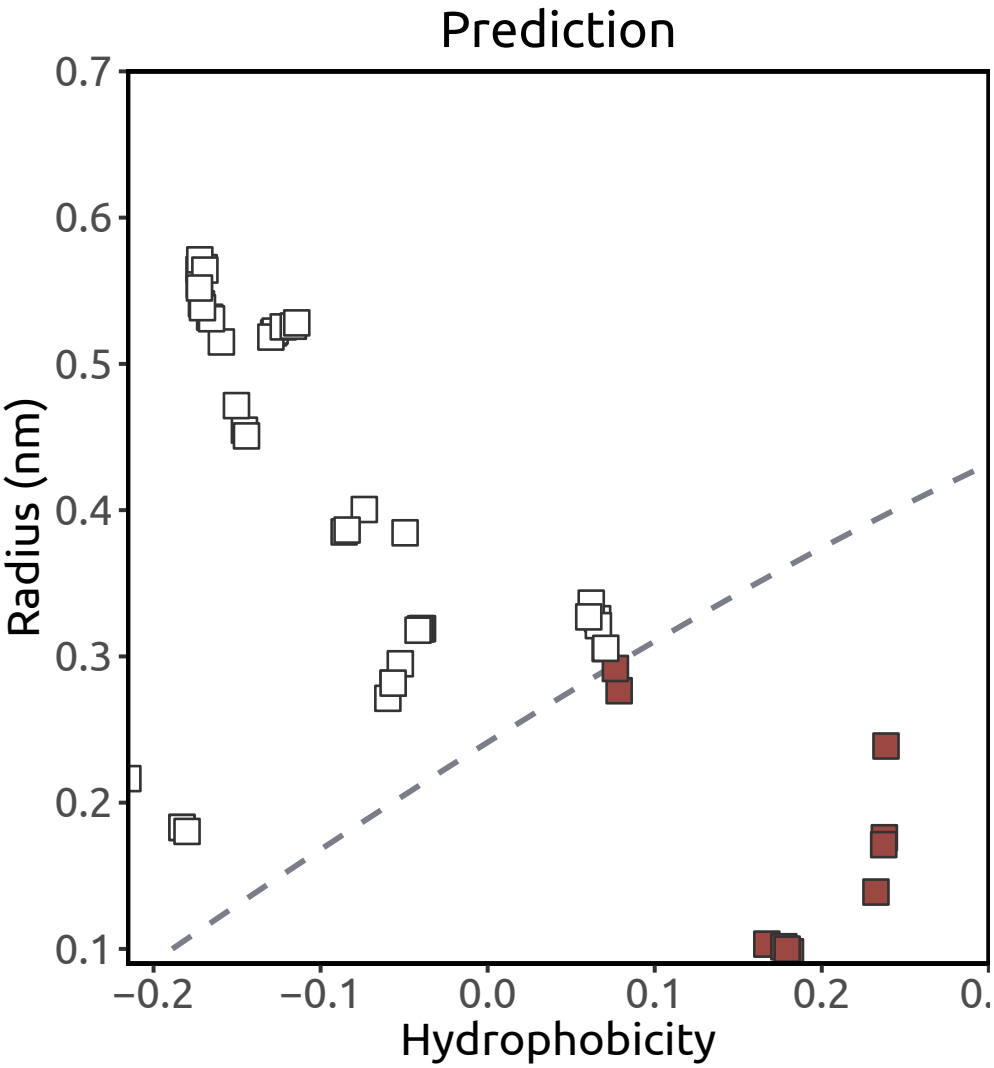
Kir6.2 (PDB ID: 6C3O)

Homo sapiens

cryo–EM (3.9 Å)

Lee et al., 2017





Heuristic score:

1.62 (n = 10)

Simulation result:

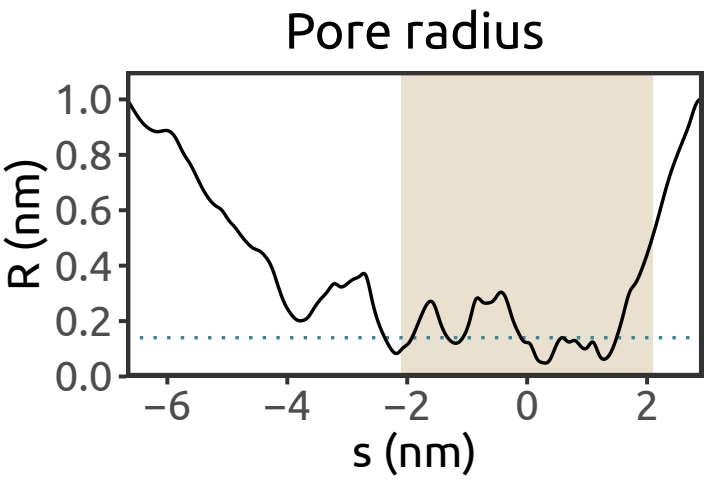
barrier to water

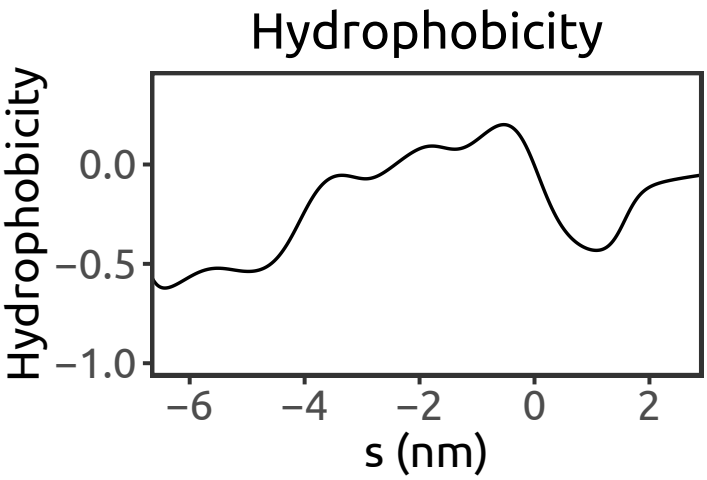
KirBac1.1 (PDB ID: 2WLL)

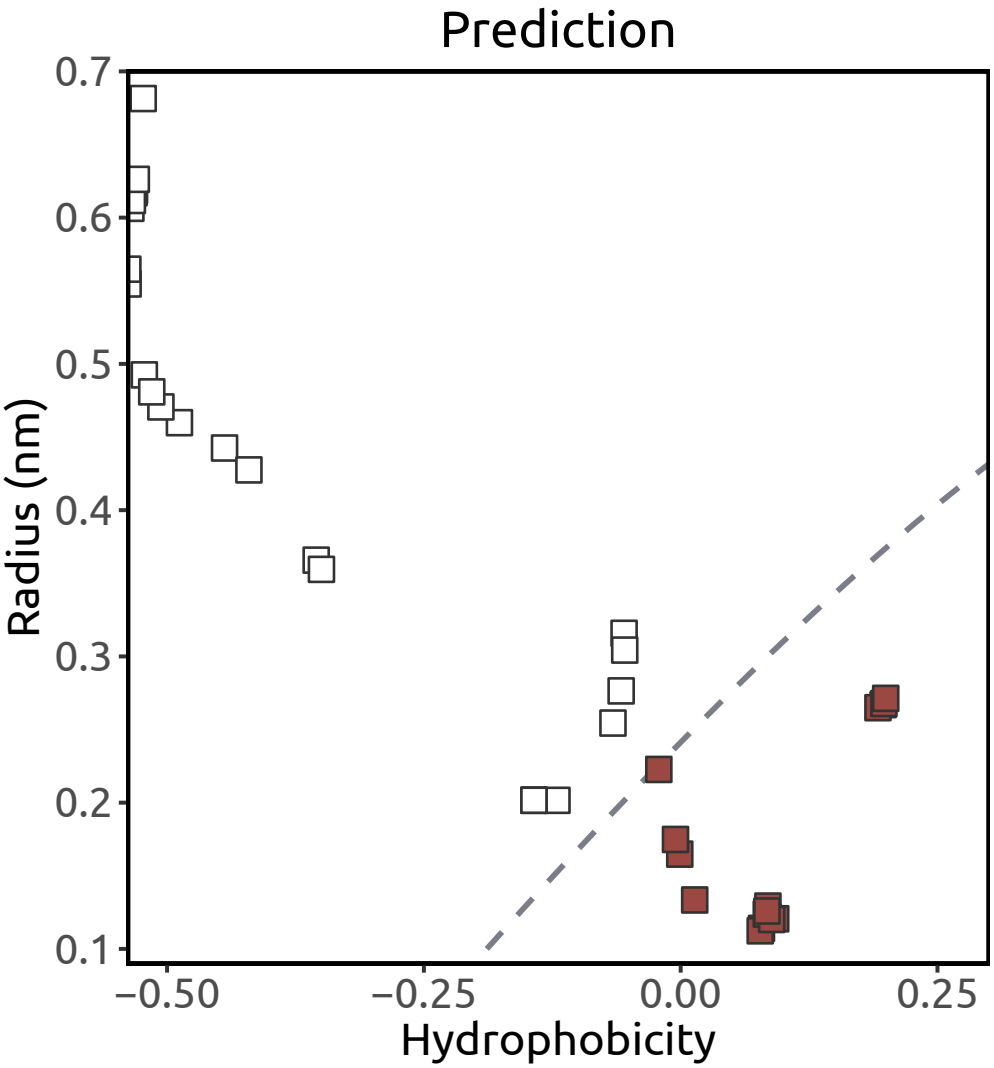
Burkholderia pseudomallei

X–ray (3.65 Å)

Kuo et al., 2003







Heuristic score:

1.74 (n = 16)

Simulation result:

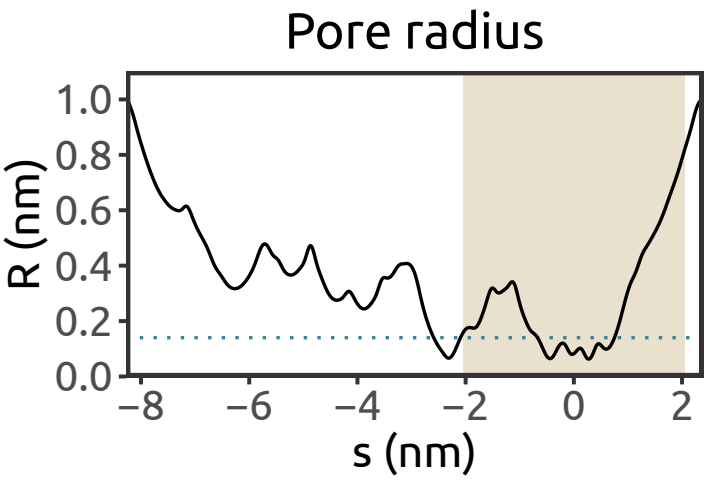
barrier to water

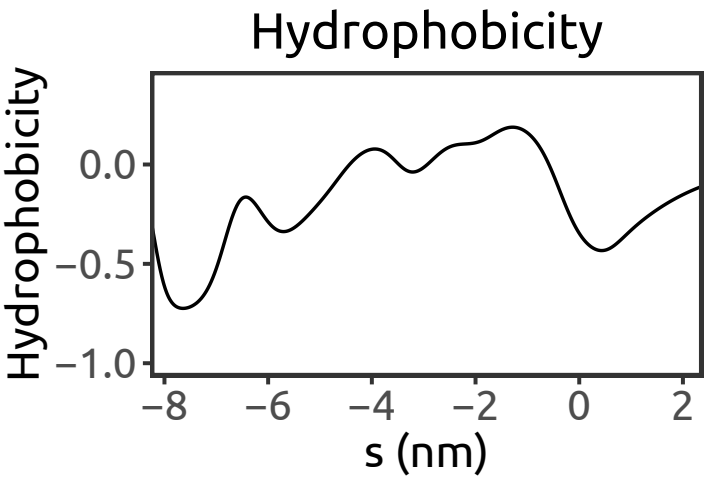
KirBac1.3 (PDB ID: 2QKS)

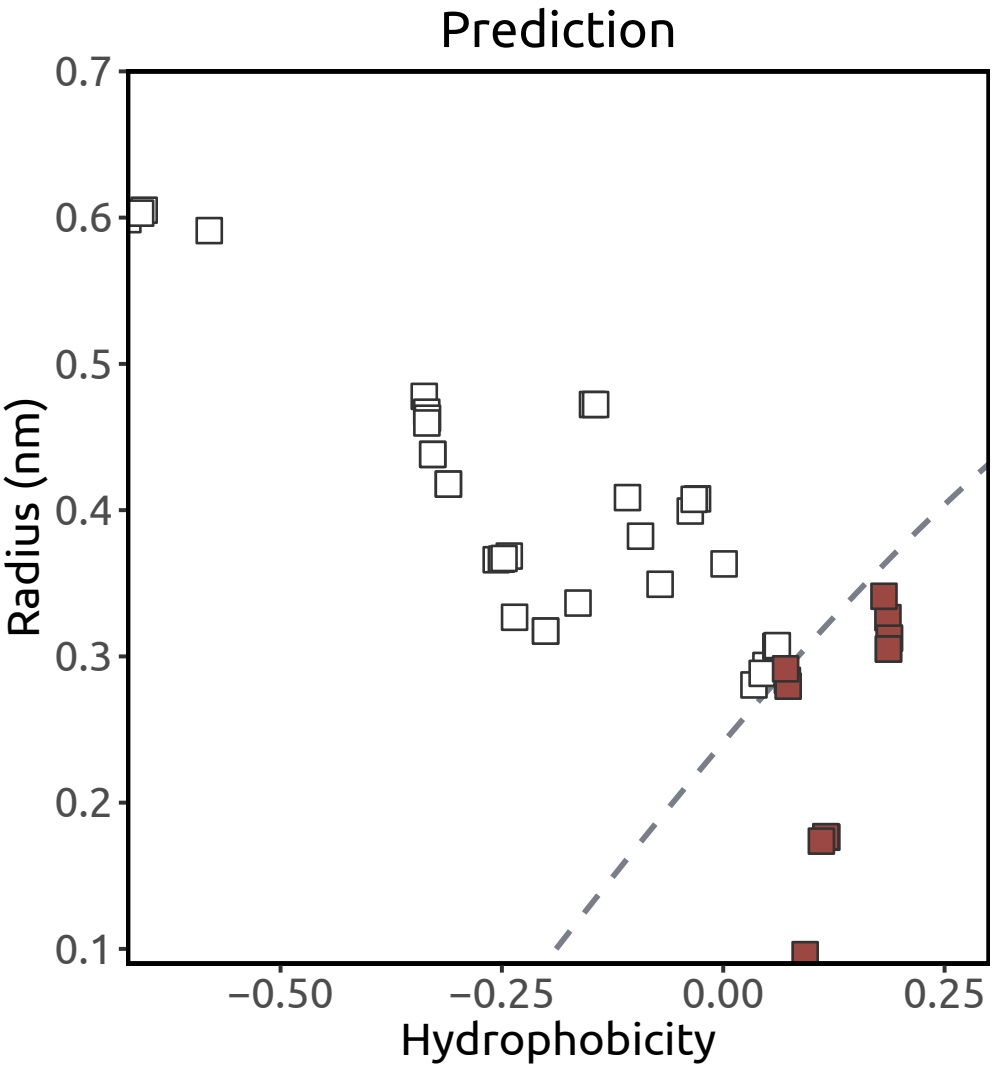
M. musculus B. xenovornas

X–ray (2.2 Å)

Nishida et al., 2007







Heuristic score:

1.49 (n = 17)

Simulation result:

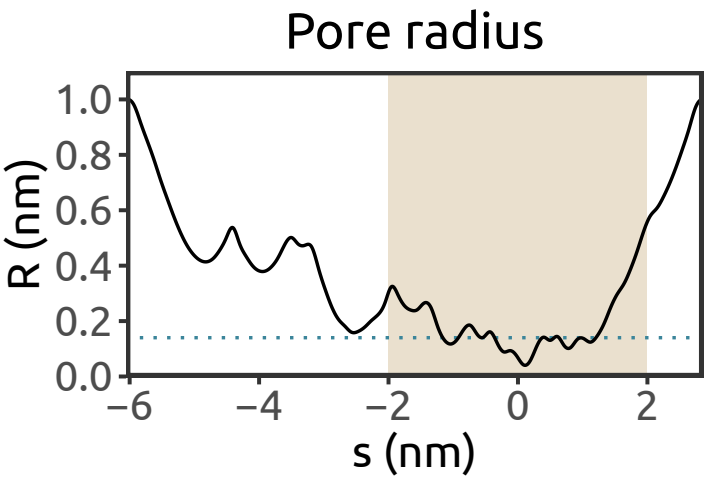
barrier to water

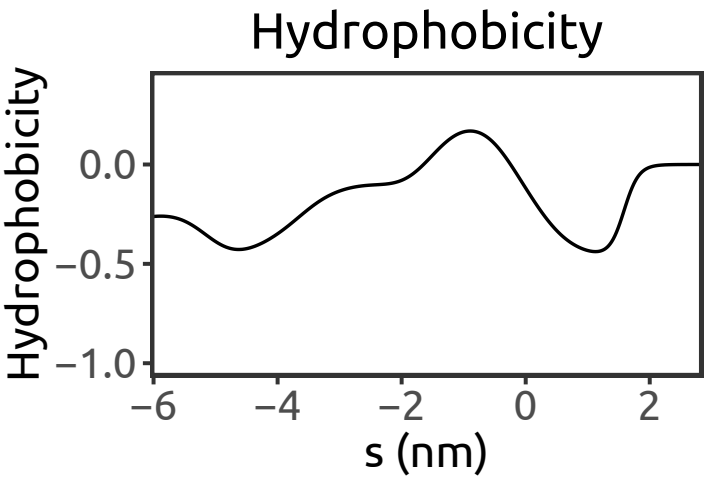
KirBac3.1 (PDB ID: 2WLH)

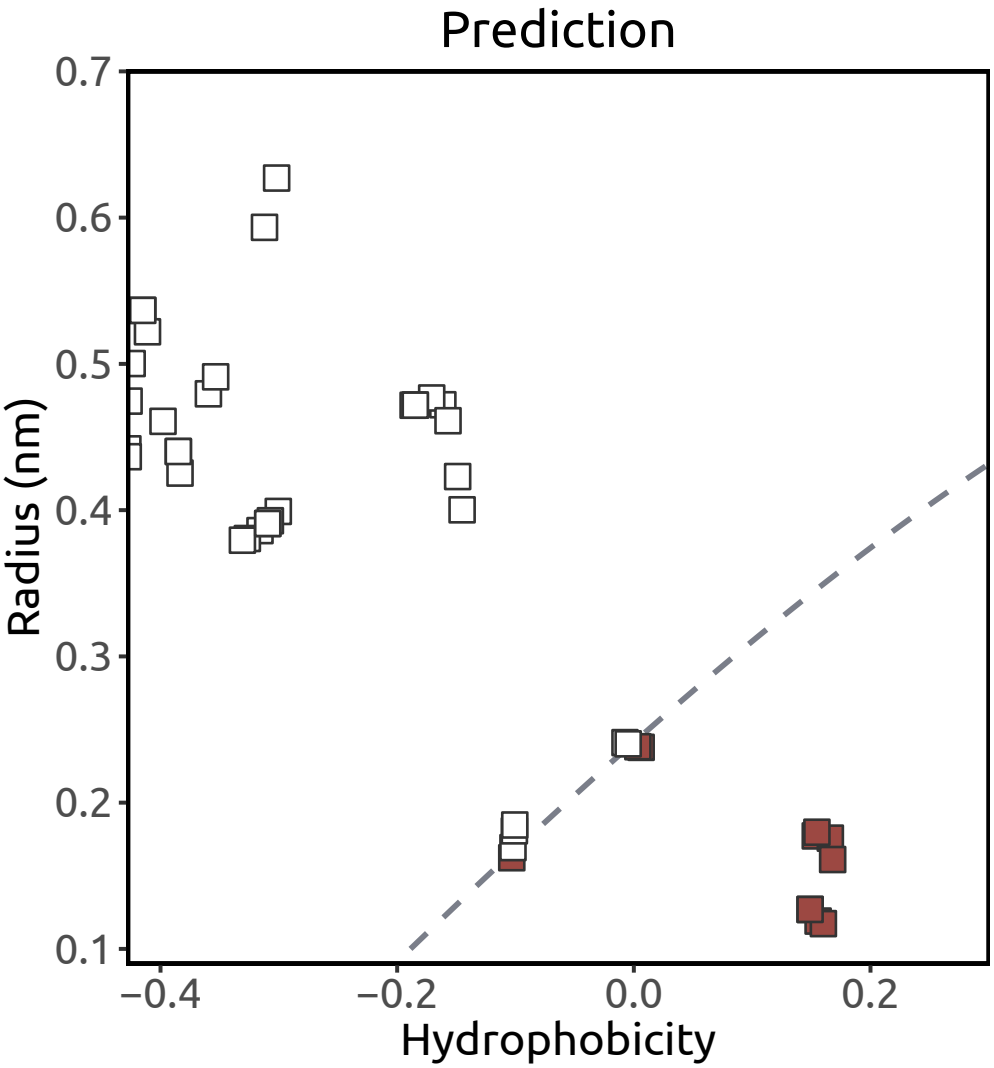
M. magnetotacticum

X–ray (3.28 Å)

Clarke et al., 2010







Heuristic score:

1.35 (n = 11)

Simulation result:

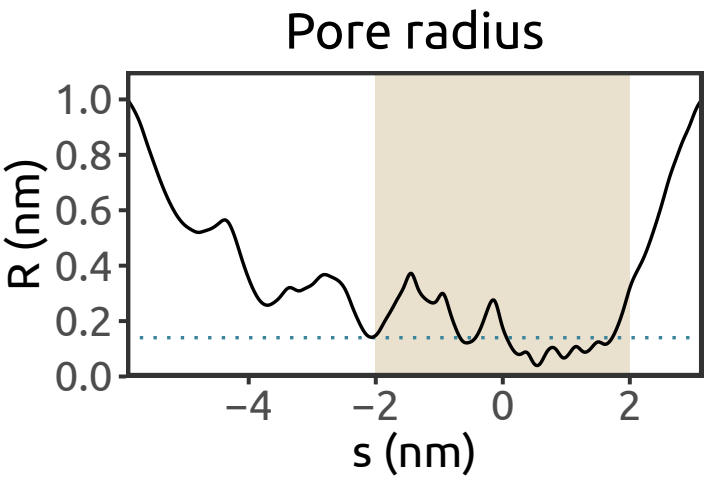
barrier to water

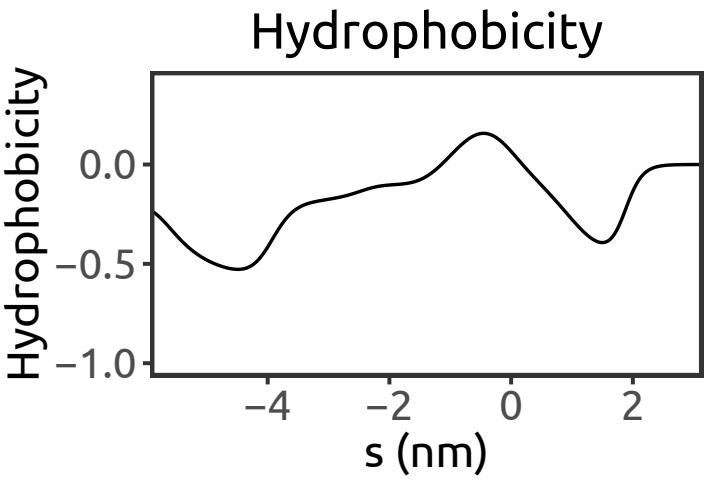
KirBac3.1 (PDB ID: 2WLI)

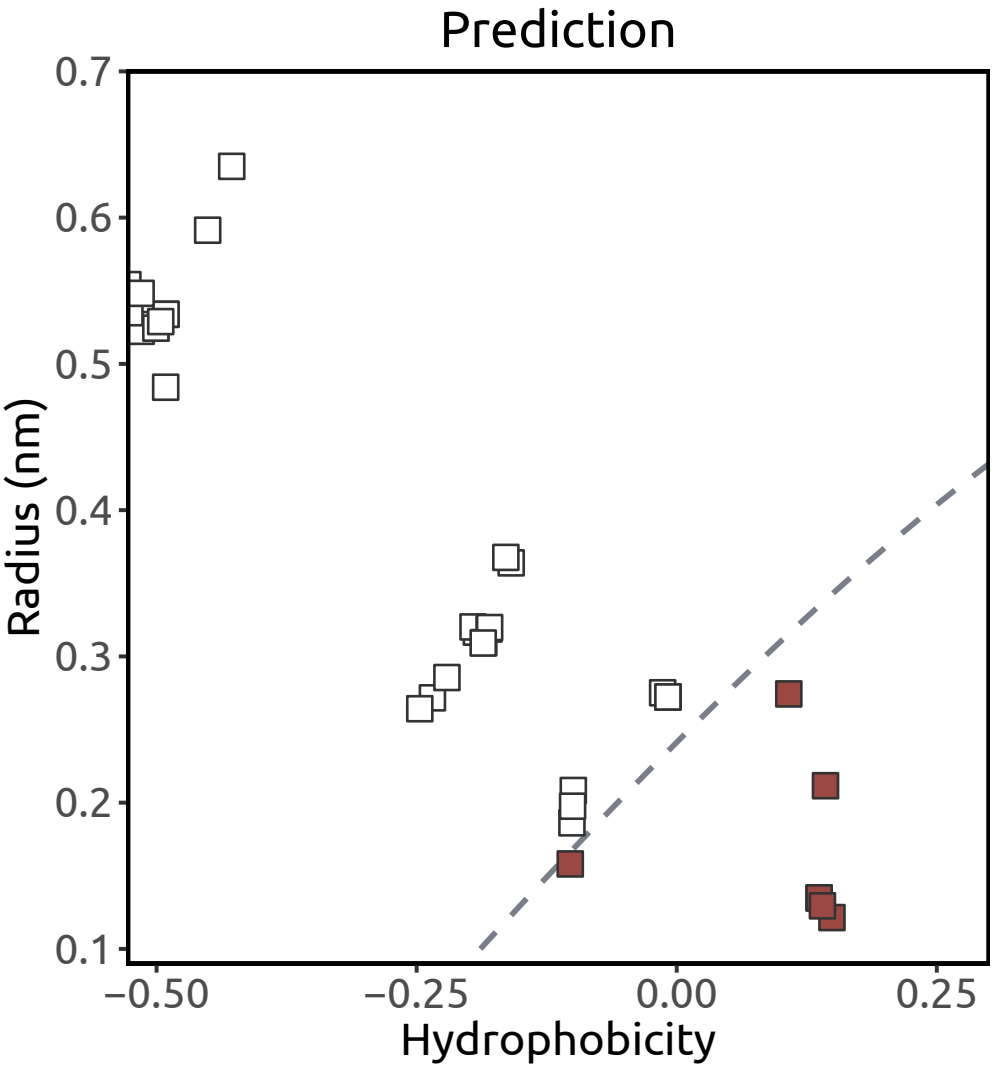
M. magnetotacticum

X–ray (3.09 Å)

Clarke et al., 2010







Heuristic score:

0.84 (n = 7)

Simulation result:

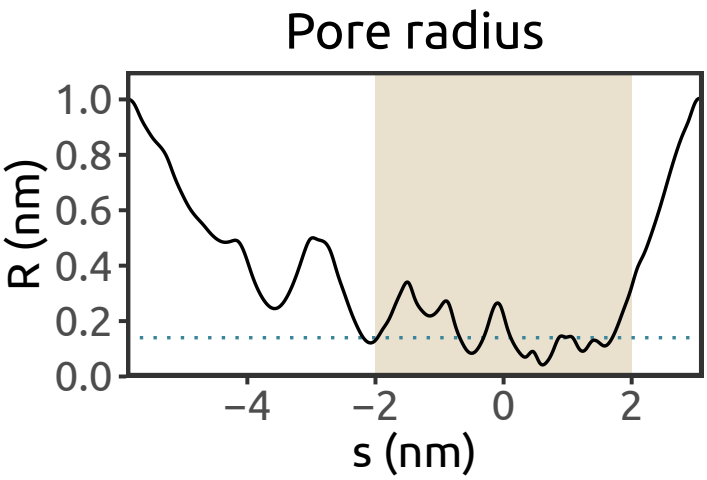
barrier to water

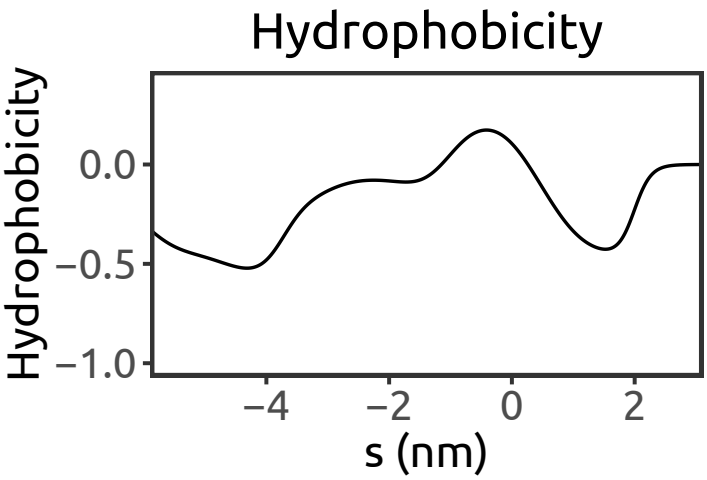
KirBac3.1 (PDB ID: 2WLJ)

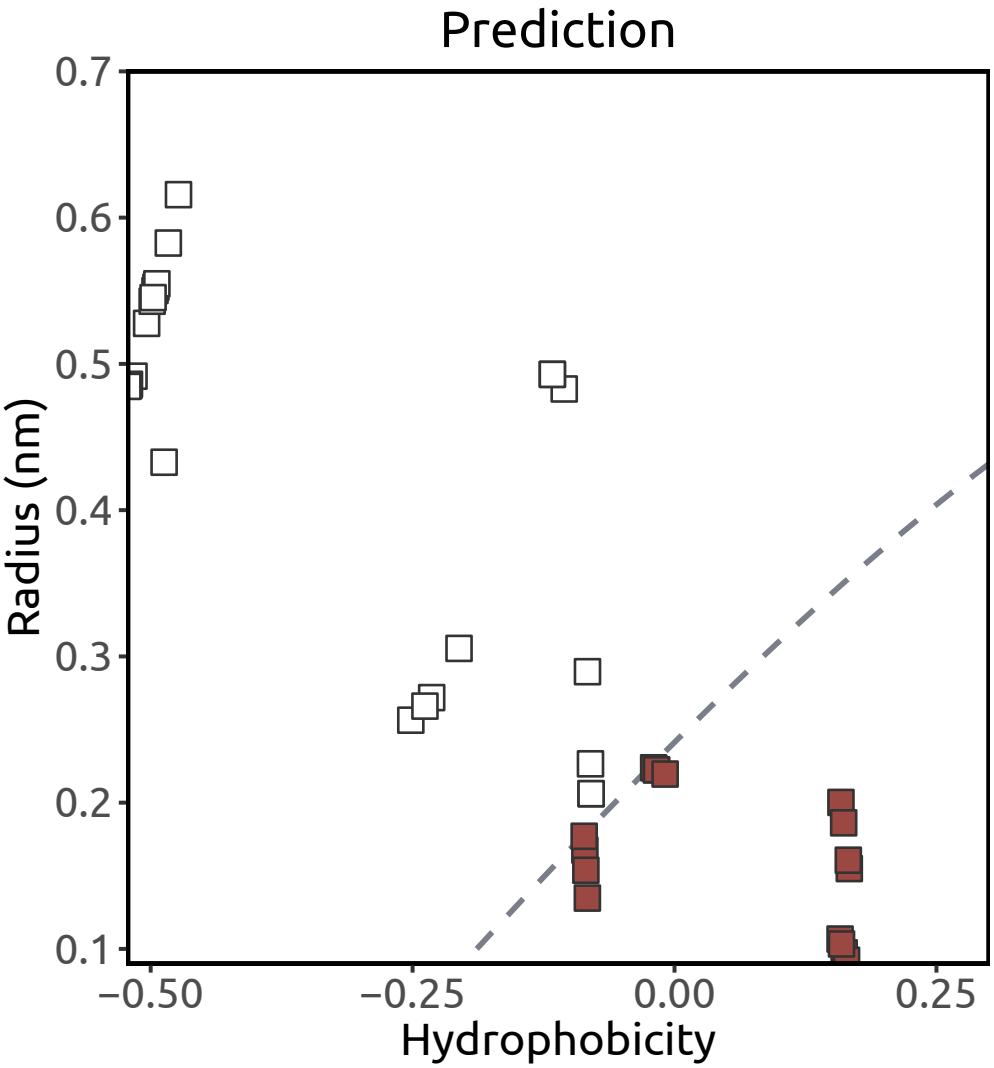
M. magnetotacticum

X–ray (2.6 Å)

Clarke et al., 2010







Heuristic score:

1.52 (n = 16)

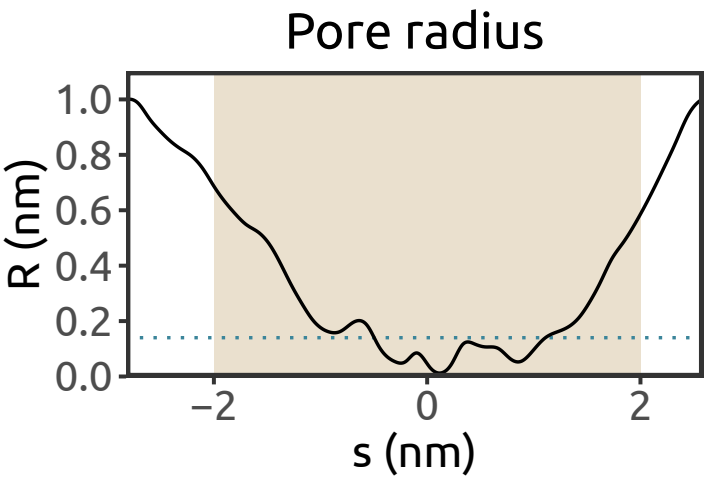
Simulation result:

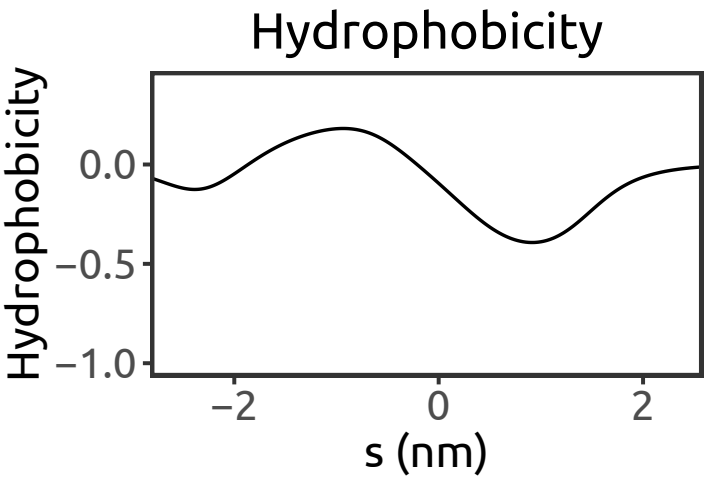
barrier to water

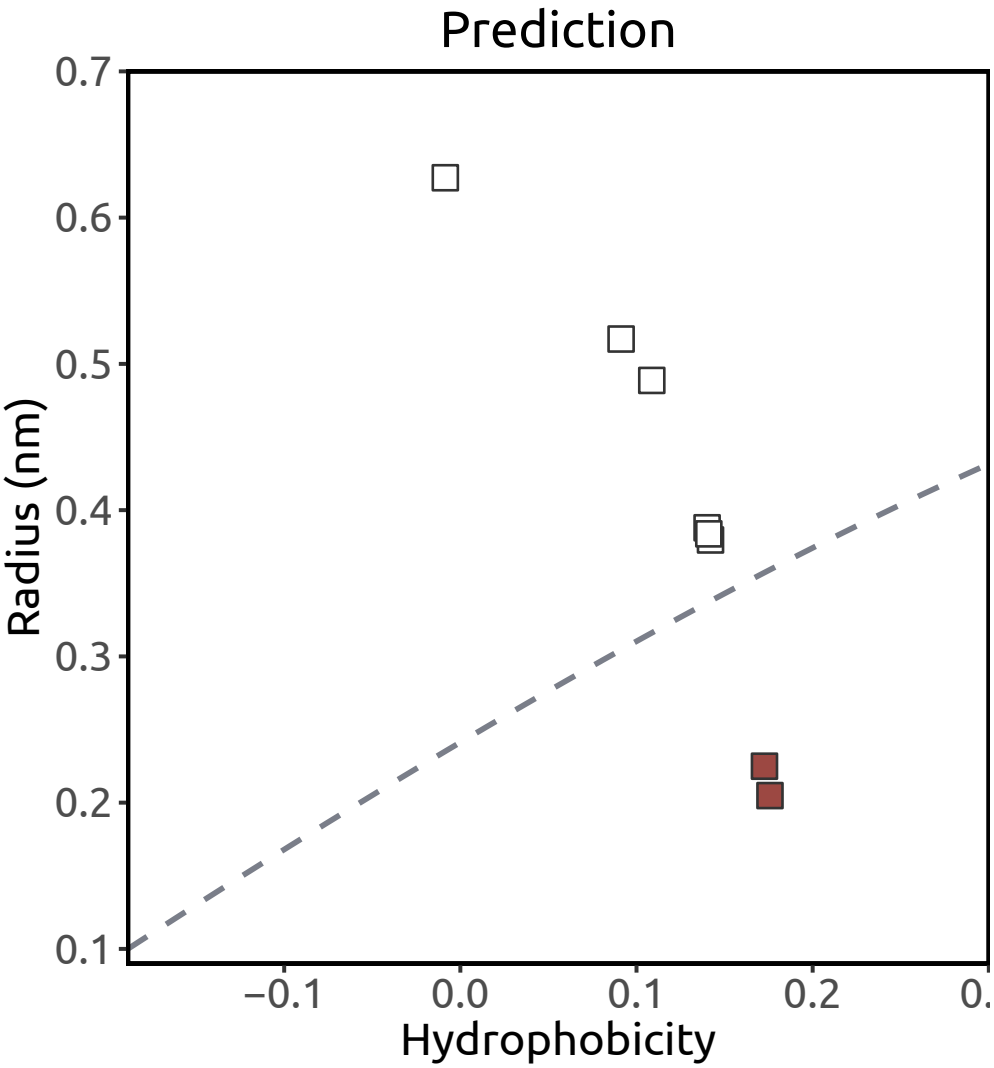
MthK (PDB ID: 1LNQ)

M. thermautotrophicus
X–ray (3.3 Å)

Jiang et al., 2002







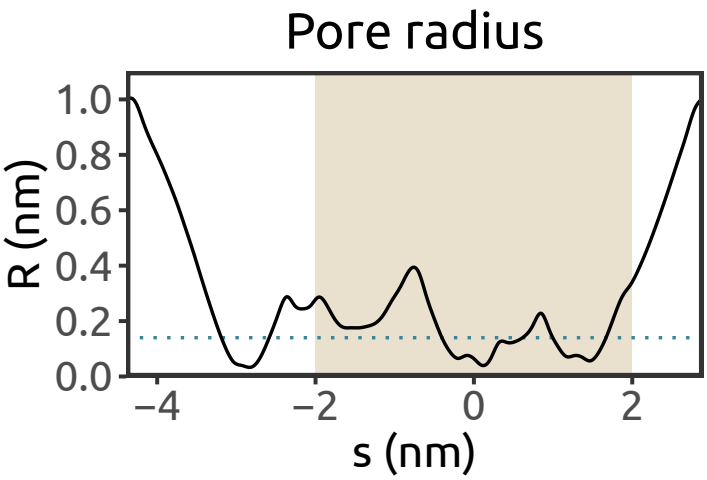
Heuristic score:
0.24 (n = 2)

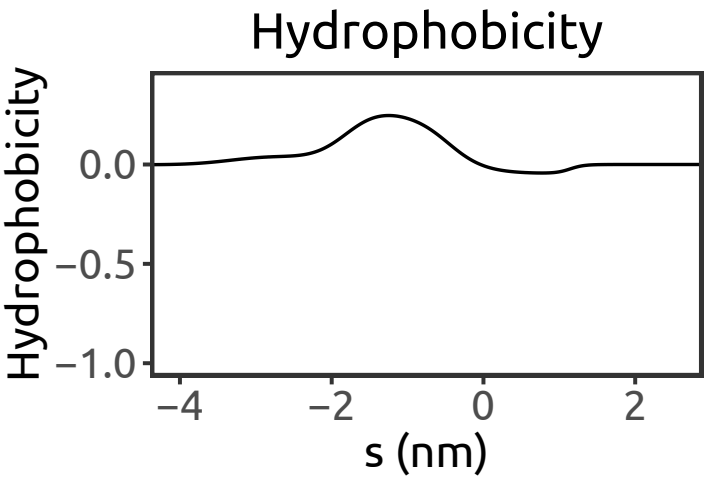
Simulation result:
hydrated channel

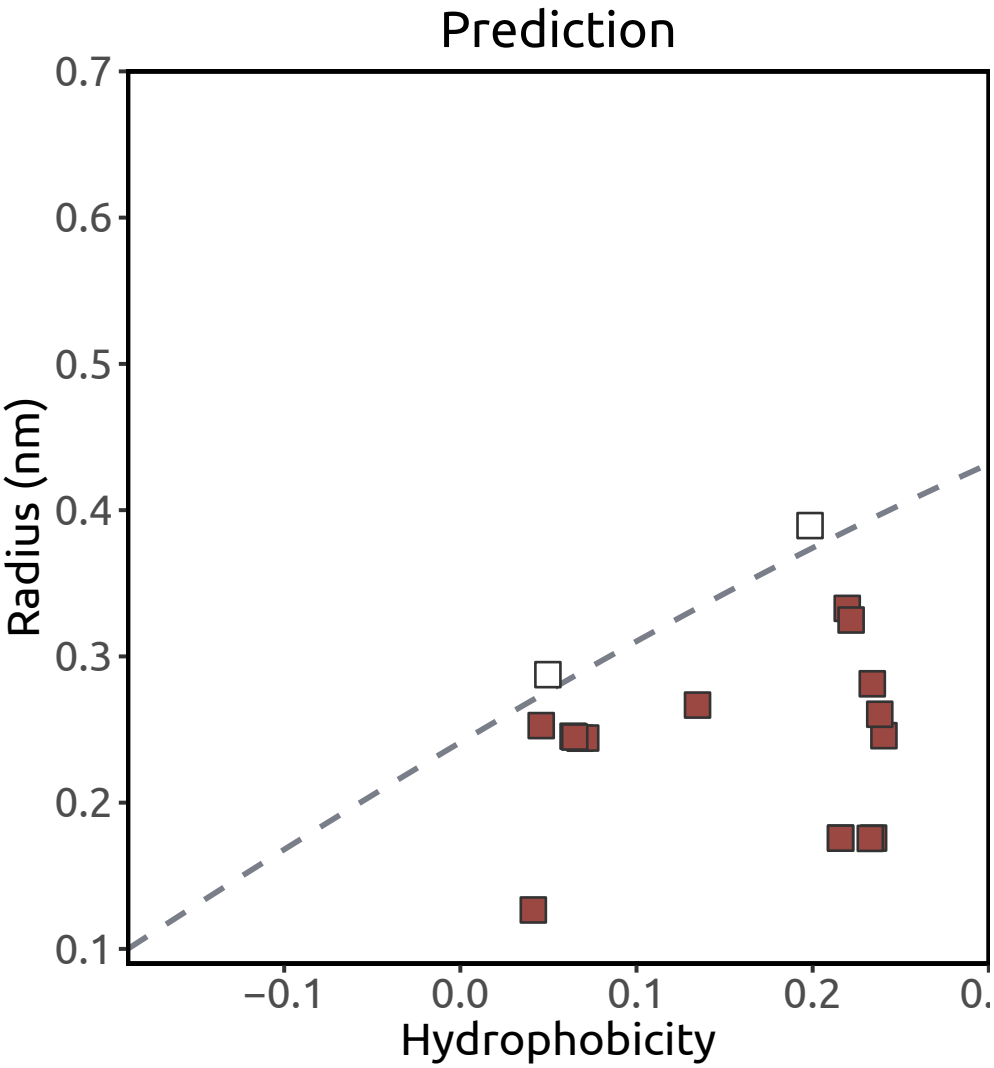
NaK (PDB ID: 2AHY)

Bacillus cereus
X–ray (2.4 Å)

Shi et al., 2006







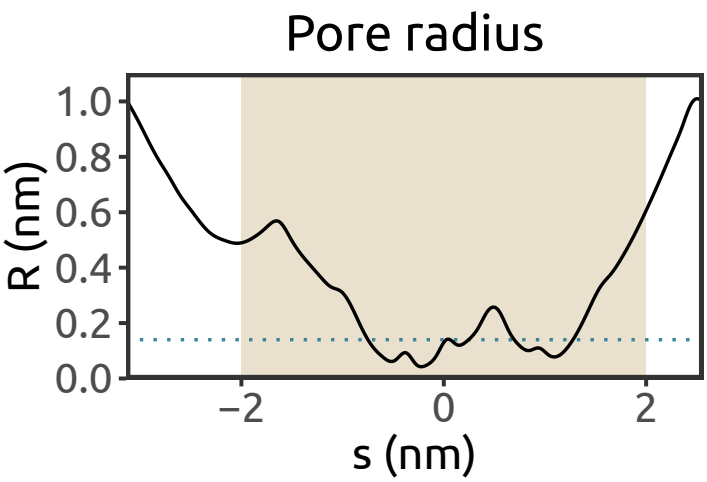
Heuristic score:
2.24 (n = 20)

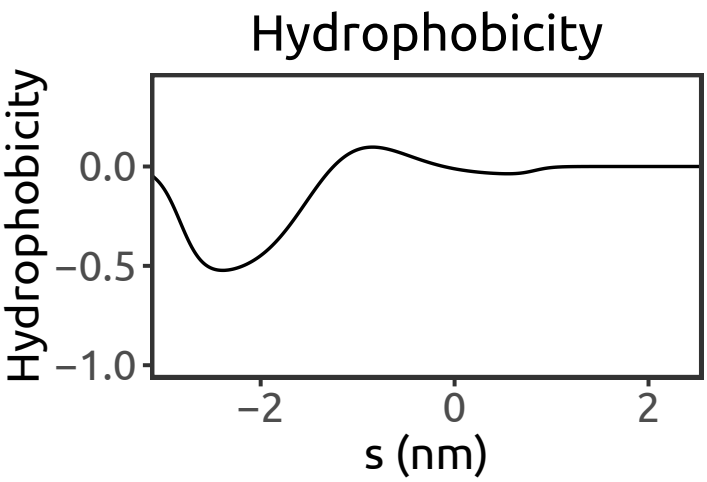
Simulation result:
barrier to water

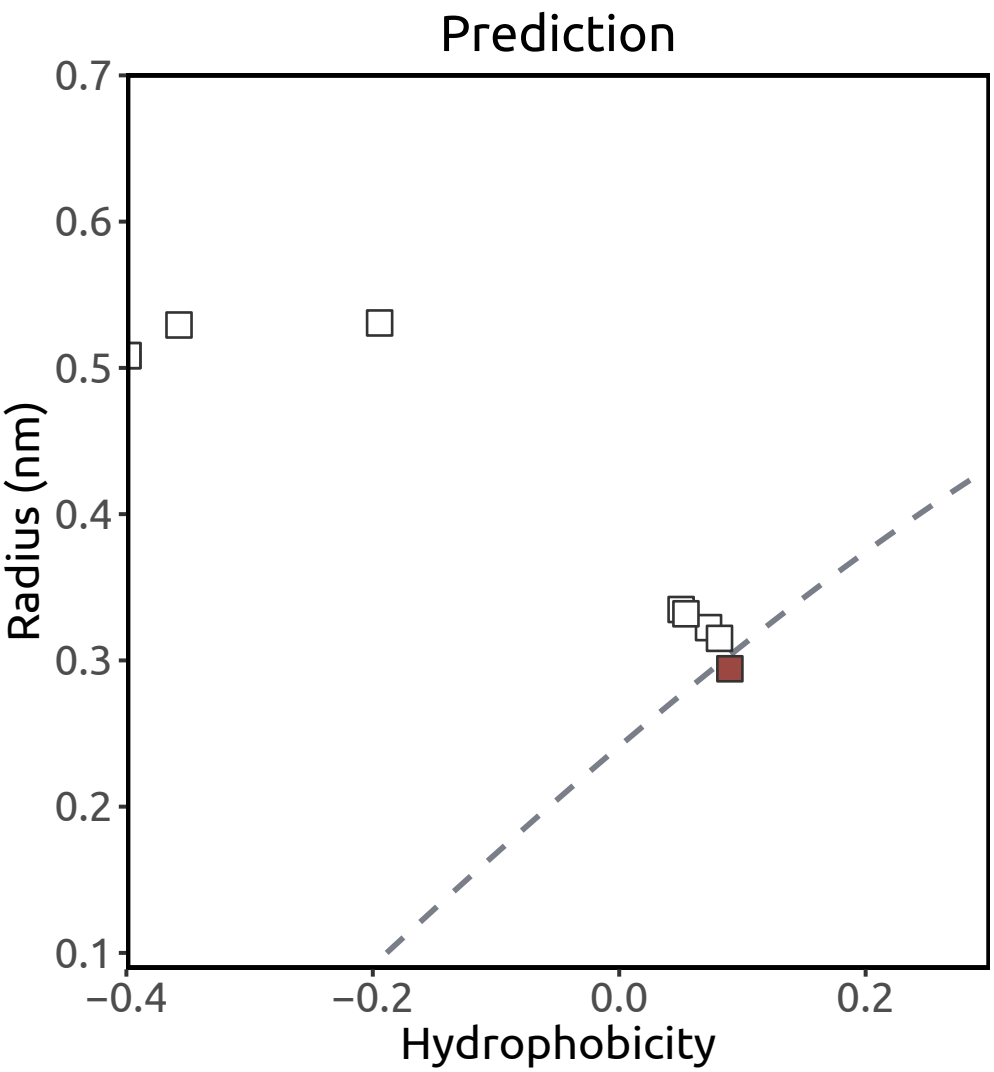
NaK (PDB ID: 3E86)

Bacillus cereus
X–ray (1.6 Å)

Alam & Jiang, 2009







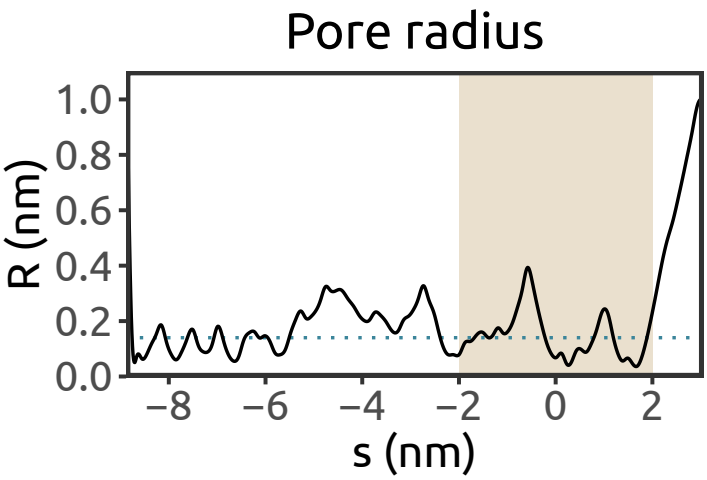
Heuristic score:
0.01 (n = 1)

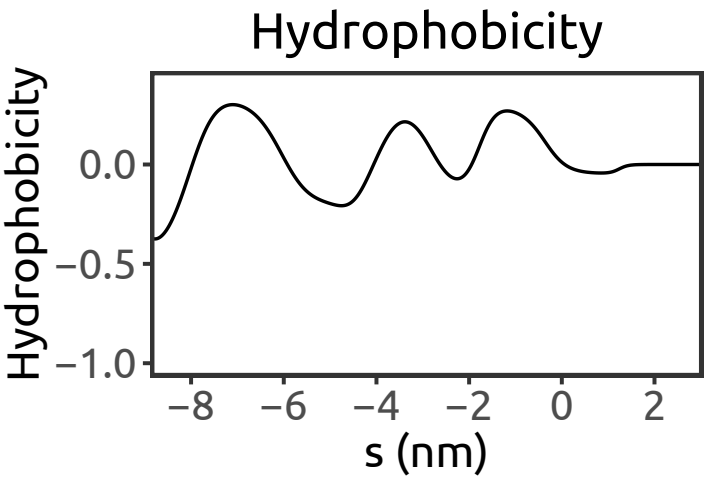
Simulation result:
hydrated channel

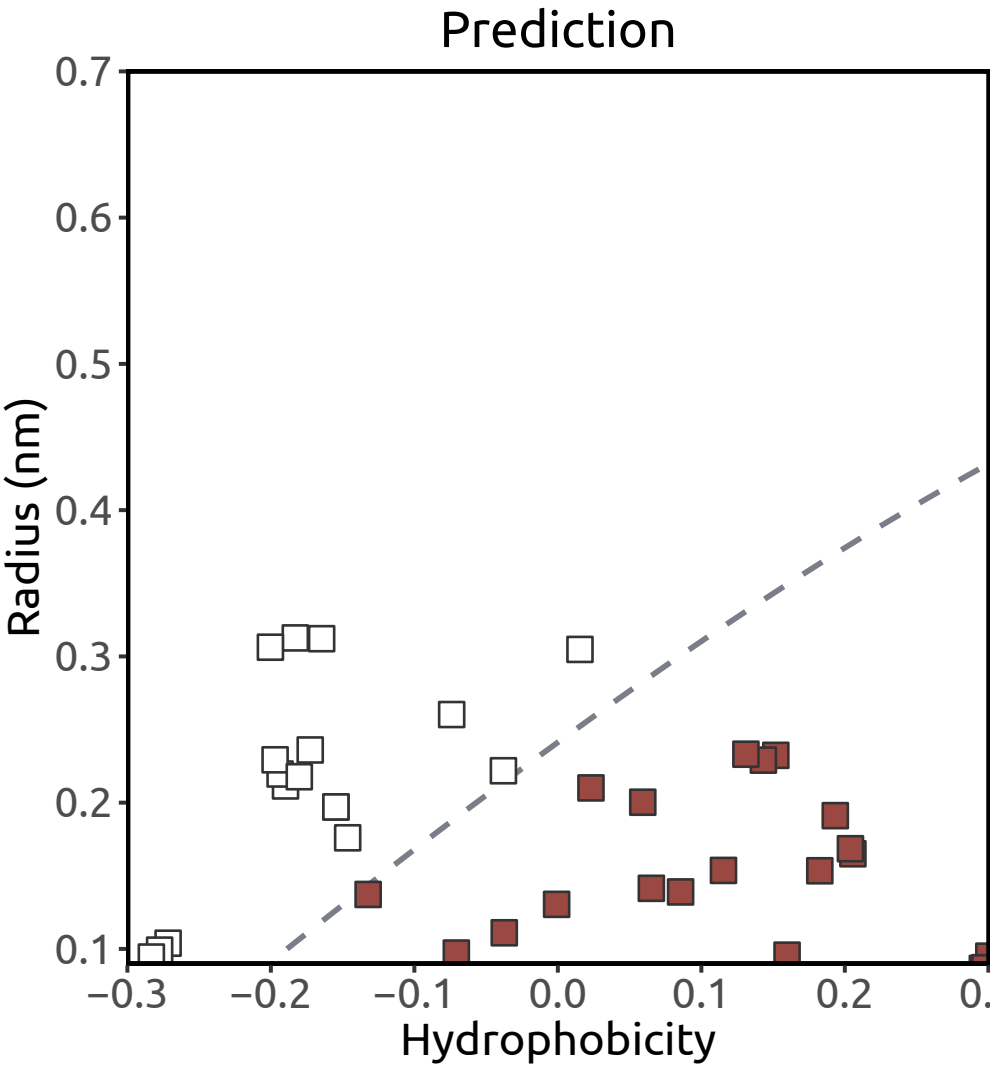
NaKNav (PDB ID: 3VOU)

B. mycoides S. pontiacus
X–ray (3.2 Å)

Irie et al., 2012







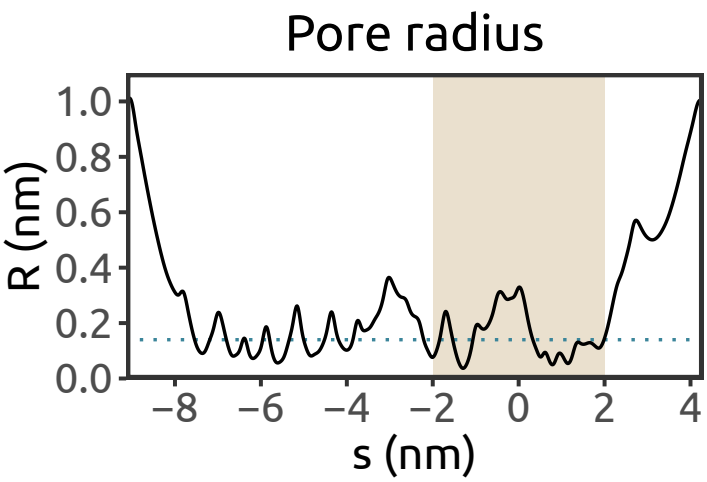
Heuristic score:
4.81 (n = 31)

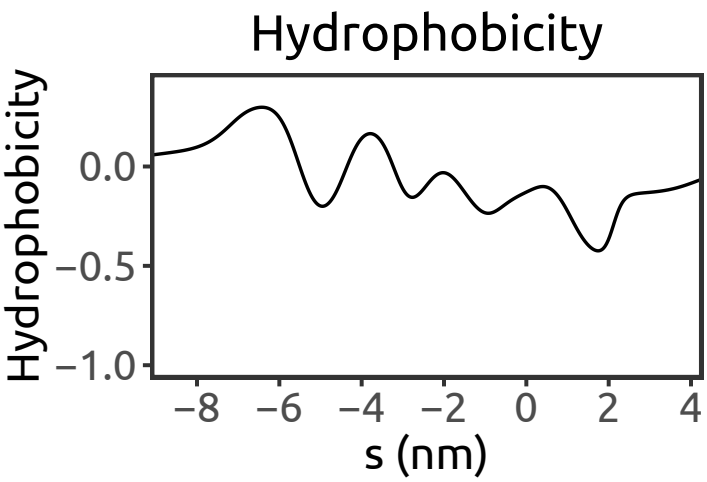
Simulation result:
barrier to water

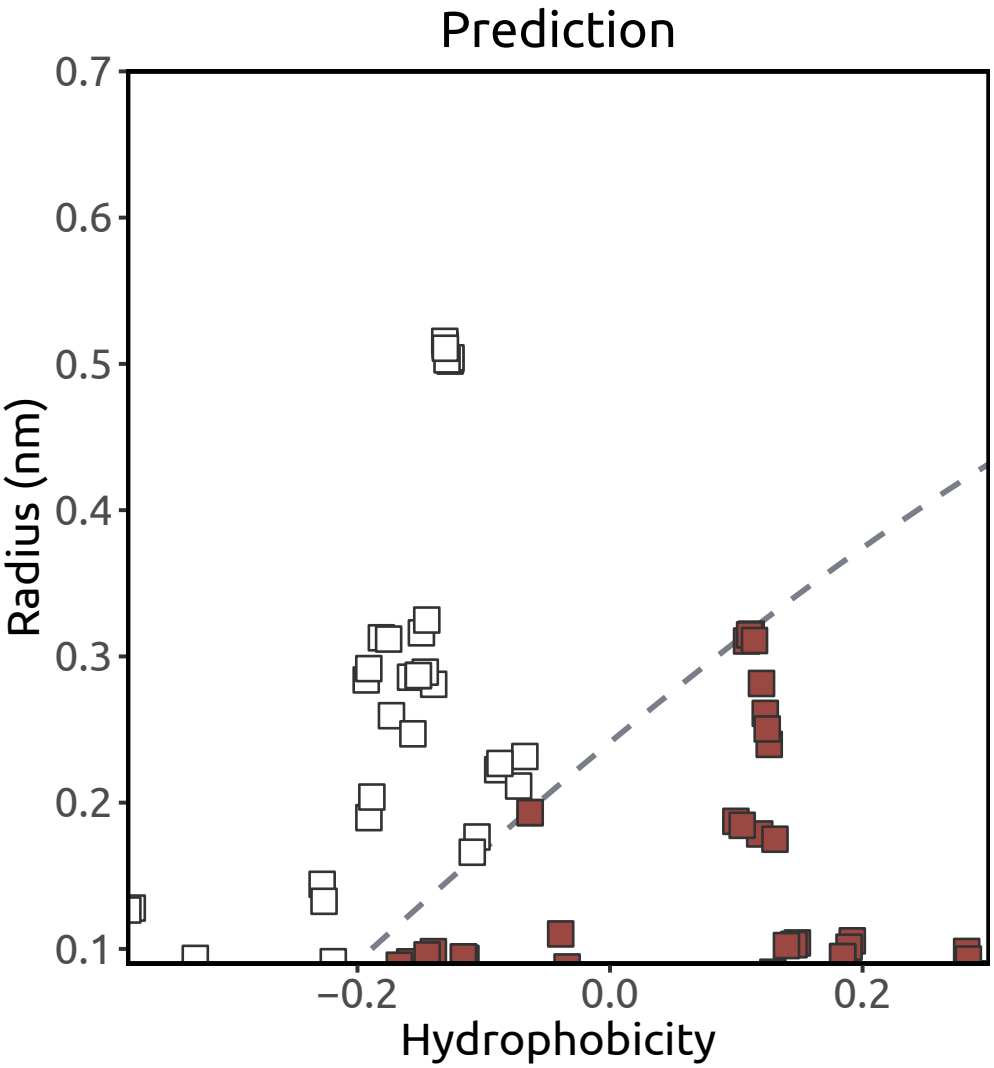
KCNQ1 (PDB ID: 5VMS)

Xenopus laevis
cryo–EM (3.7 Å)

Sun & MacKinnon, 2017







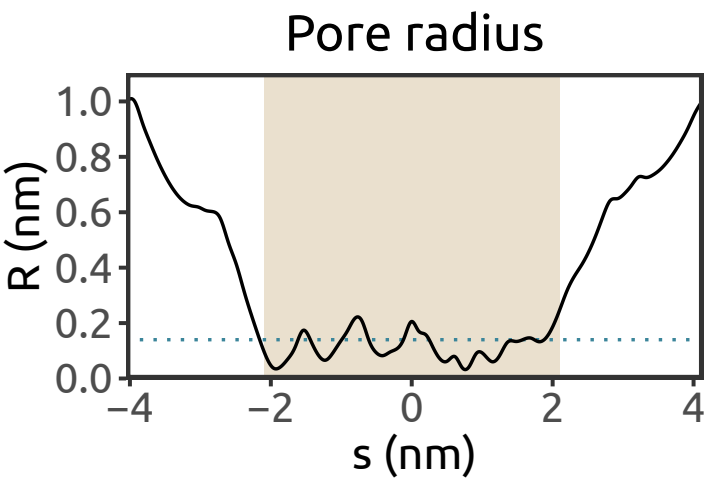
Heuristic score:
6.44 (n = 50)

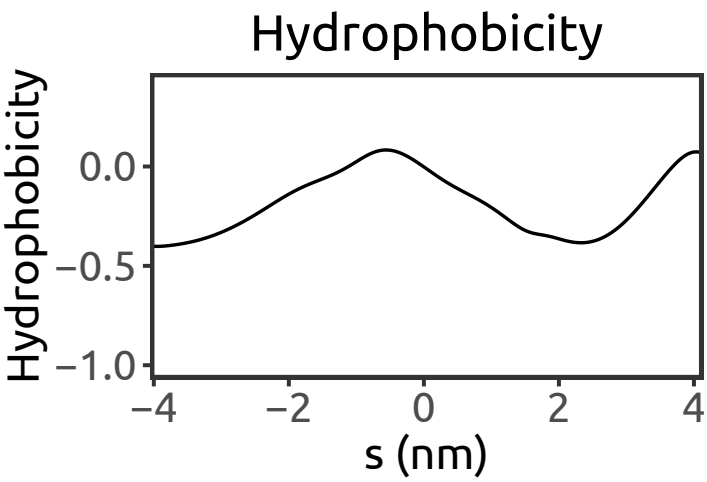
Simulation result:
barrier to water

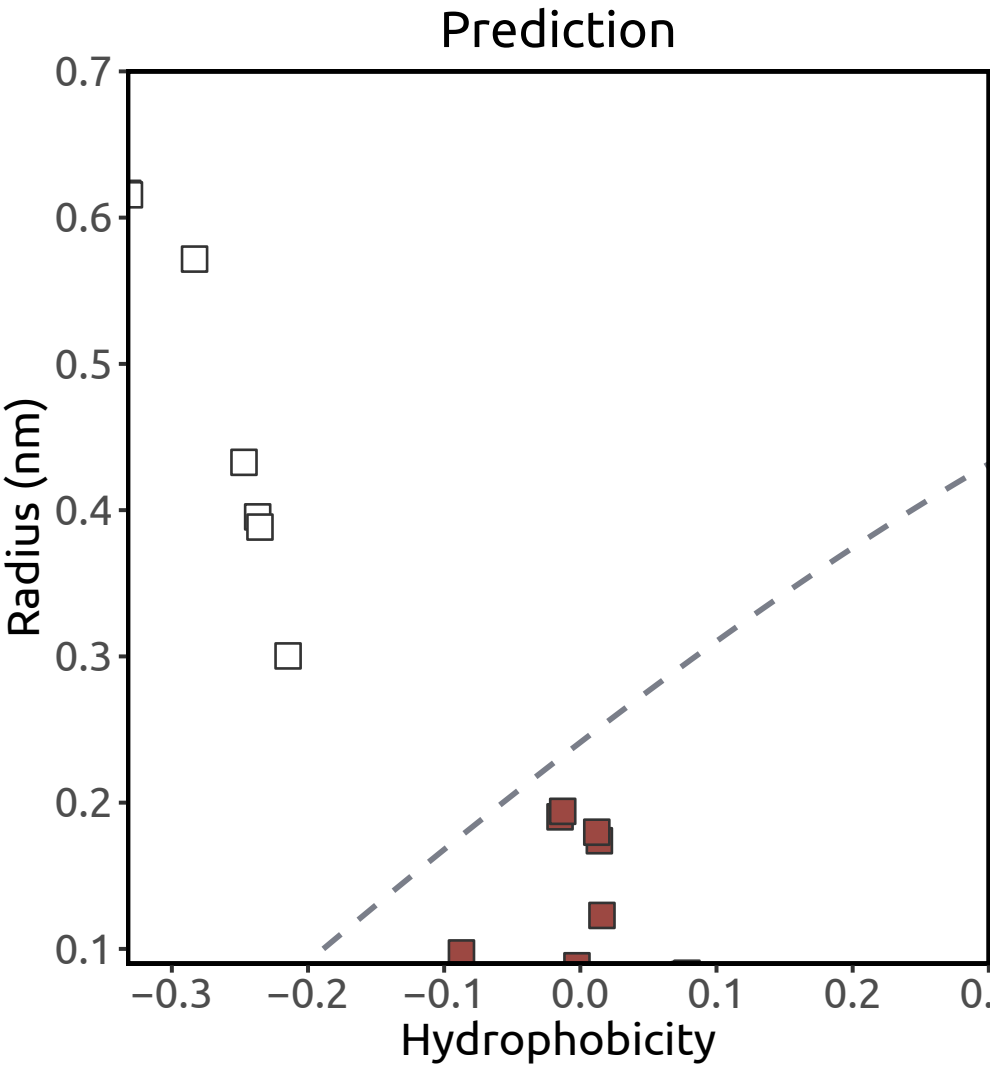
Kv10.1 (PDB ID: 5K7L)

Rattus norvegicus
cryo–EM (3.78 Å)

Whicher & MacKinnon, 2016







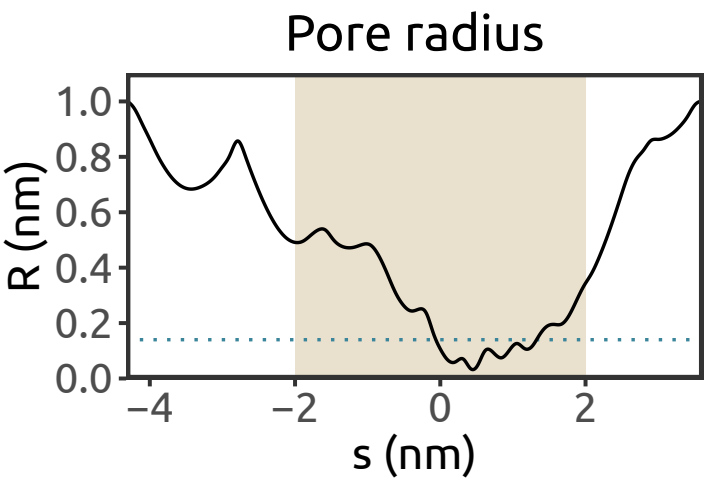
Heuristic score:
1.69 (n = 16)

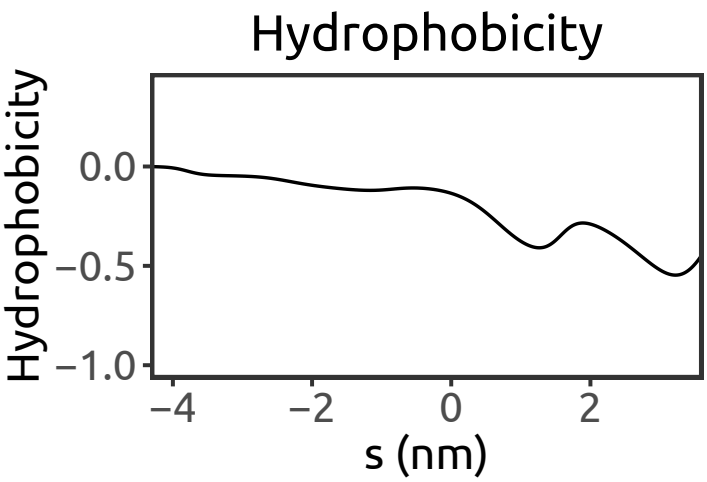
Simulation result:
barrier to water

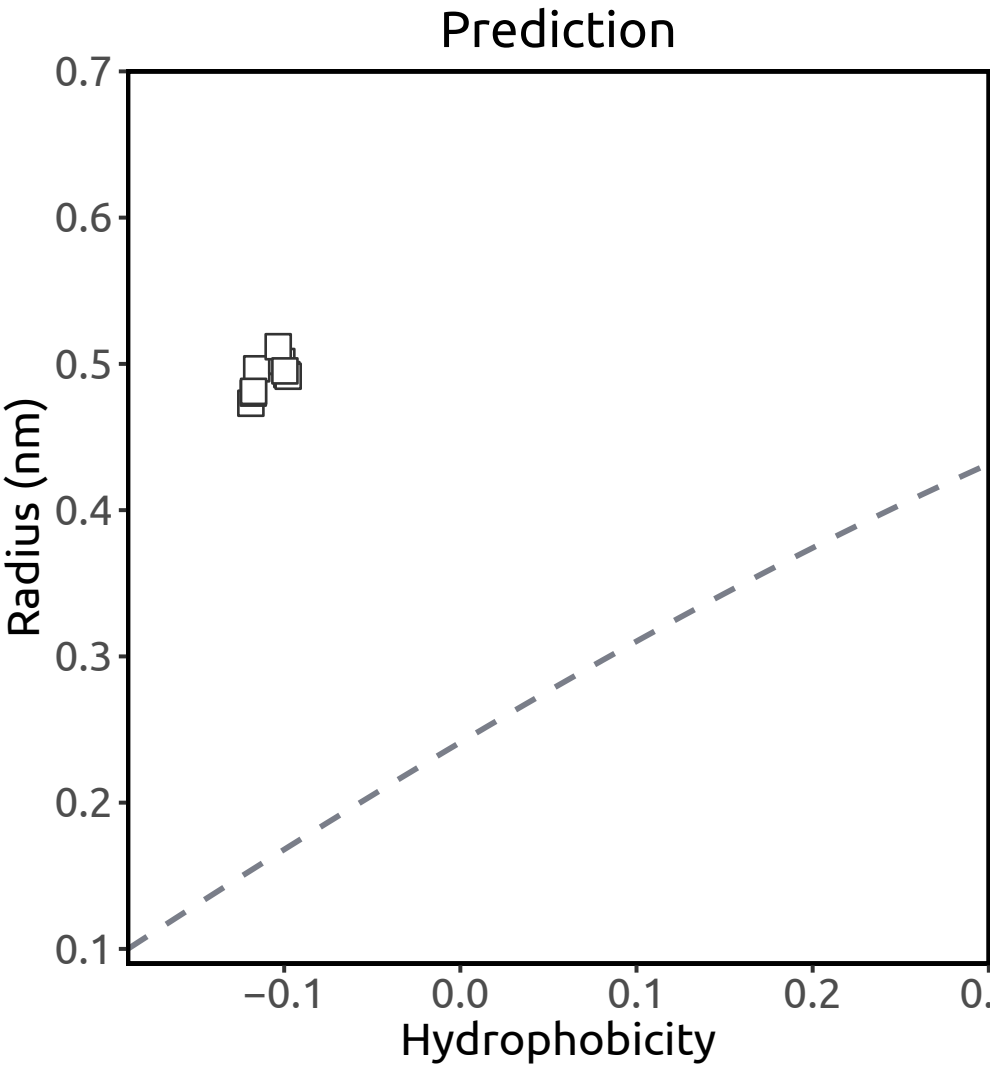
Kv11.1 (PDB ID: 5VA1)

Homo sapiens
cryo–EM (3.7 Å)

Wang & MacKinnon, 2017







Heuristic score:
0 (n = 0)

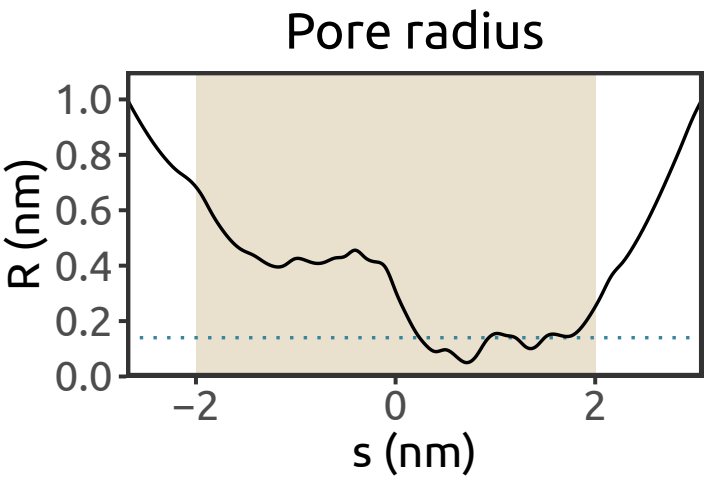
Simulation result:
hydrated channel

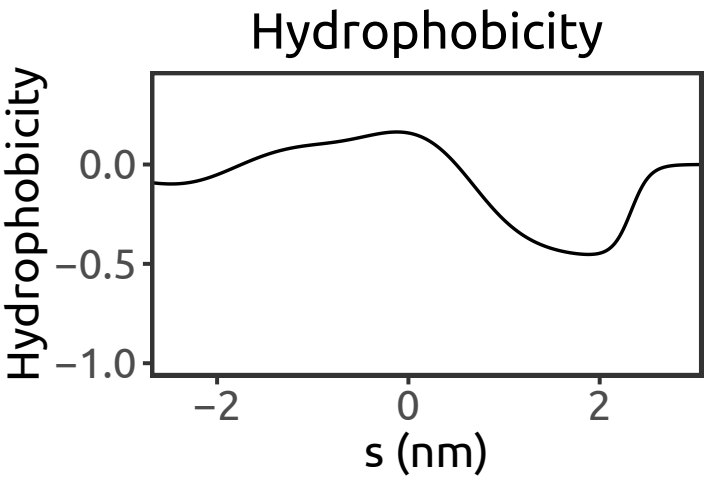
Kv1.2 (PDB ID: 2A79)

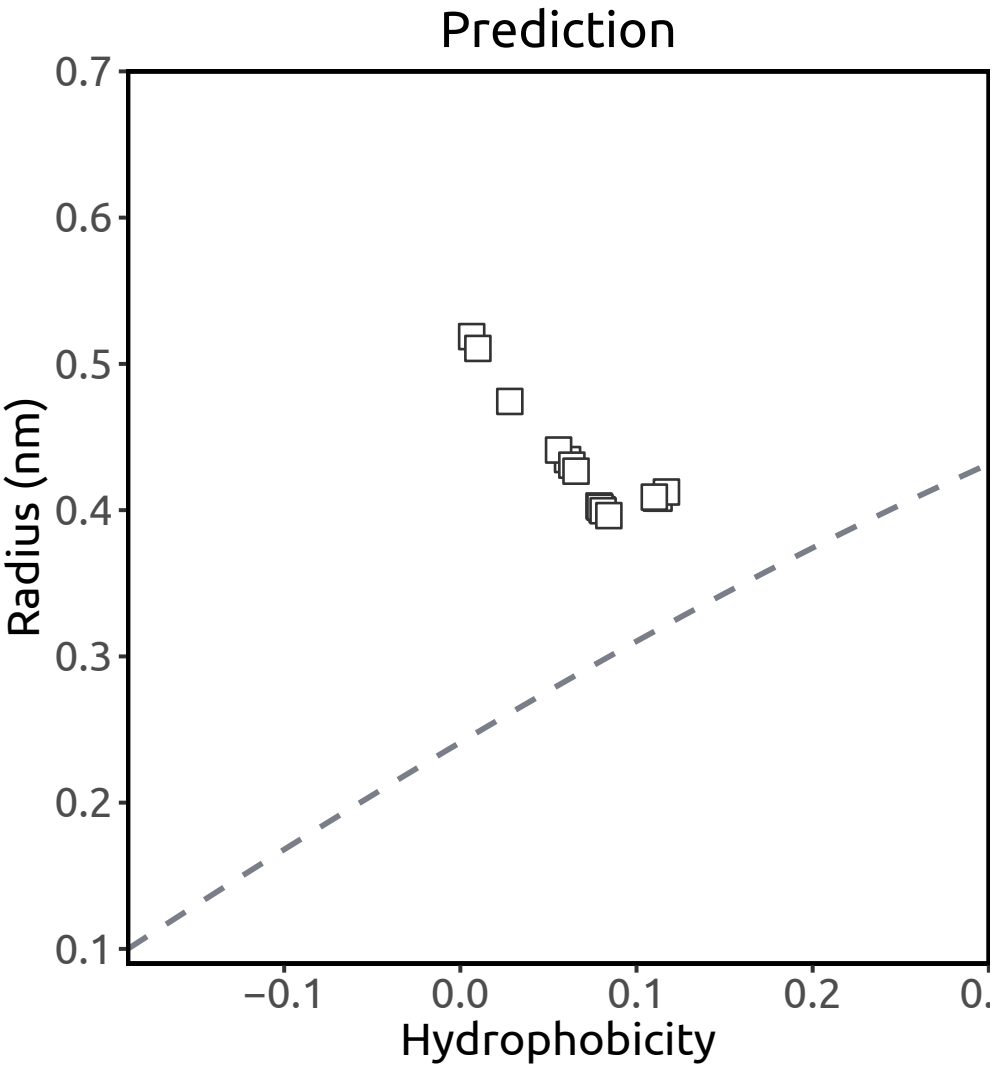
Rattus norvegicus

X–ray (2.9 Å)

Long et al., 2005







Heuristic score:

0 (n = 0)

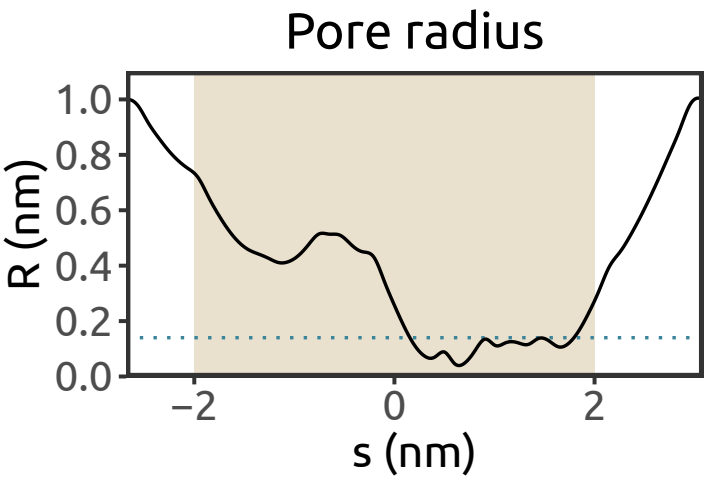
Simulation result:

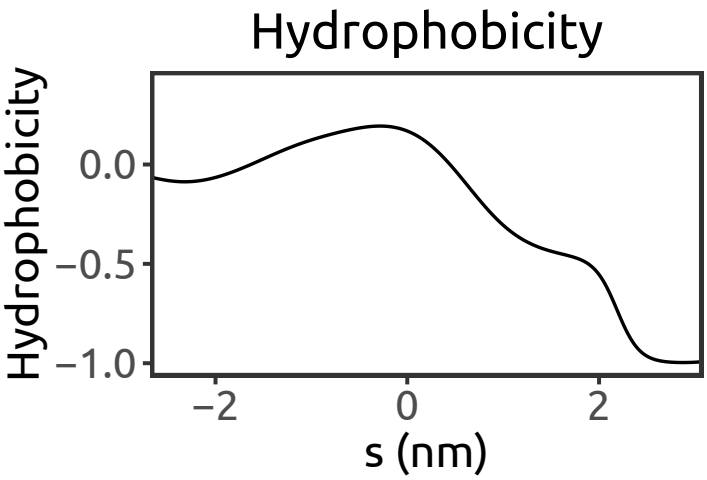
hydrated channel

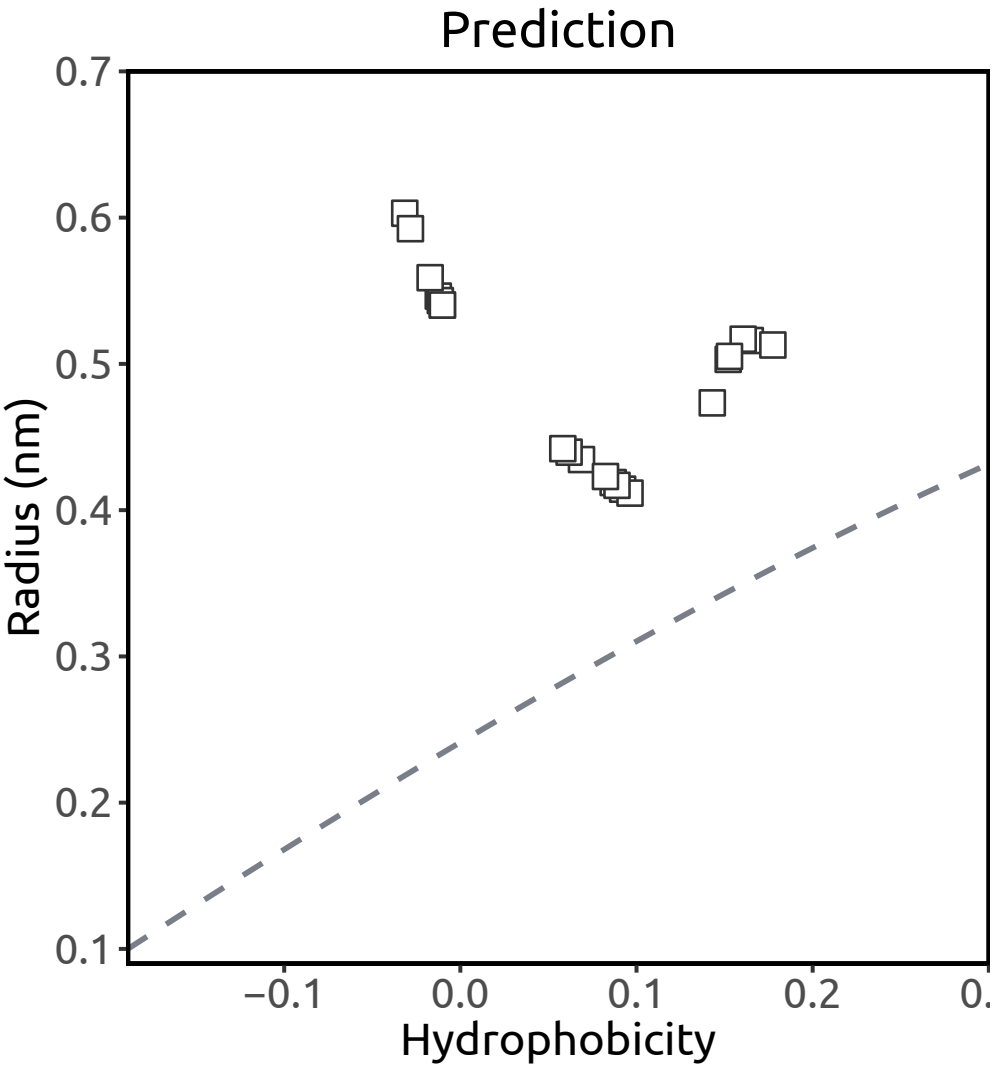
Kv1.2 (PDB ID: 2R9R)

Rattus norvegicus
X–ray (2.4 Å)

Long et al., 2007







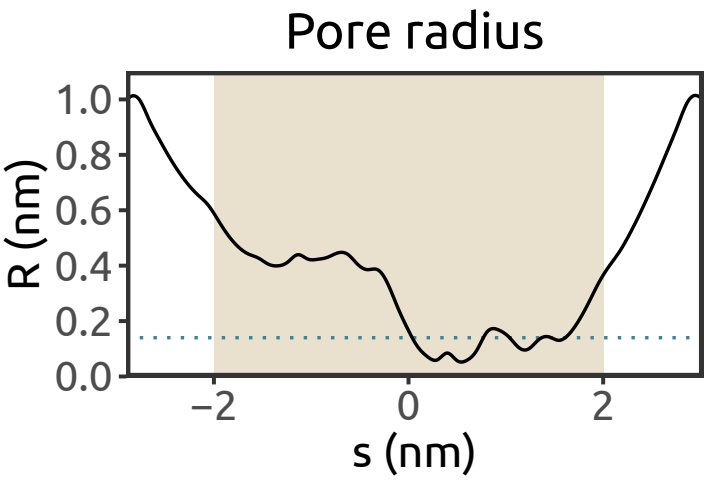
Heuristic score:
0 (n = 0)

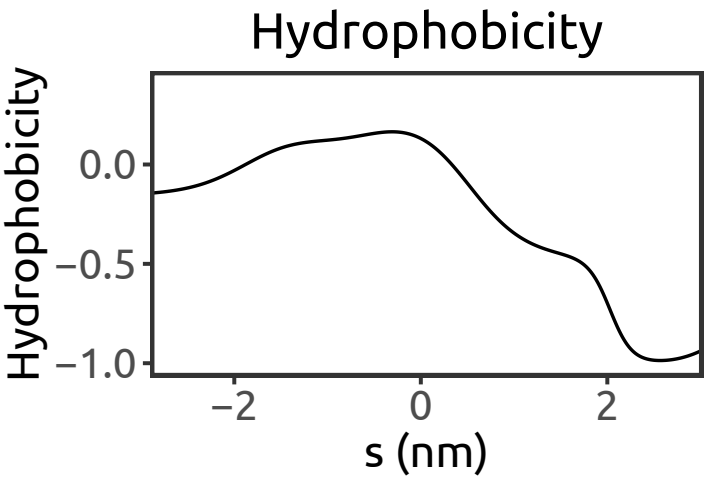
Simulation result:
hydrated channel

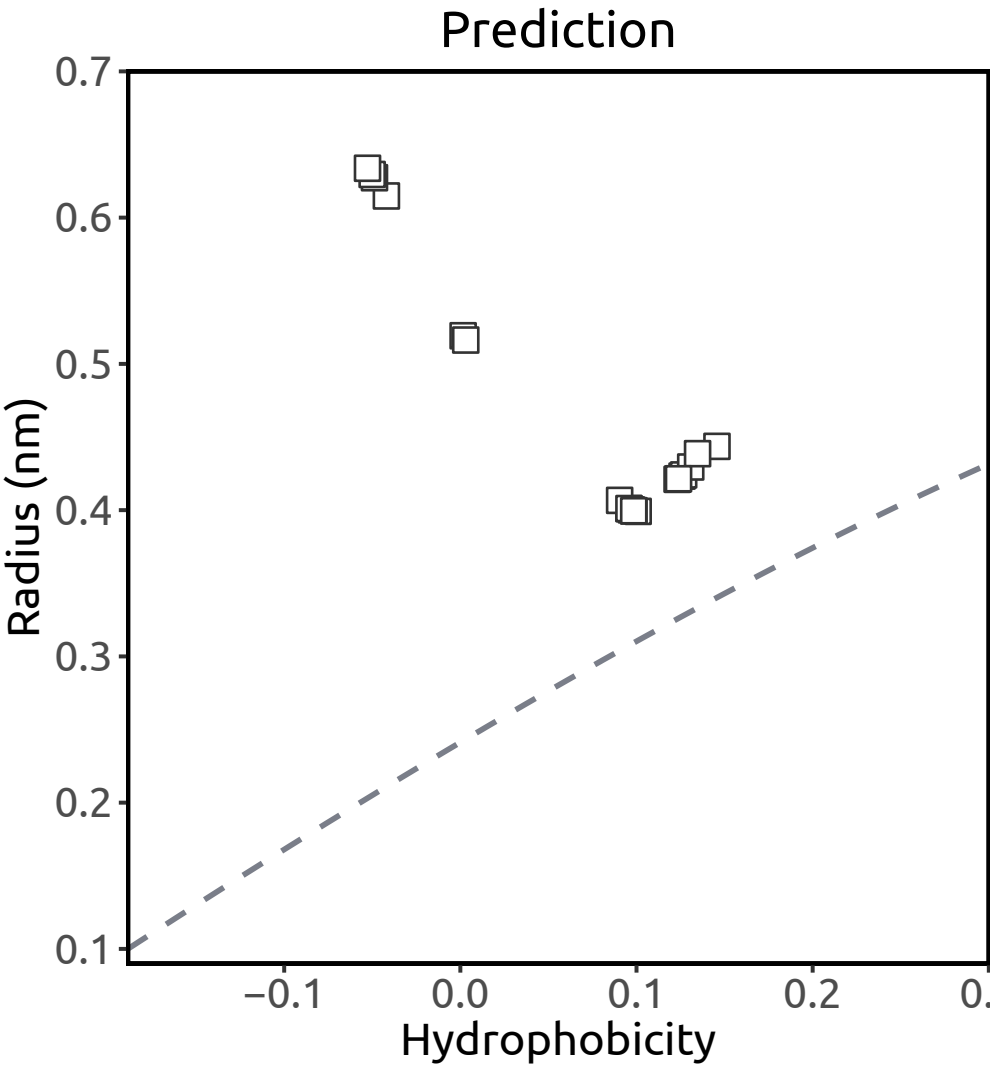
Kv1.2 (PDB ID: 3LUT)

Rattus norvegicus
X–ray (2.9 Å)

Chen et al., 2010







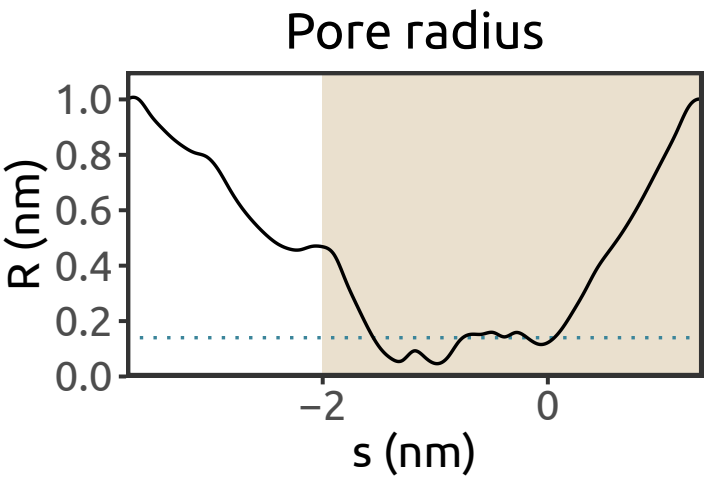
Heuristic score:
0 (n = 0)

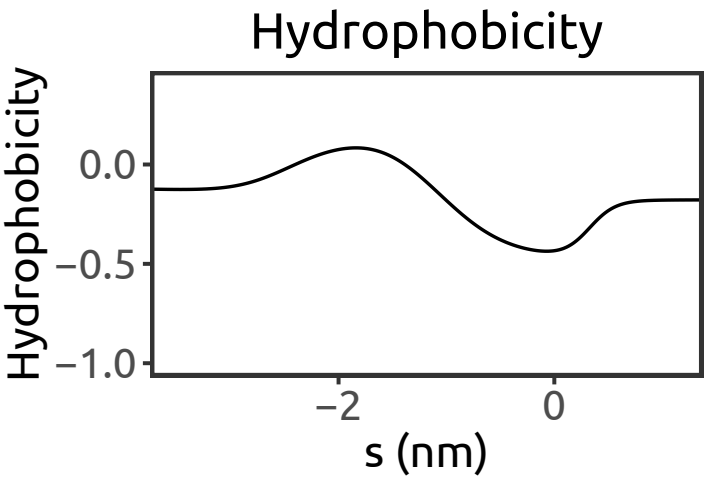
Simulation result:
hydrated channel

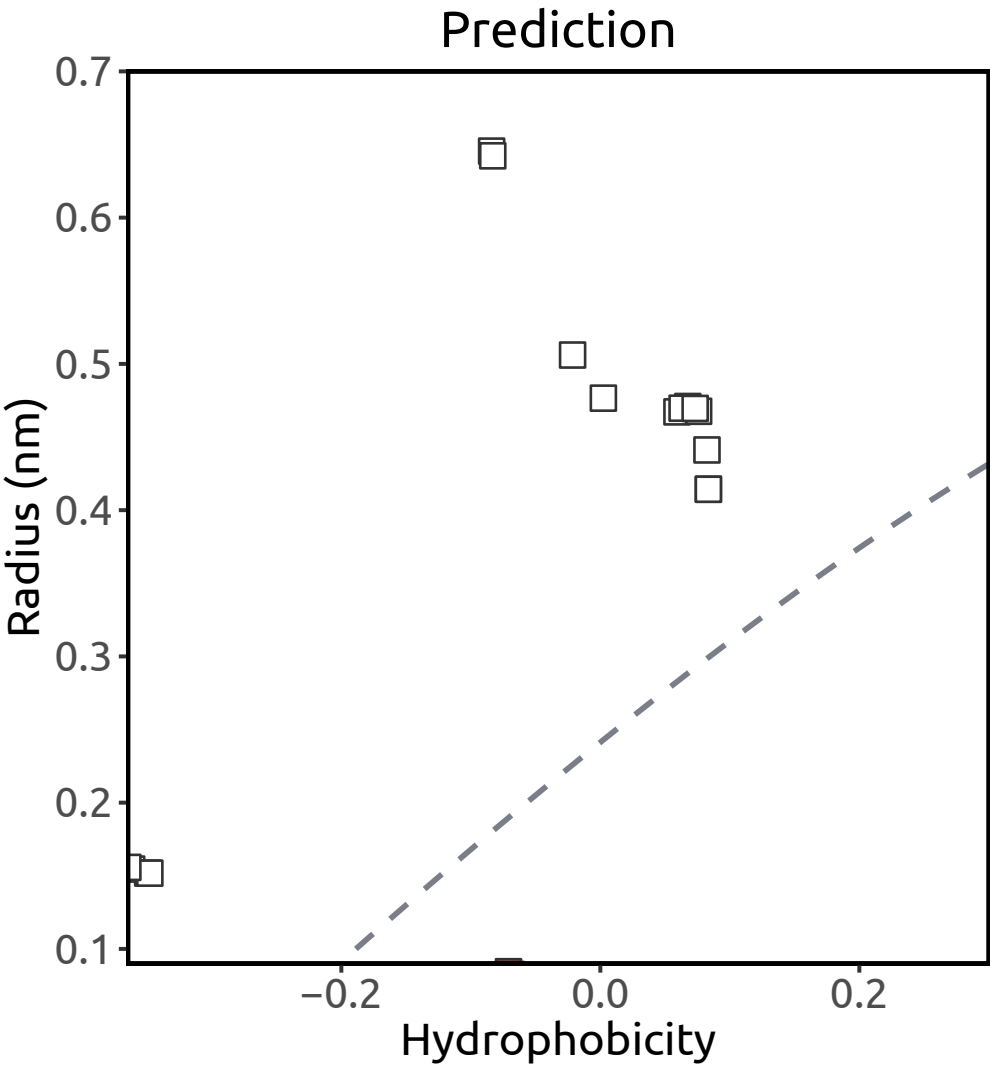
KvAp (PDB ID: 1ORQ)

Aeropyrum pernix
X–ray (3.2 Å)

Jiang et al., 2003







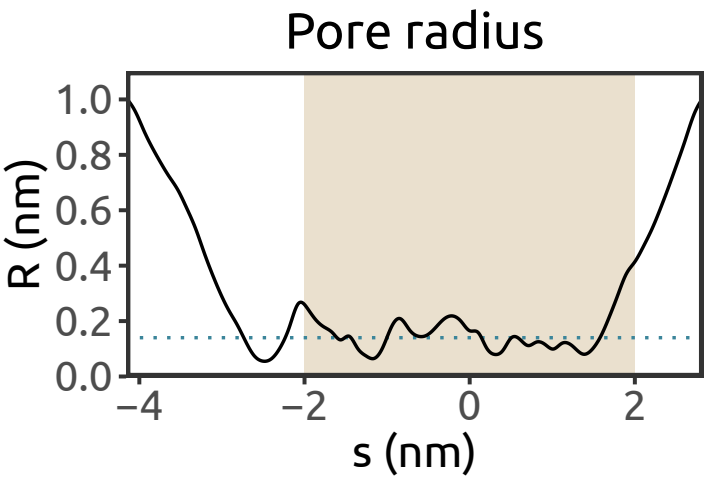
Heuristic score:
0.38 (n = 4)

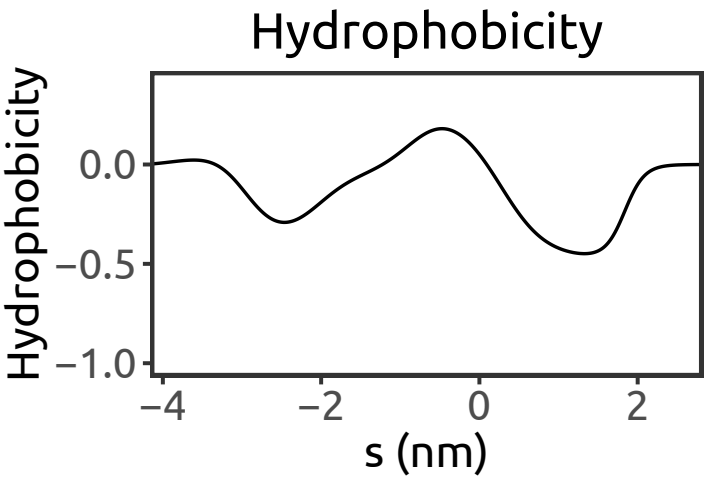
Simulation result:
barrier to water

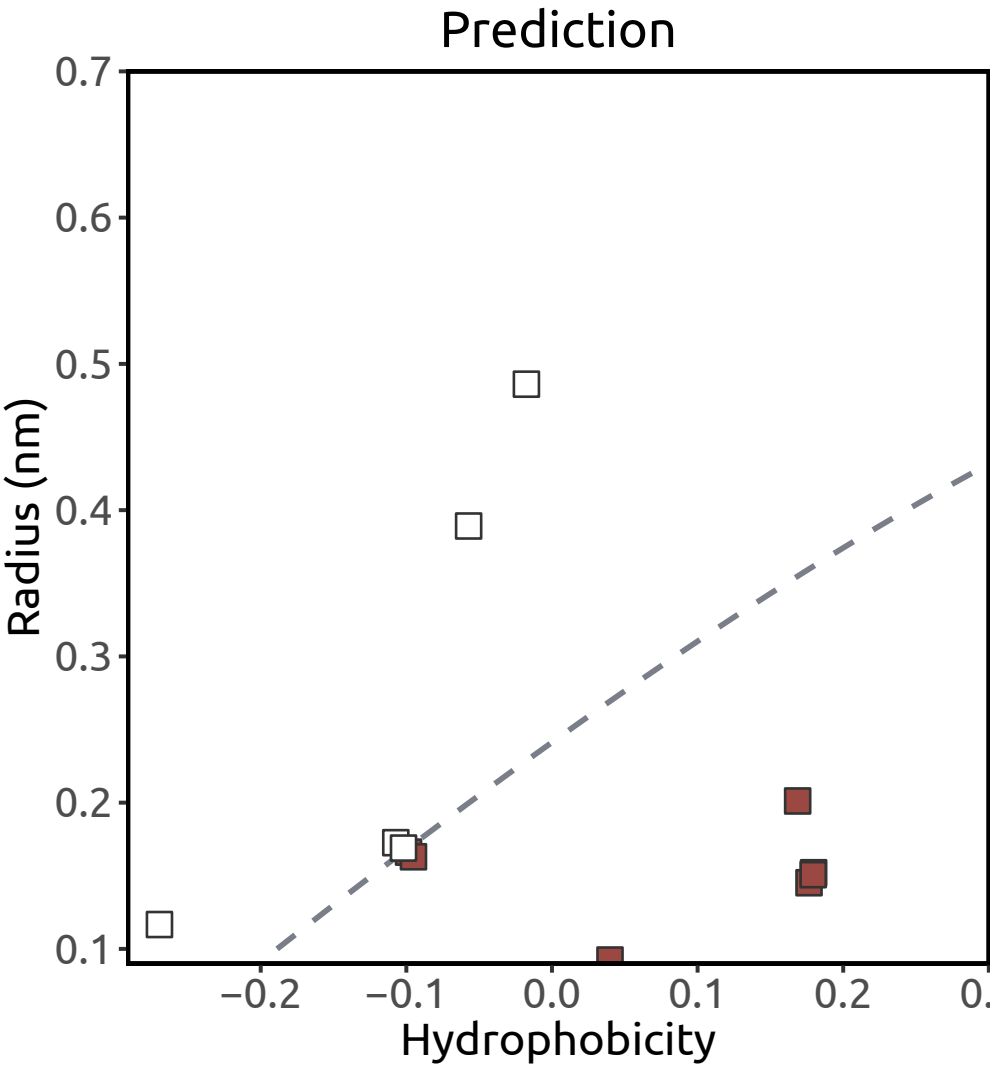
KvLm (PDB ID: 4H33)

Listeria monocytogenes
X–ray (3.1 Å)

Santos et al., 2012







Heuristic score:
1.25 (n = 10)

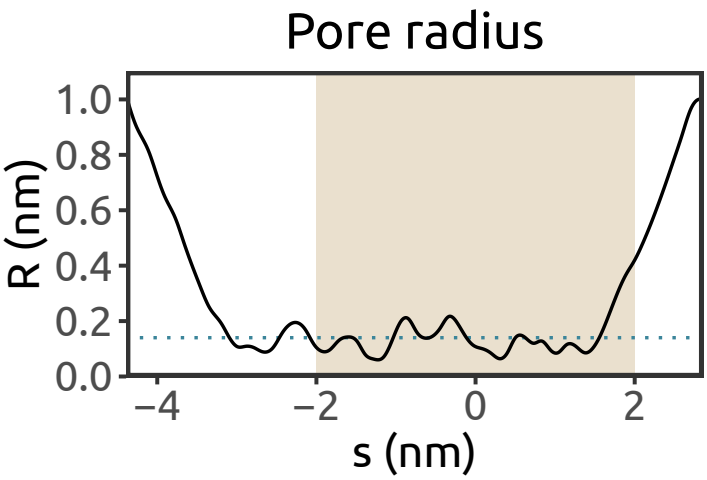
Simulation result:
barrier to water

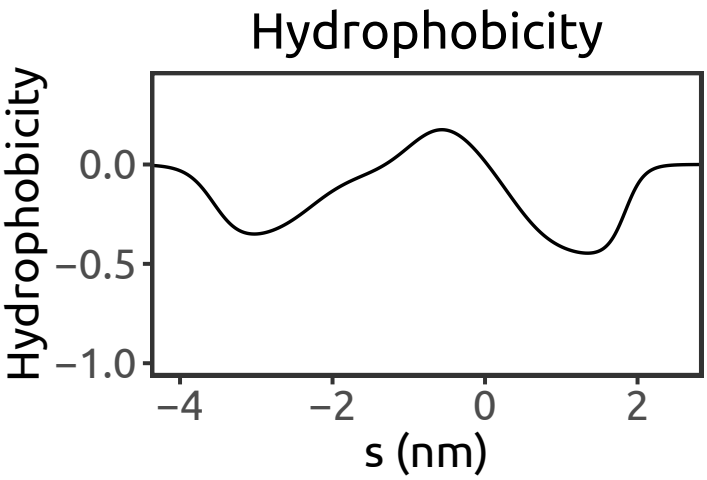
KvLm (PDB ID: 4H37)

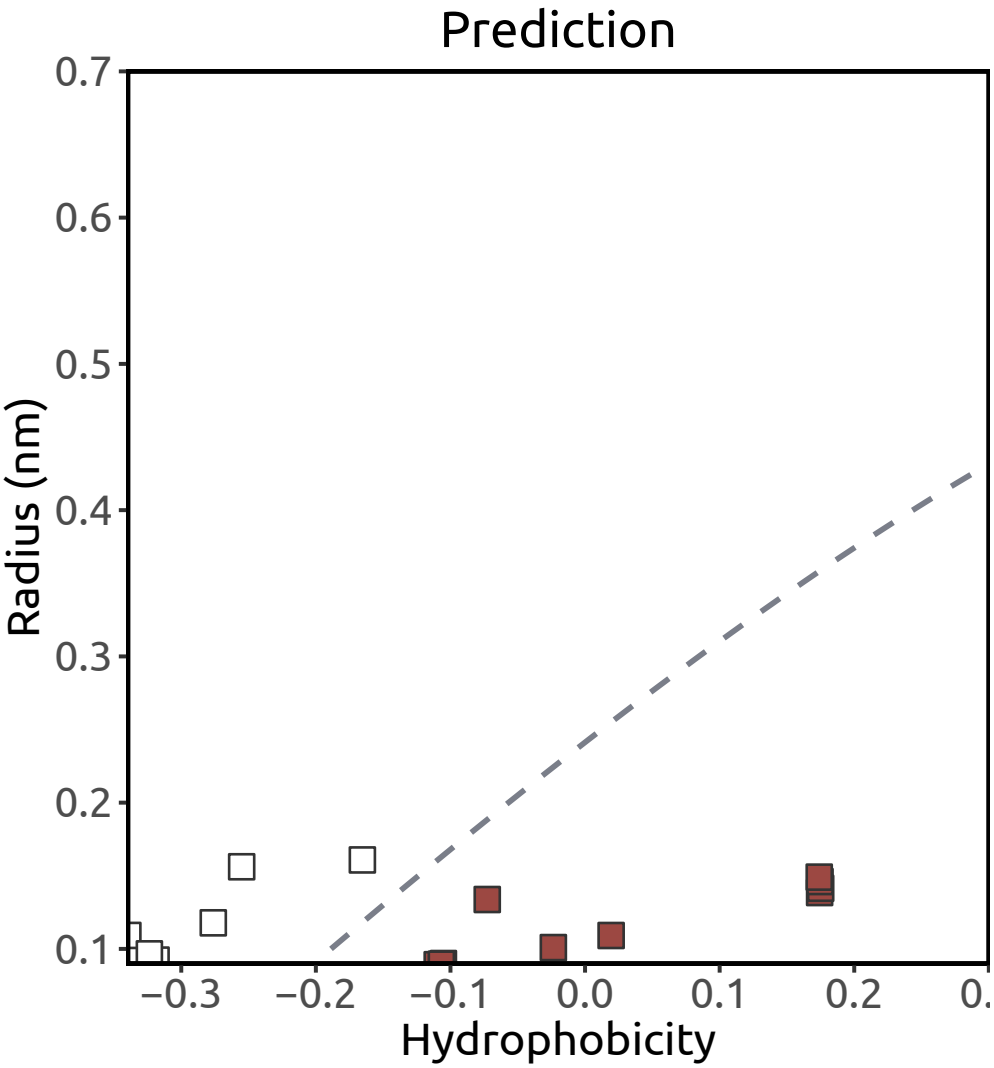
Listeria monocytogenes

X–ray (3.35 Å)

Santos et al., 2012







Heuristic score:

1.76 (n = 14)

Simulation result:

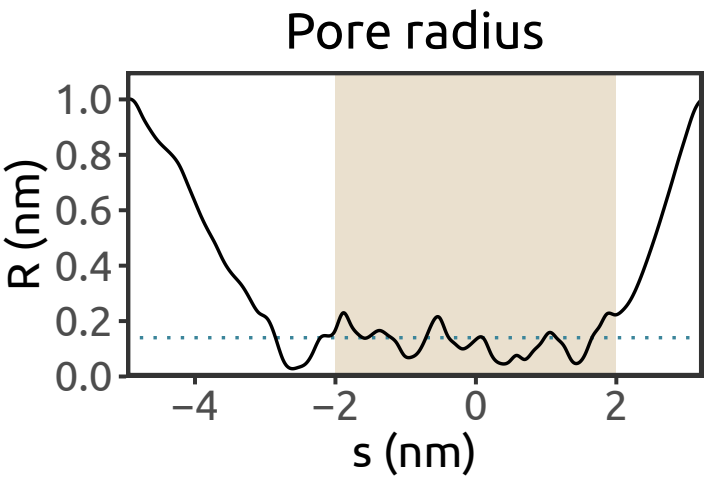
barrier to water

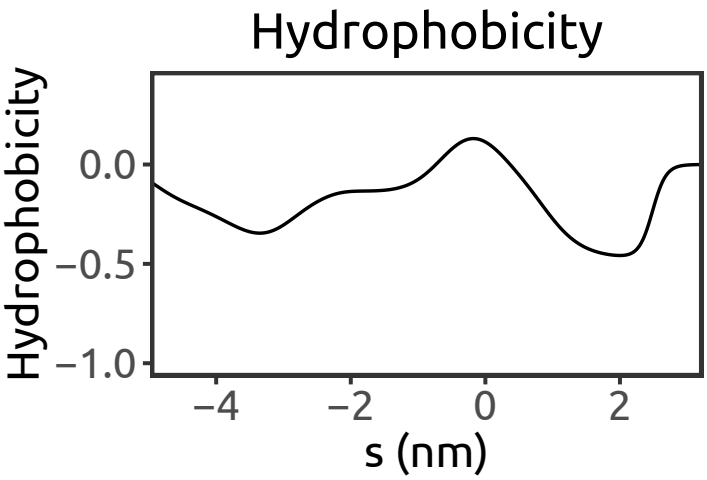
MloK1 (PDB ID: 3BEH)

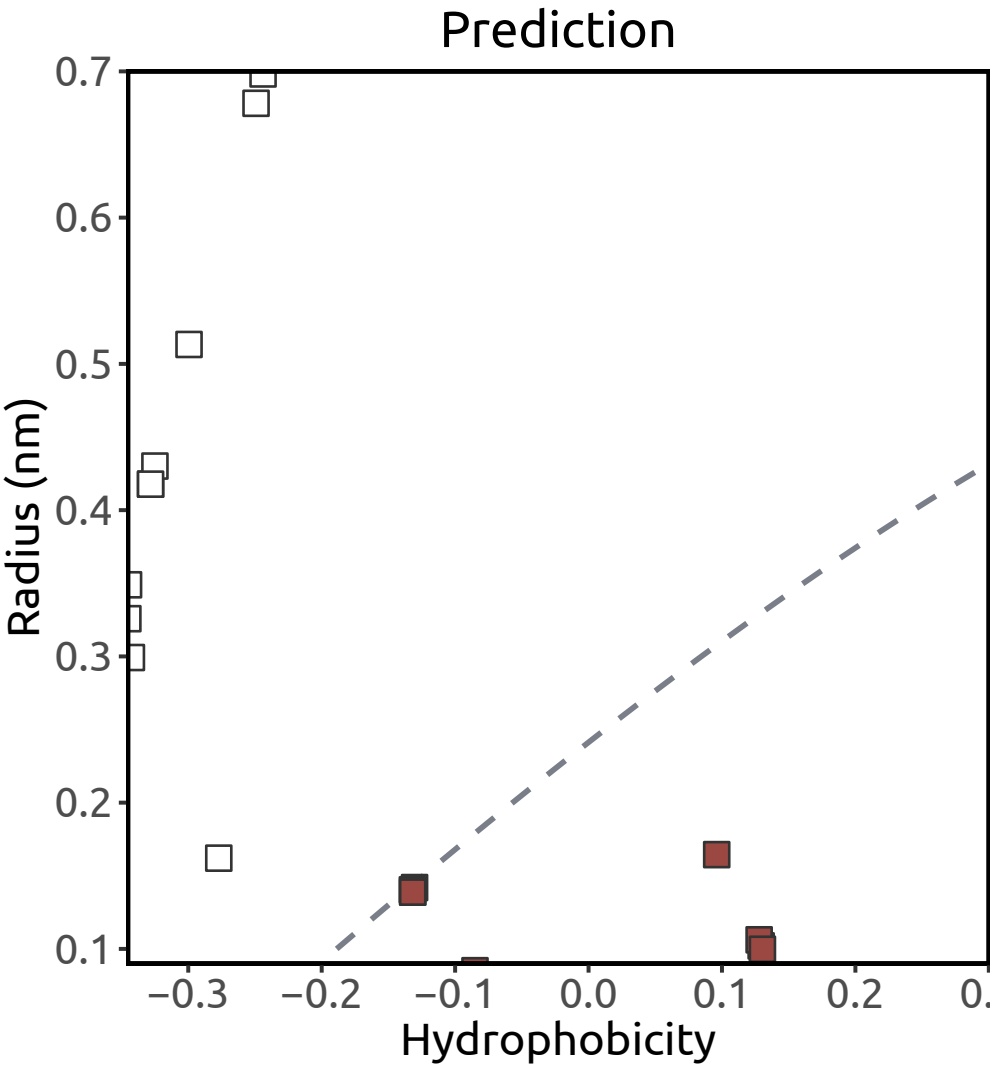
Mesorhizobium loti

X–ray (3.1 Å)

Clayton et al., 2008







Heuristic score:

1.13 (n = 13)

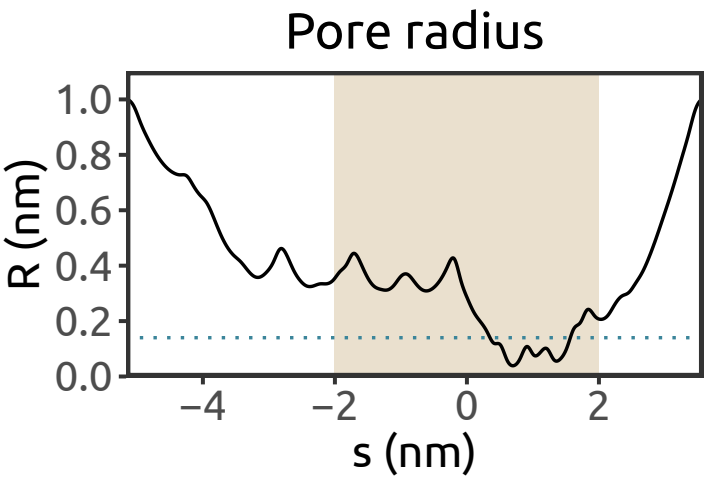
Simulation result:

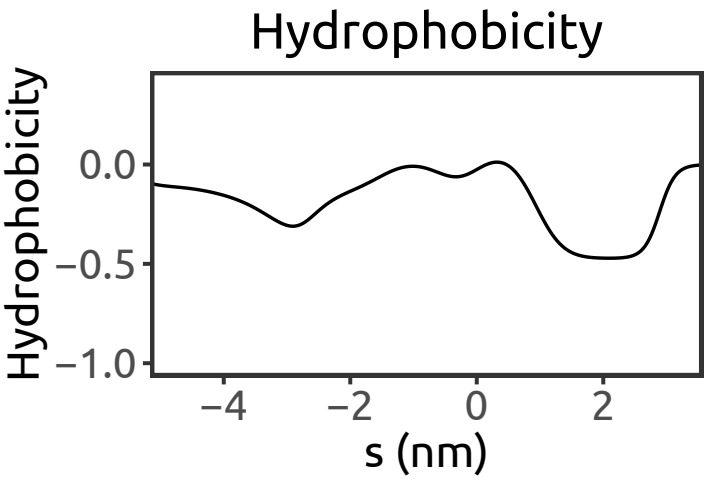
barrier to water

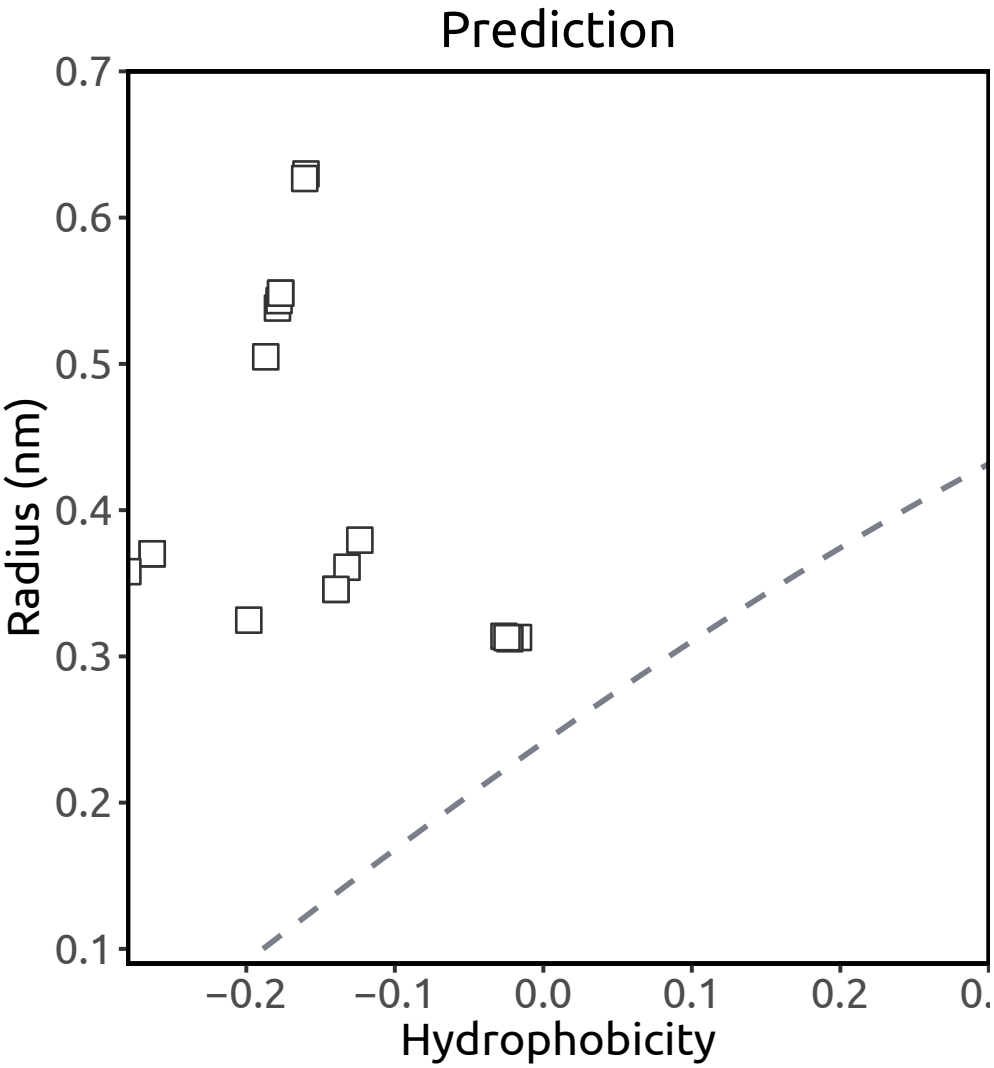
MloK1 (PDB ID: 6EO1)

Mesorhizobium loti
cryo–EM (4.5 Å)

Kowal et al., 2018







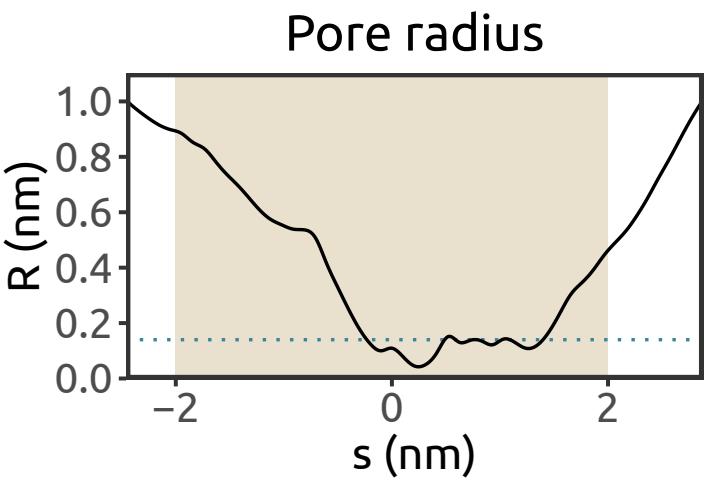
Heuristic score:
0 (n = 0)

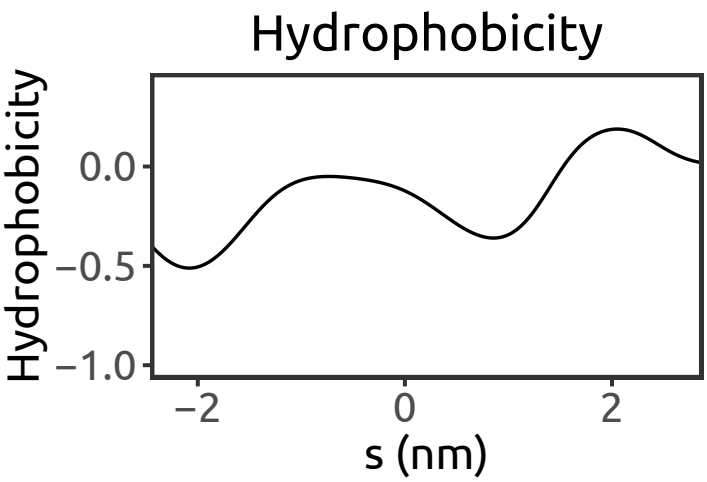
Simulation result:
hydrated channel

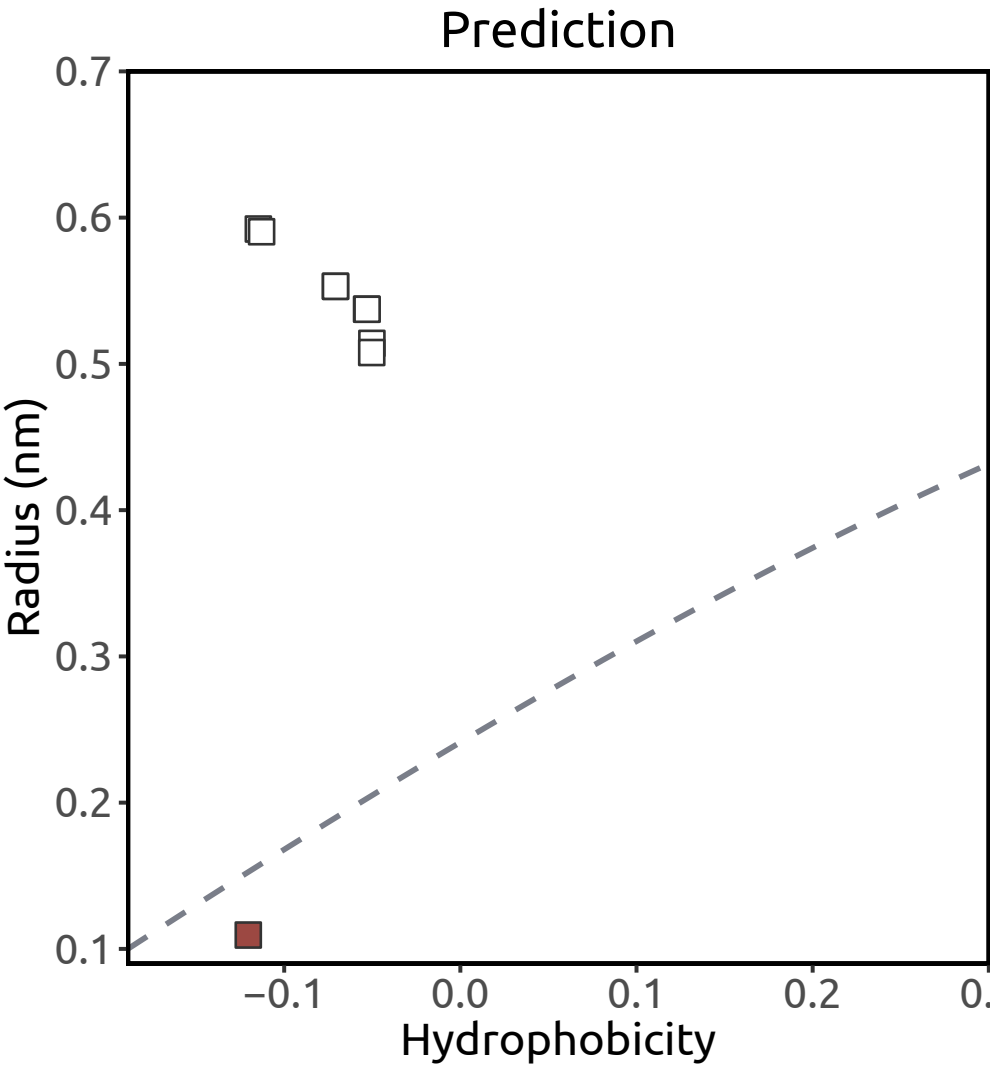
Slo1 (PDB ID: 5TJ6)

Aplysia californica
cryo–EM (3.5 Å)

Tao el al, 2017







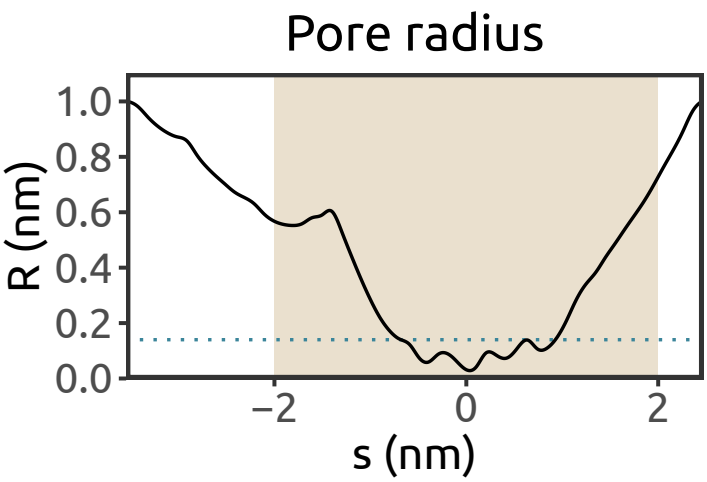
Heuristic score:
0.03 (n = 1)

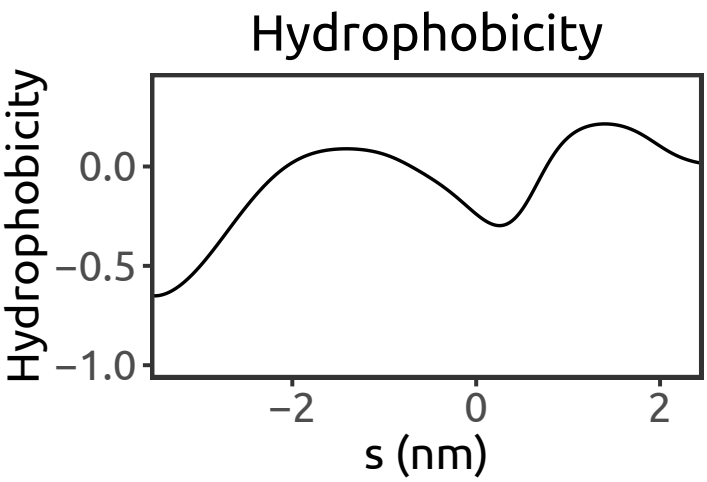
Simulation result:
hydrated channel

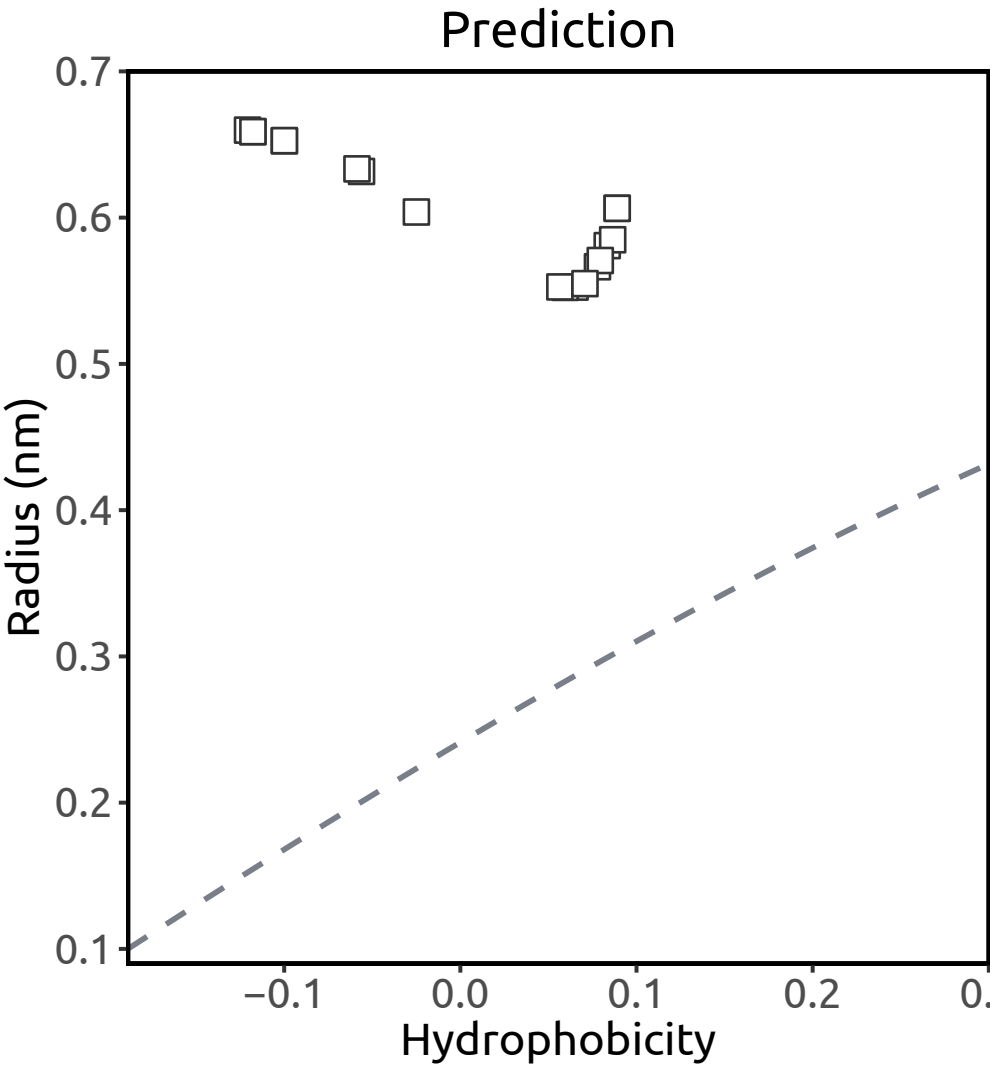
Slo1 (PDB ID: 5TJI)

Aplysia californica
cryo–EM (3.8 Å)

Hite et al., 2017







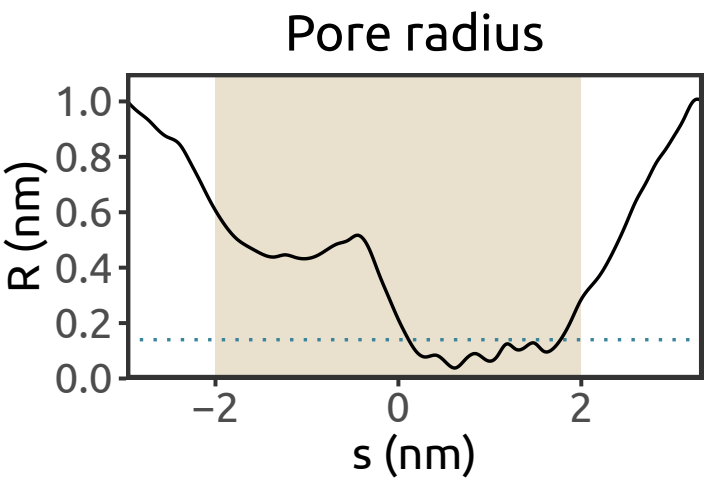
Heuristic score:
0 (n = 0)

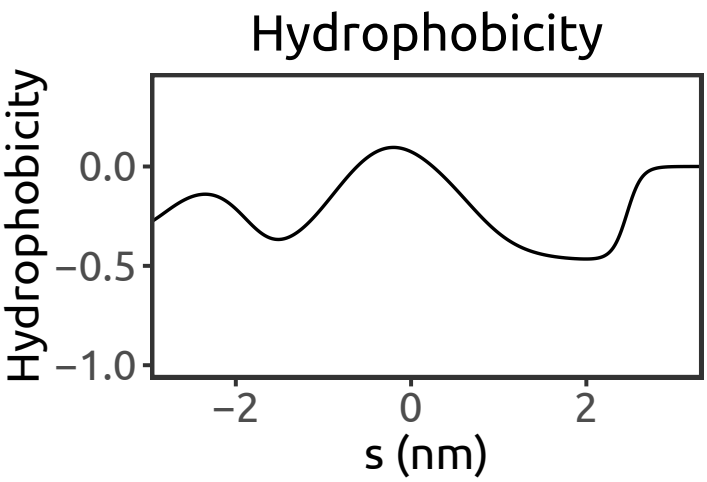
Simulation result:
hydrated channel

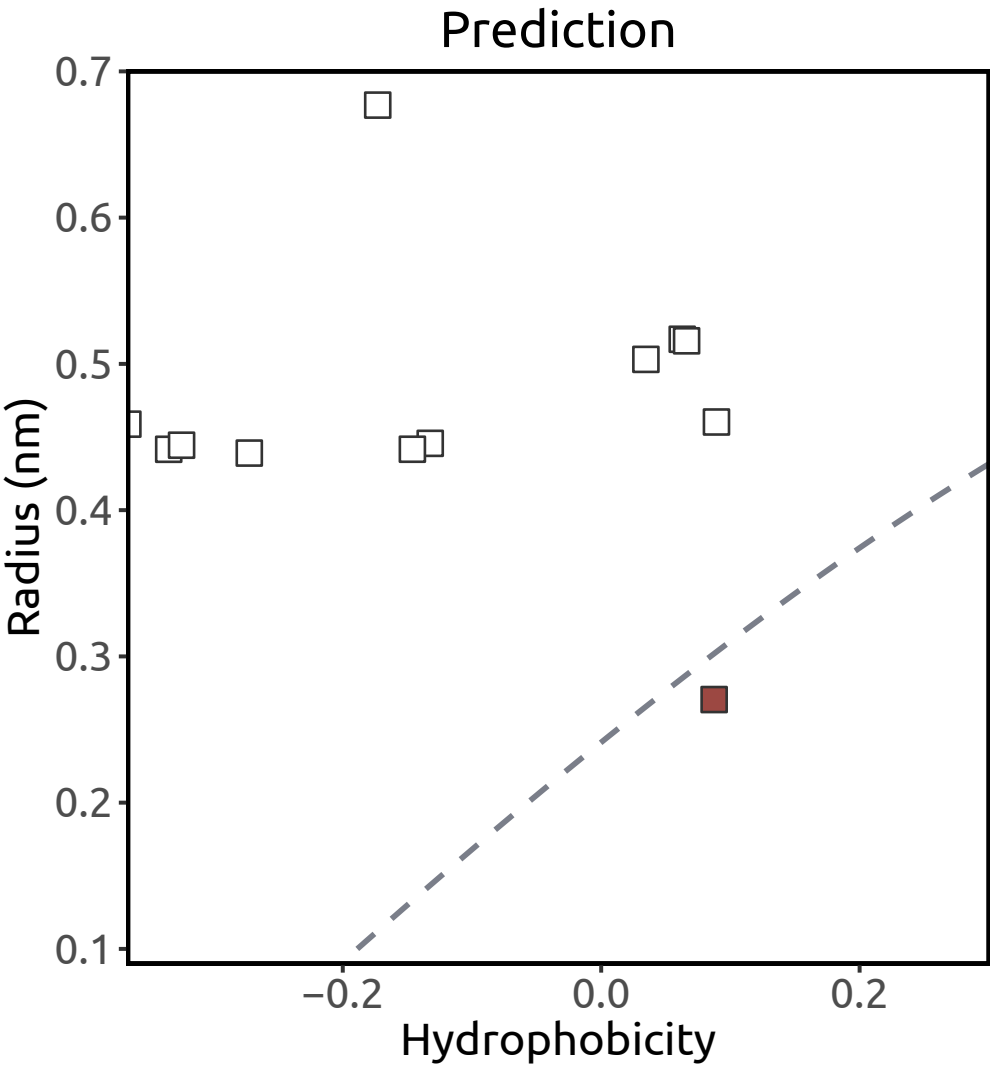
Slo2.2 (PDB ID: 5U70)

Gallus gallus
cryo–EM (3.76 Å)

Hite & MacKinnon, 2017







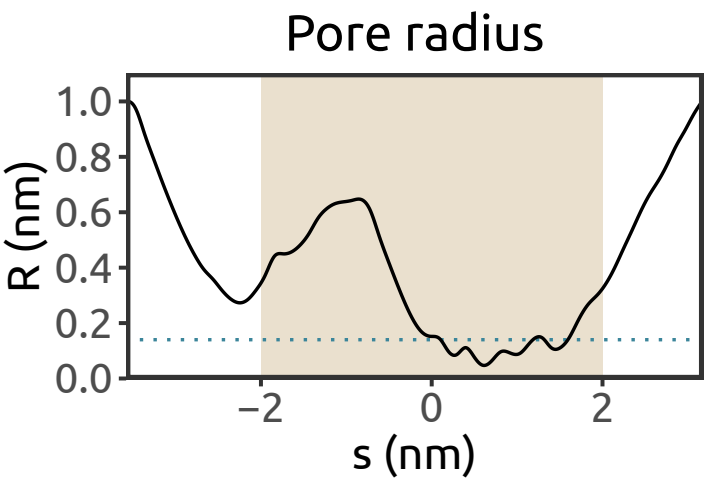
Heuristic score:
0.03 (n = 1)

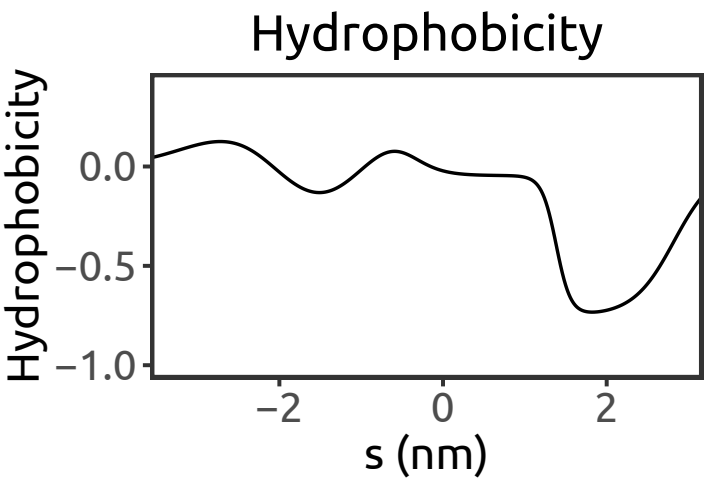
Simulation result:
hydrated channel

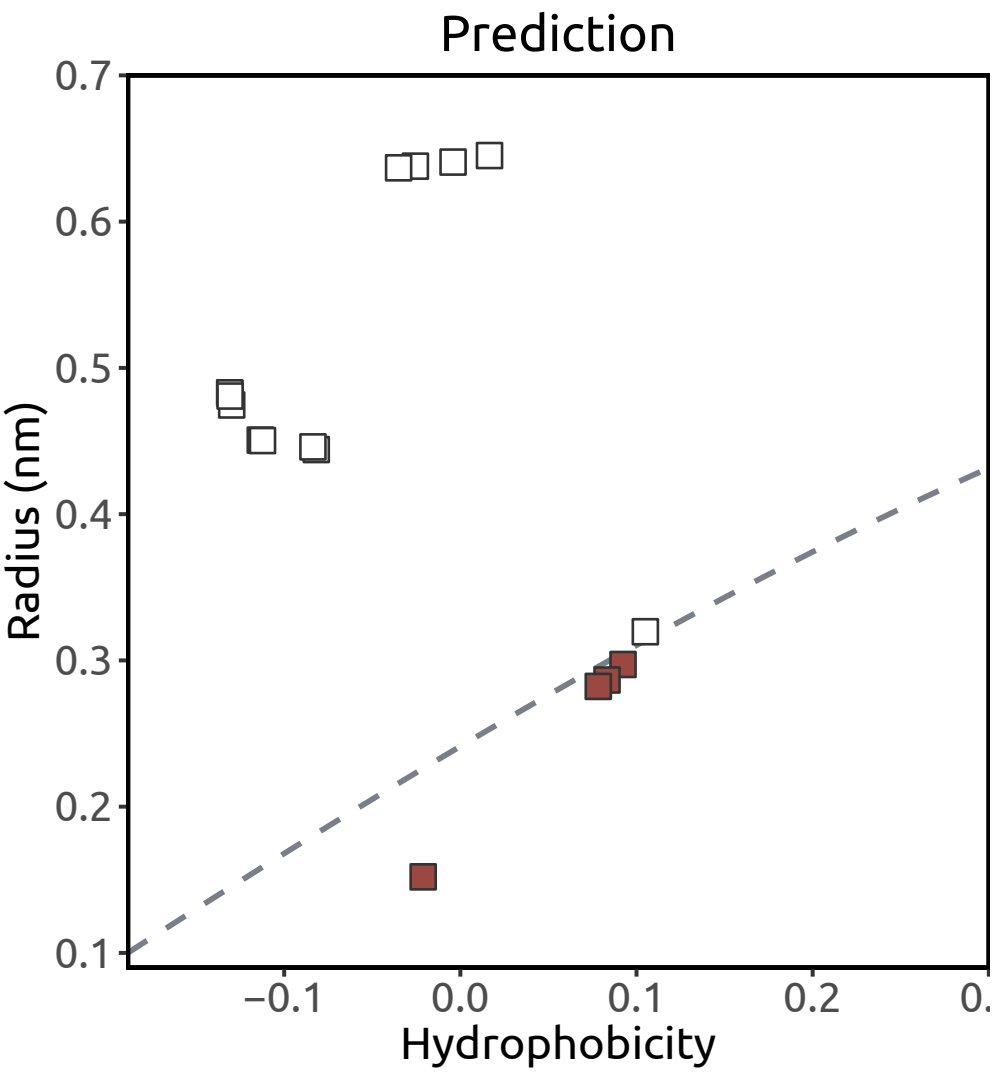
Slo2.2 (PDB ID: 5U76)

Gallus gallus
cryo–EM (3.76 Å)

Hite & MacKinnon, 2017







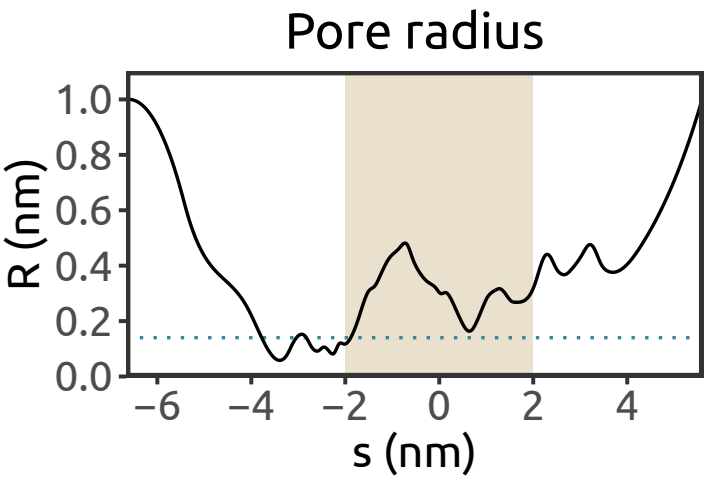
Heuristic score:
0.09 (n = 4)

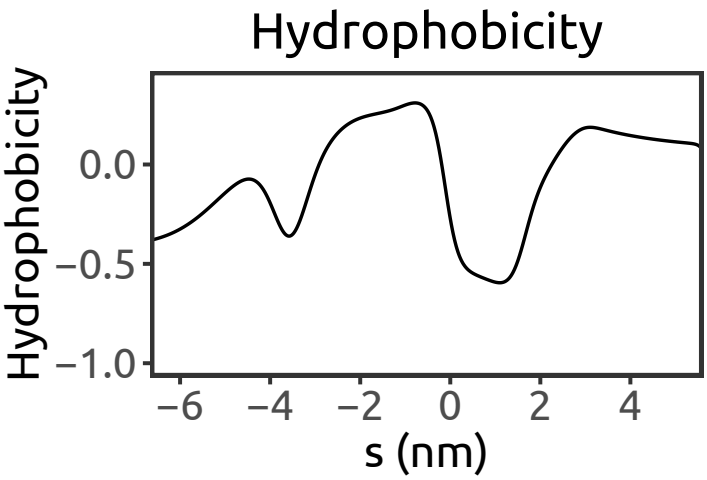
Simulation result:
hydrated channel

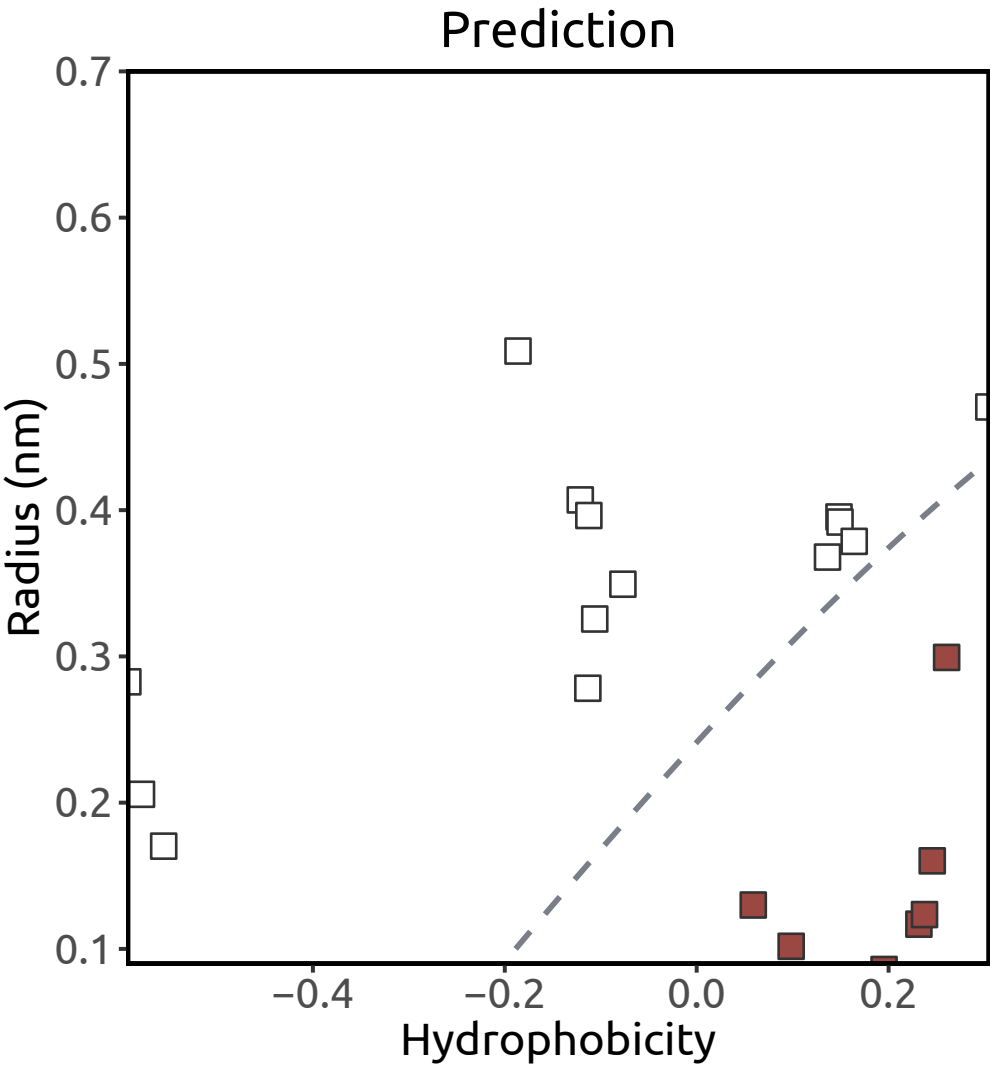
Cav1.1 (PDB ID: 5GJV)

Oryctolagus cuniculus
cryo–EM (3.6 Å)

Wu et al., 2016







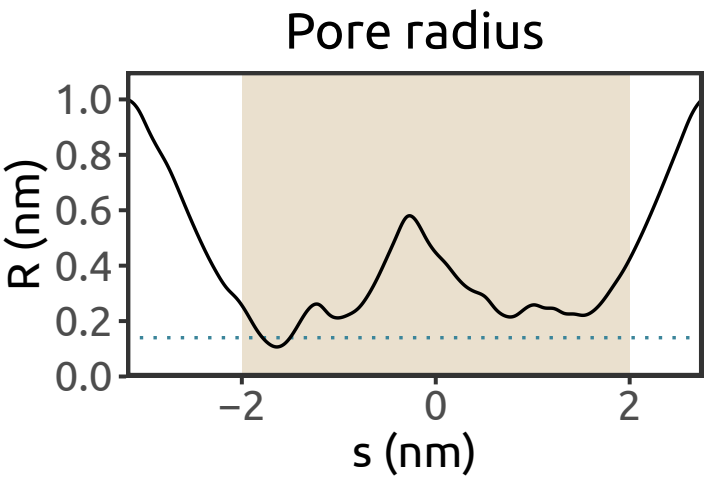
Heuristic score:
1.3 (n = 7)

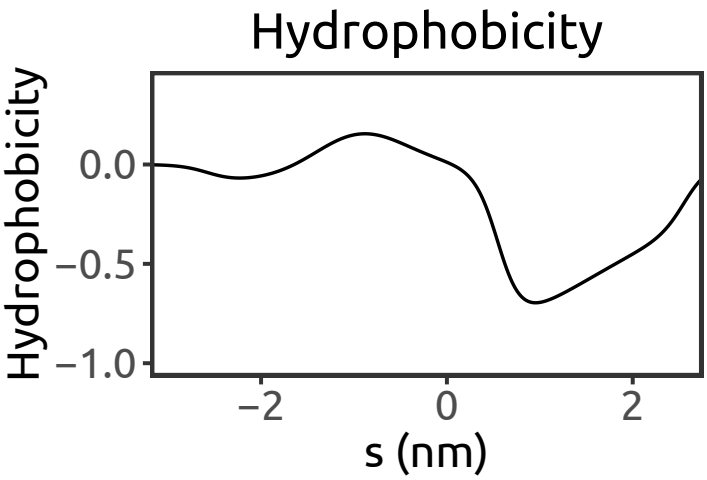
Simulation result:
barrier to water

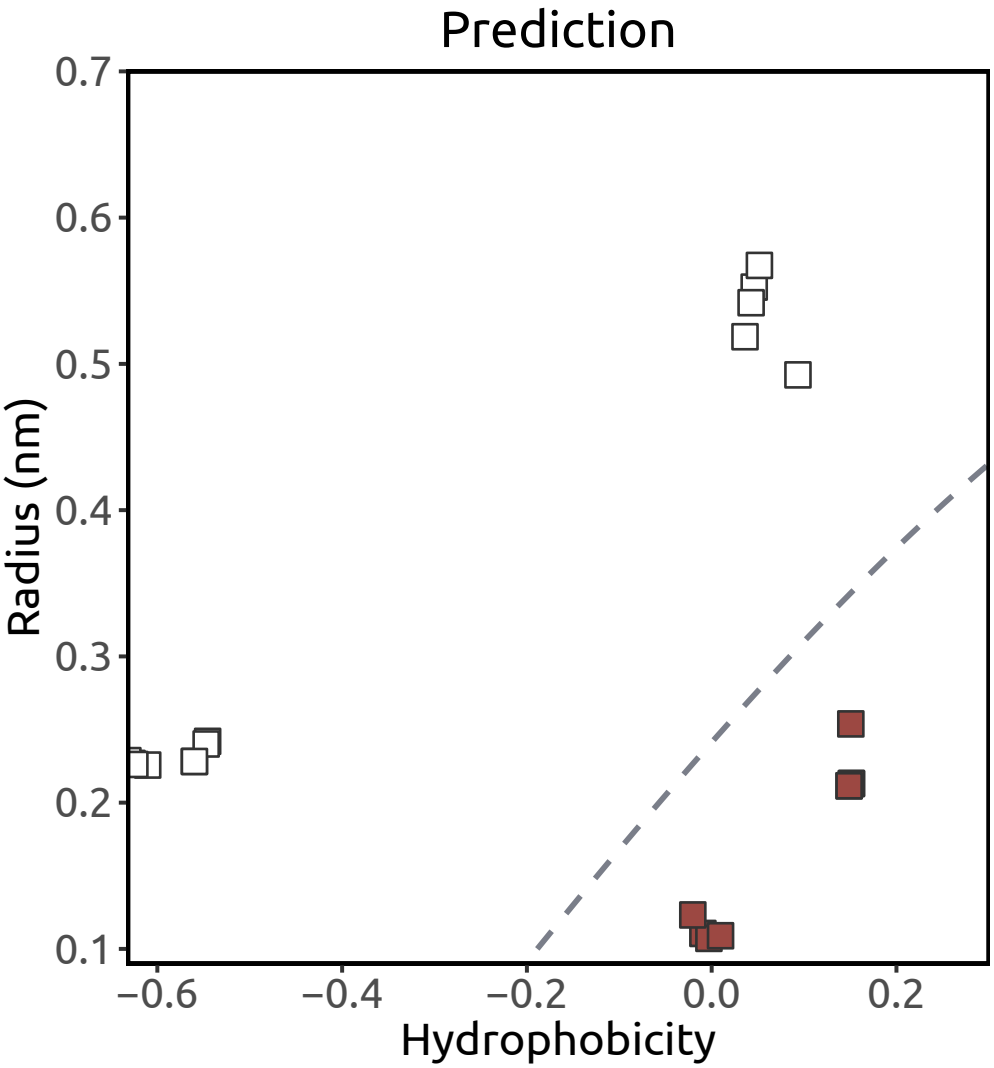
CavAb (PDB ID: 4MVM)

Arcobacter butzleri
X–ray (3.20 Å)

Tang et al., 2014







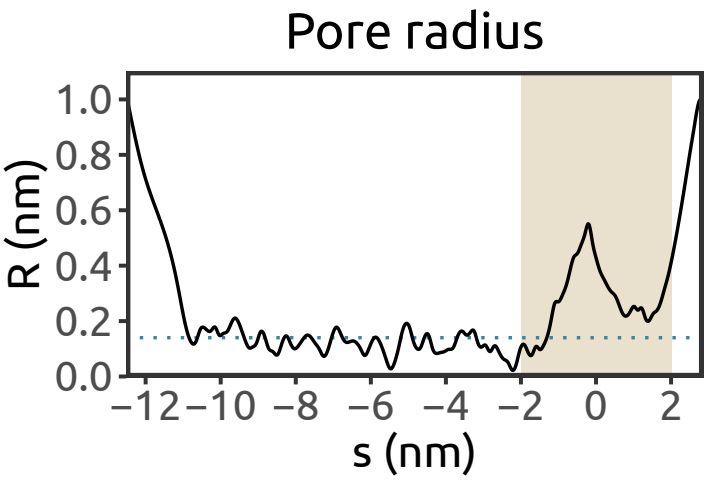
Heuristic score:
0.92 (n = 9)

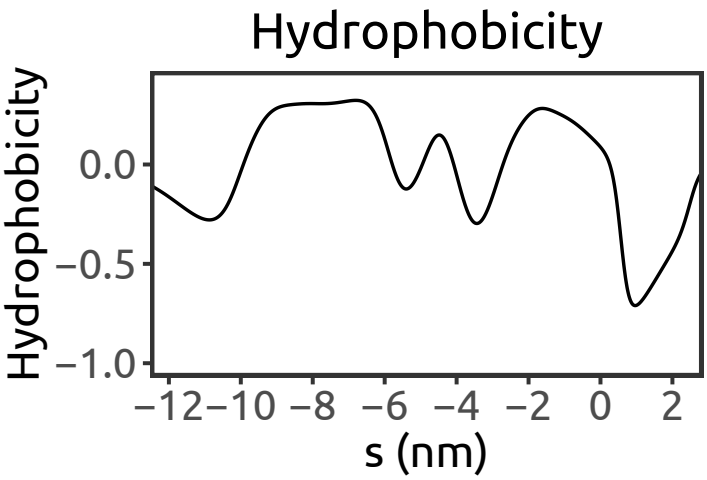
Simulation result:
barrier to water

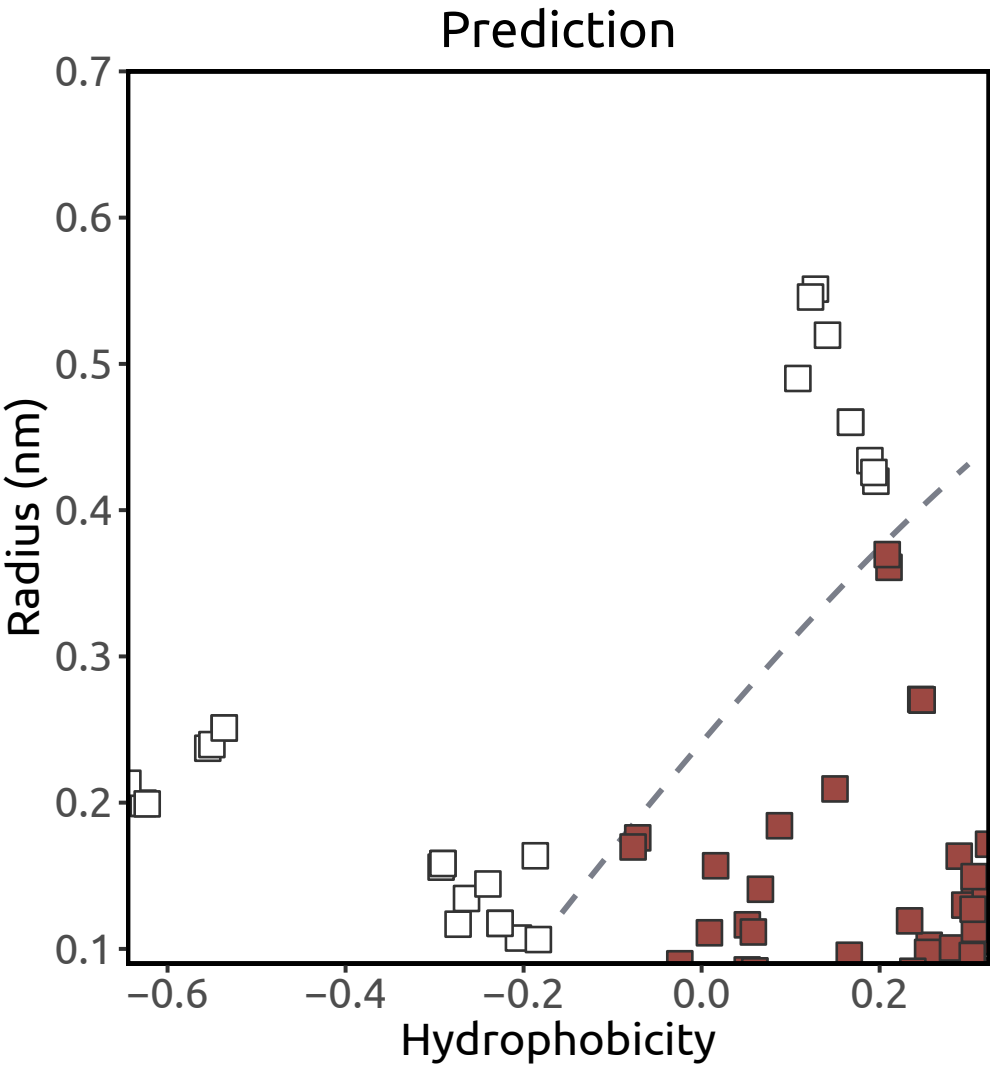
CavAb (PDB ID: 5KLB)

Arcobacter butzleri
X–ray (2.7 Å)

Tang et al., 2016







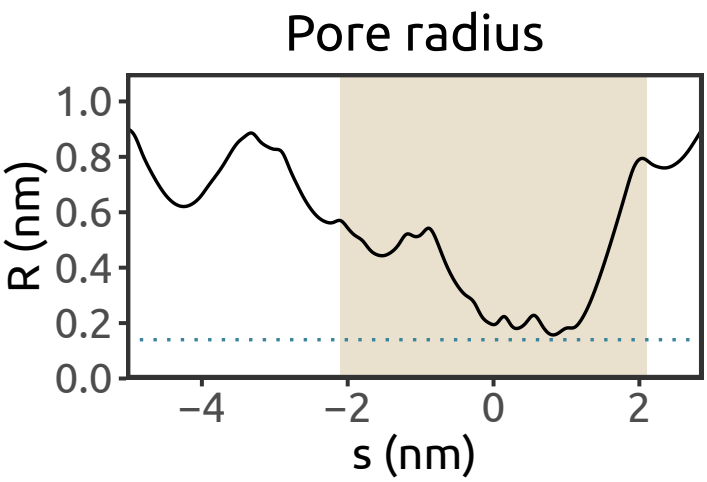
Heuristic score:
9.44 (n = 50)

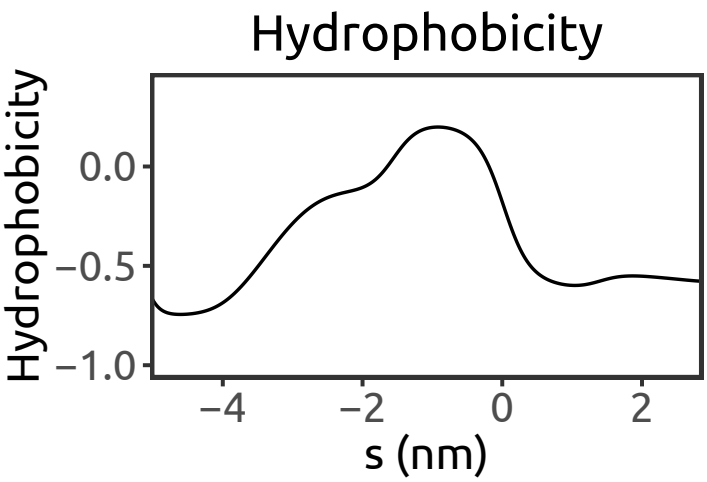
Simulation result:
barrier to water

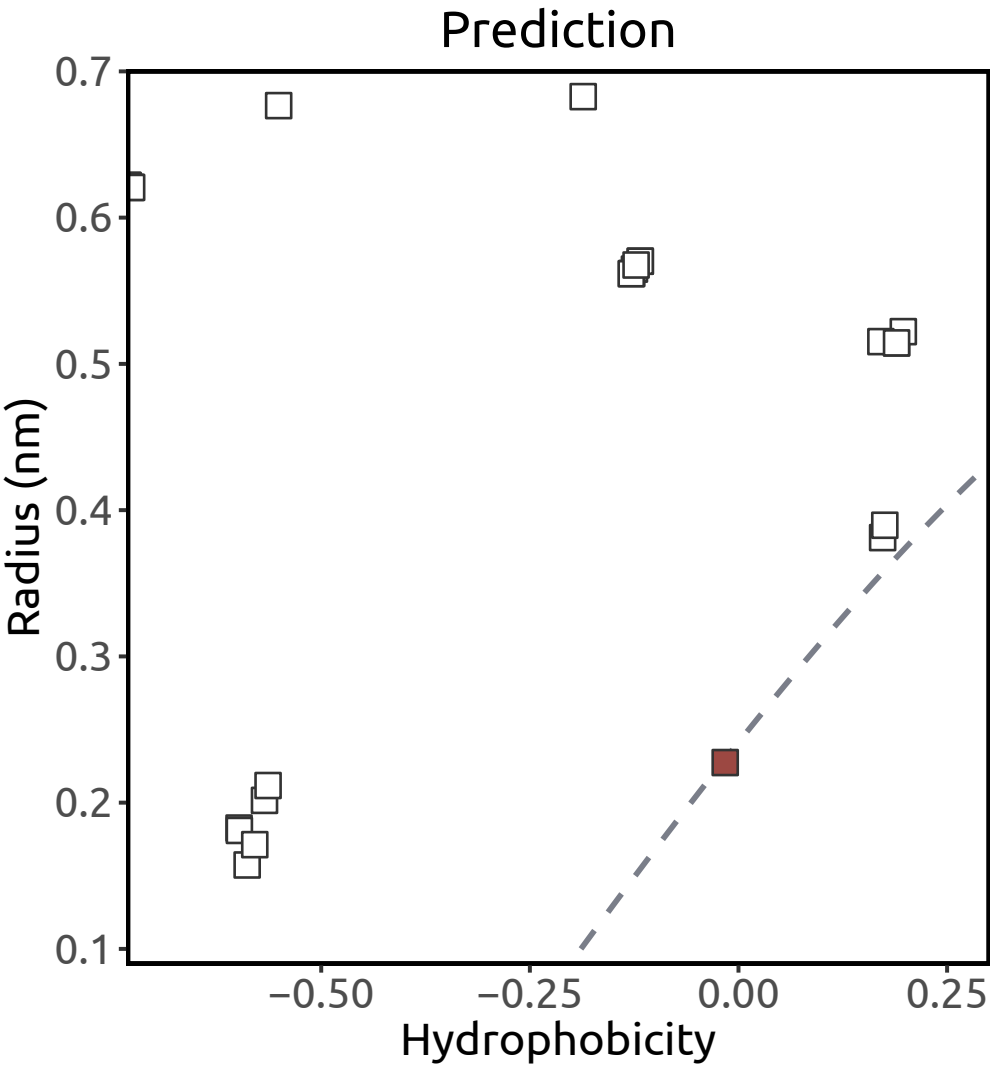
CNG (PDB ID: 5H3O)

Caenorhabditis elegans
cryo–EM (3.5 Å)

Li et al., 2017







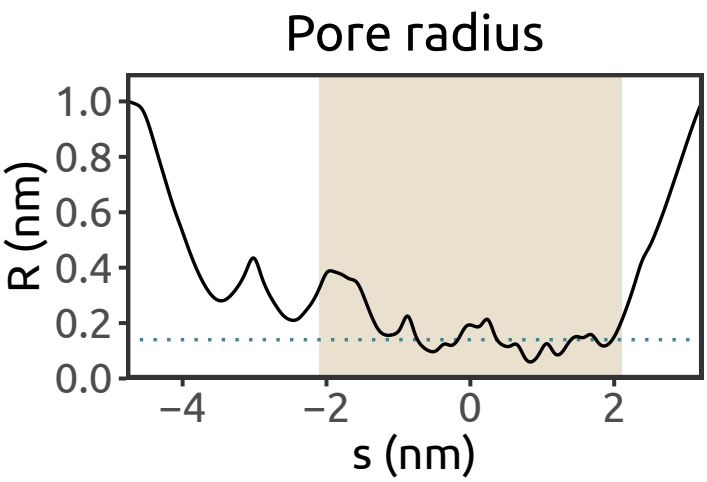
Heuristic score:
0 (n = 1)

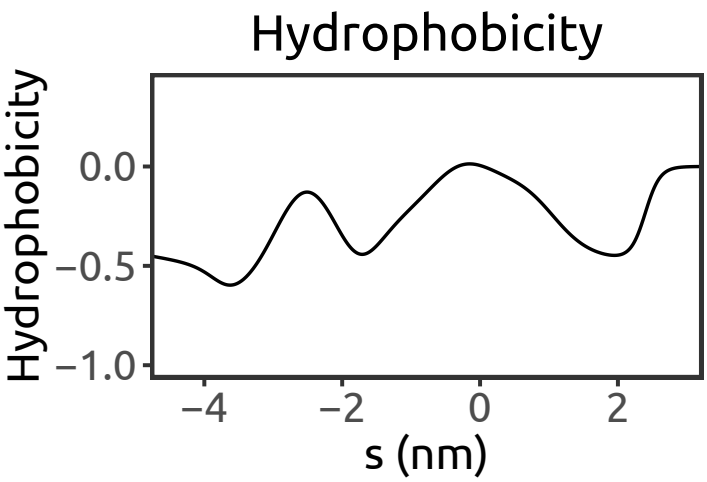
Simulation result:
hydrated channel

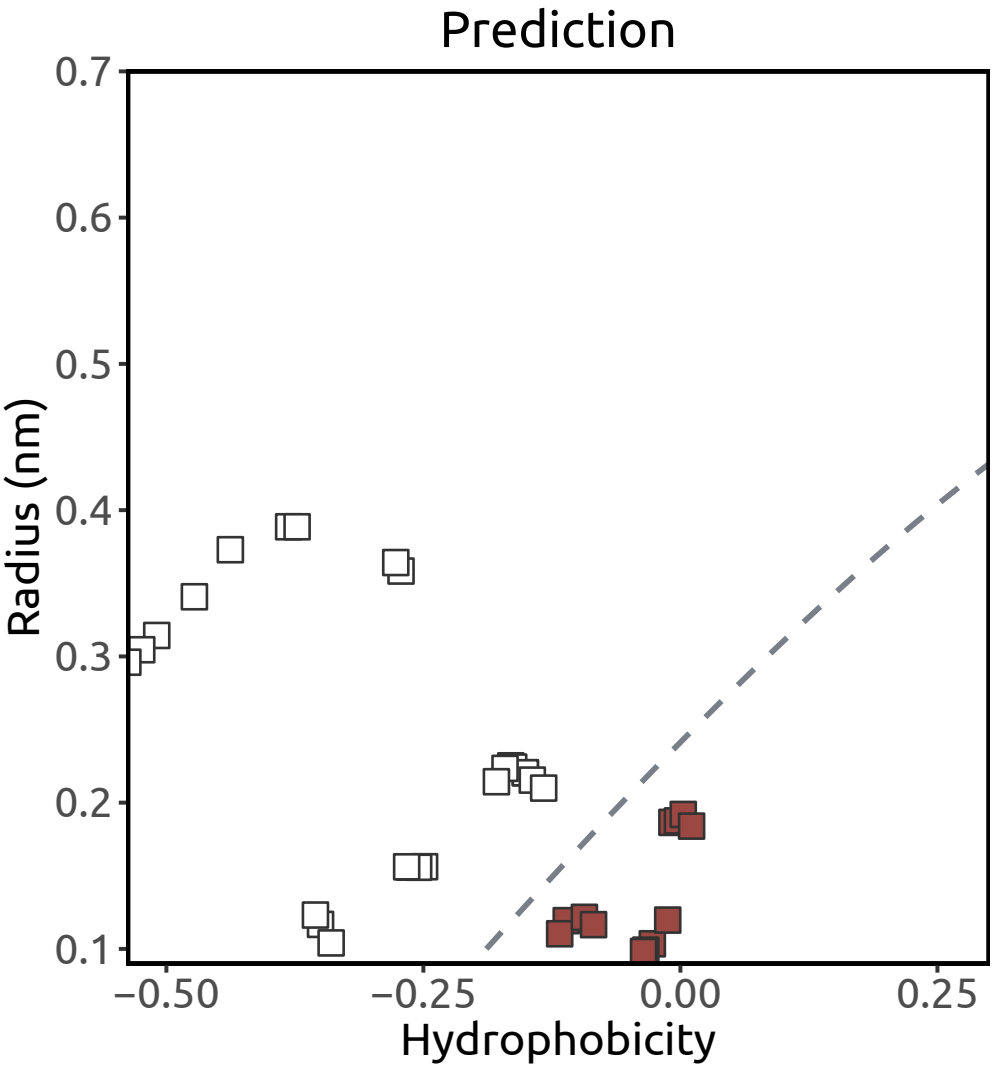
CNG (PDB ID: 5V4S)

Leptospira licerasiae
cryo–EM (4.2 Å)

James et al., 2017







Heuristic score:
0.71 (n = 12)

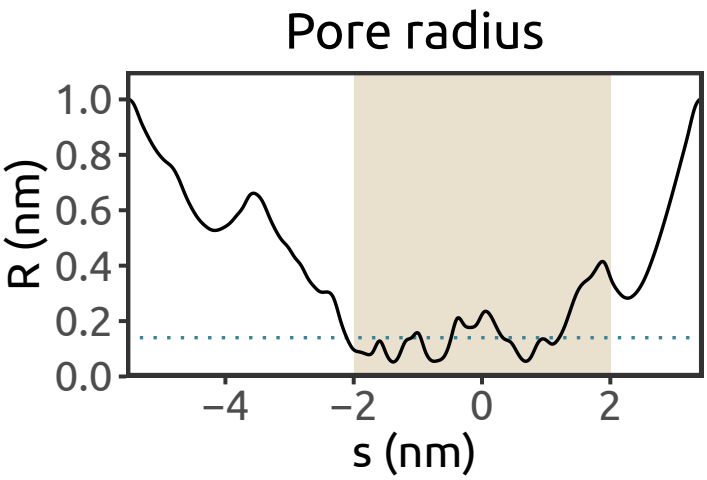
Simulation result:
barrier to water

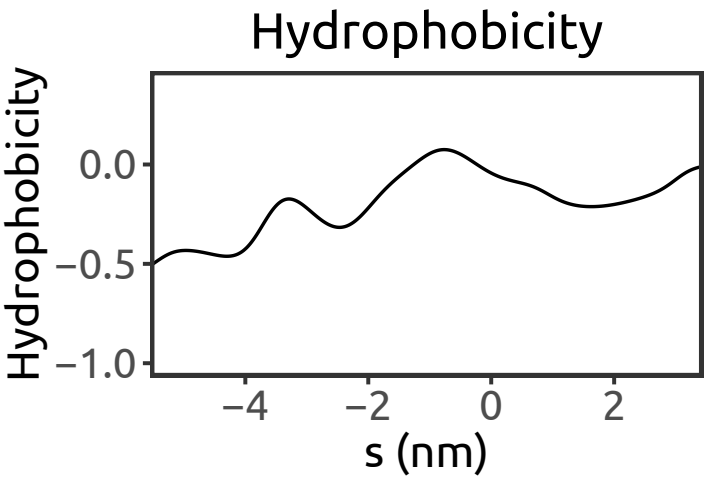
HCN1 (PDB ID: 5U6O)

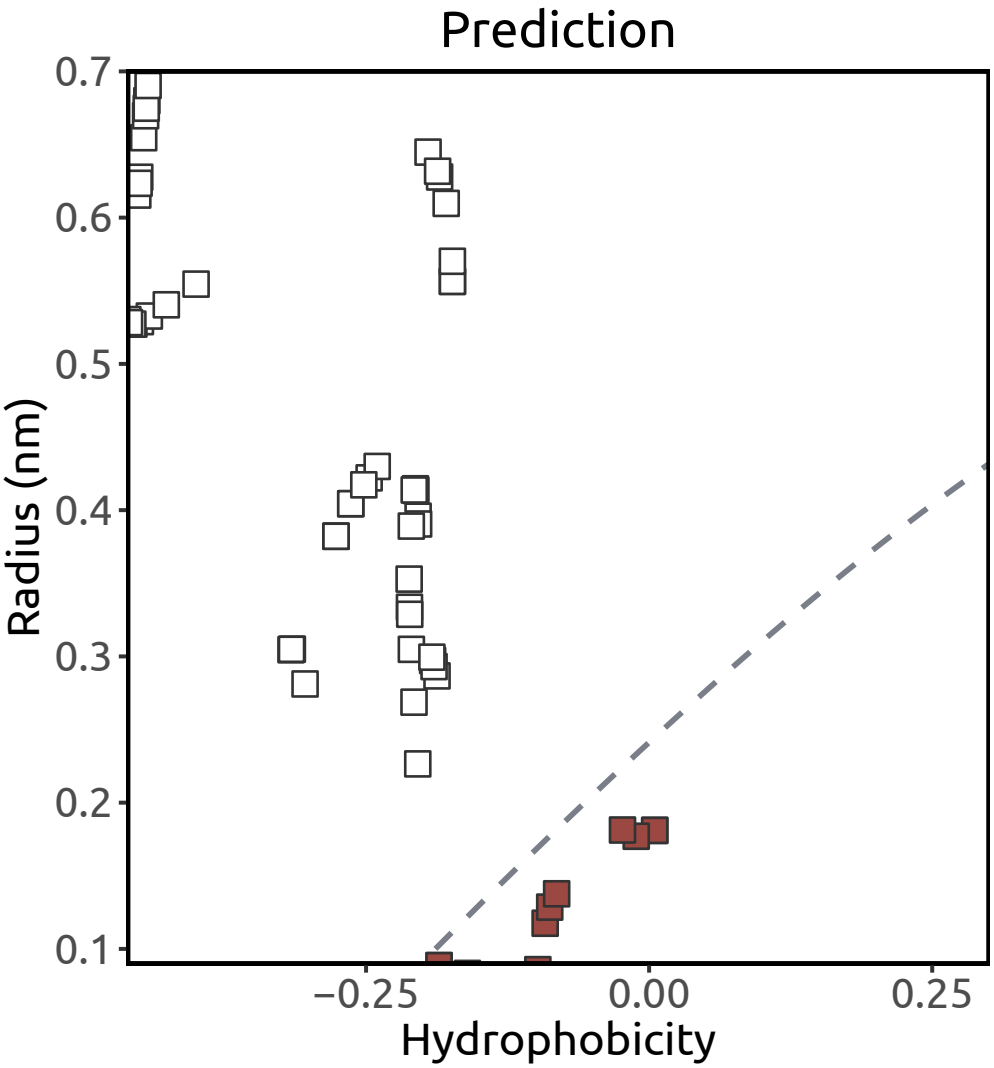
Homo sapiens

cryo–EM (3.5 Å)

Lee & MacKinnon, 2017







Heuristic score:

1.78 (n = 20)

Simulation result:

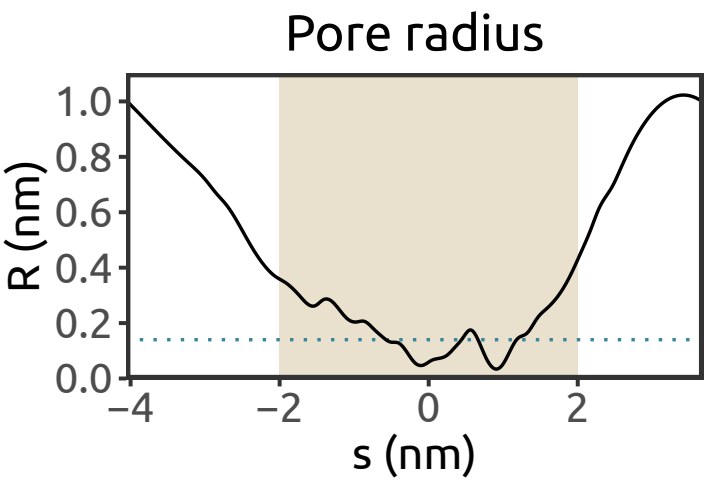
barrier to water

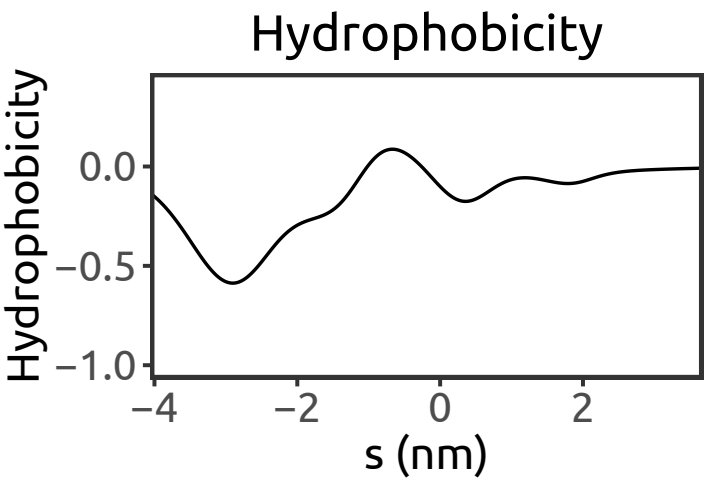
Hv1 (PDB ID: 3WKV)

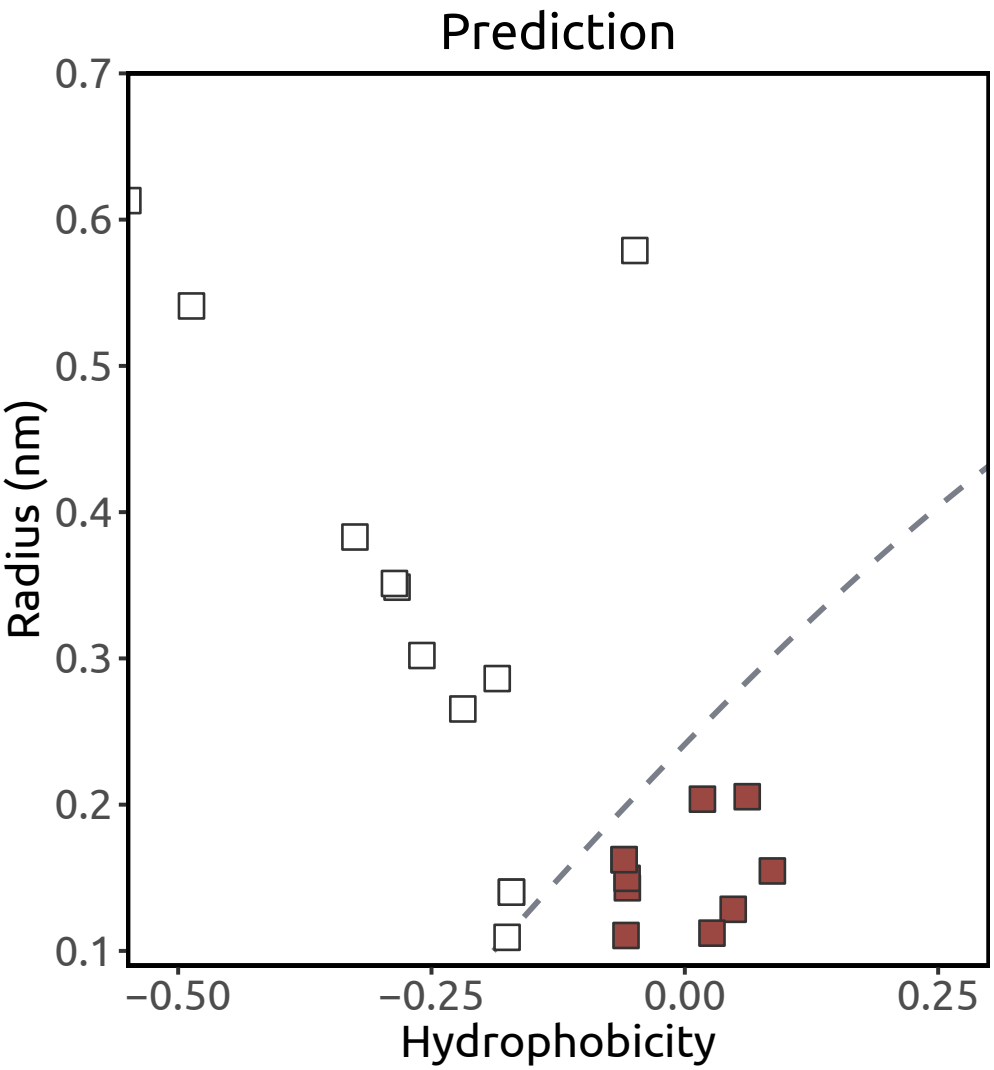
Mus musculus

X–ray (3.45 Å)

Takeshita et al., 2014







Heuristic score:

1.35 (n = 17)

Simulation result:

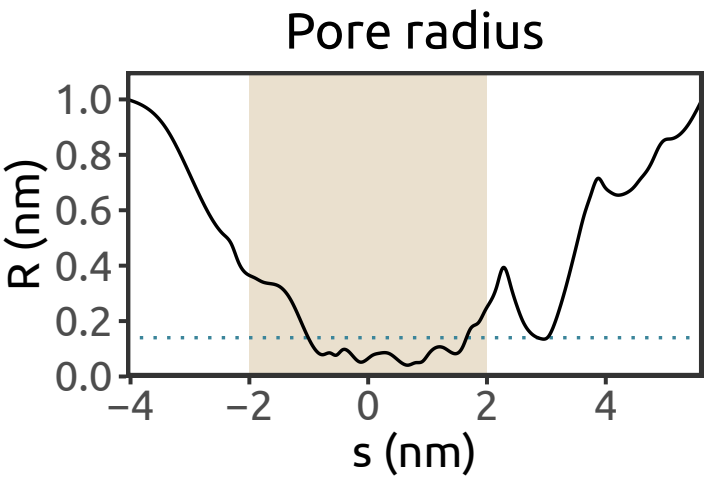
barrier to water

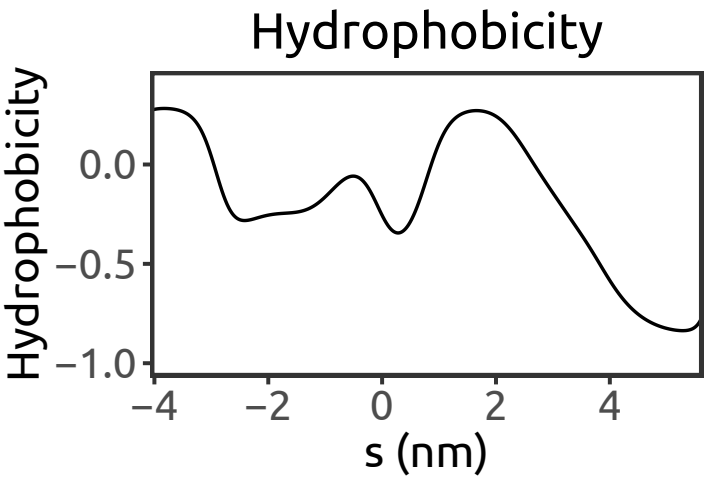
InsP3R1 (PDB ID: 3JAV)

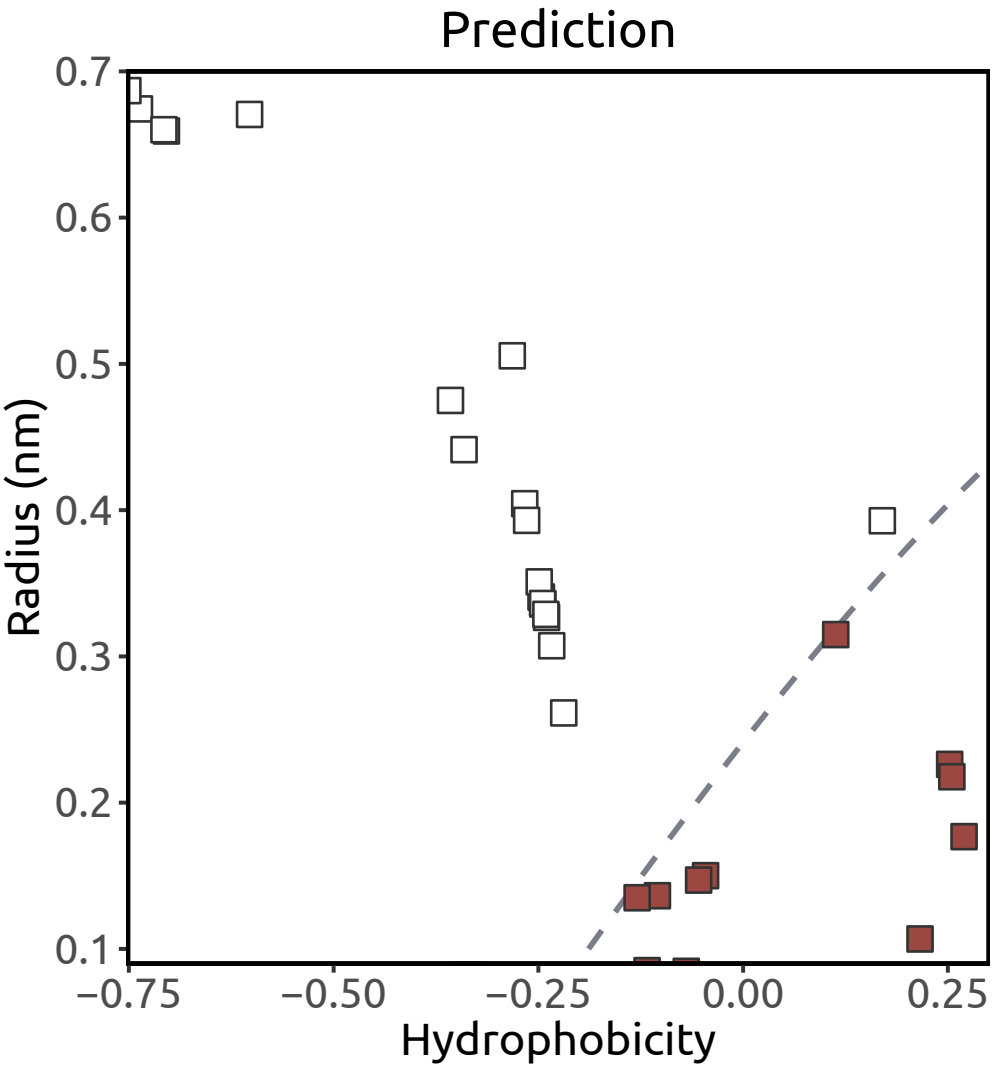
Rattus norvegicus

cryo–EM (4.7 Å)

Fan et al., 2015







Heuristic score:

1.02 (n = 11)

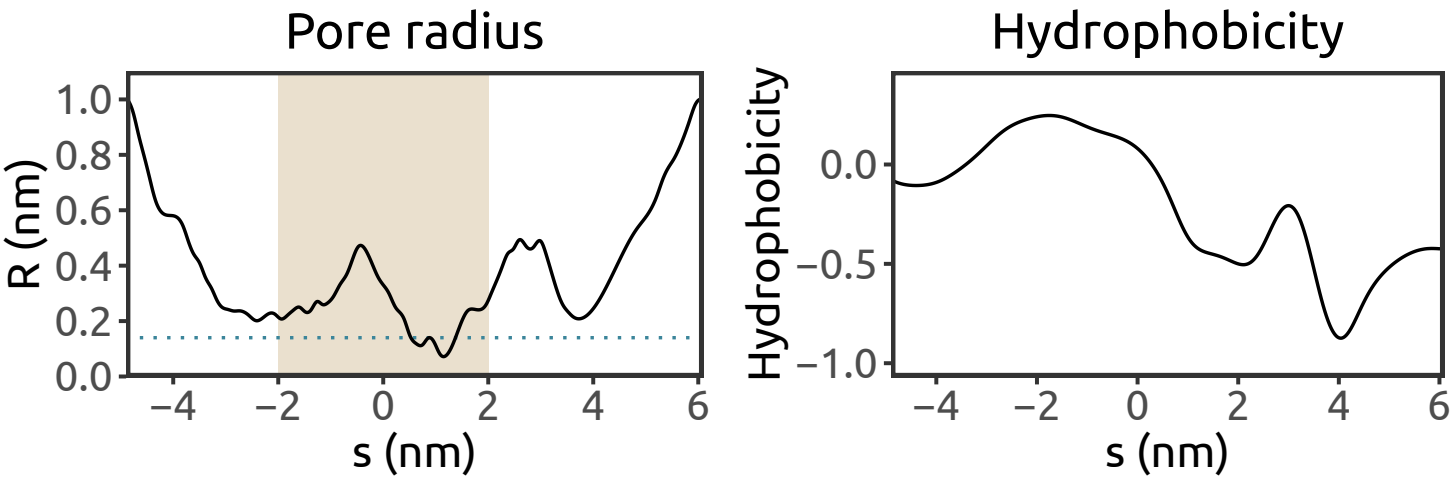
Simulation result:

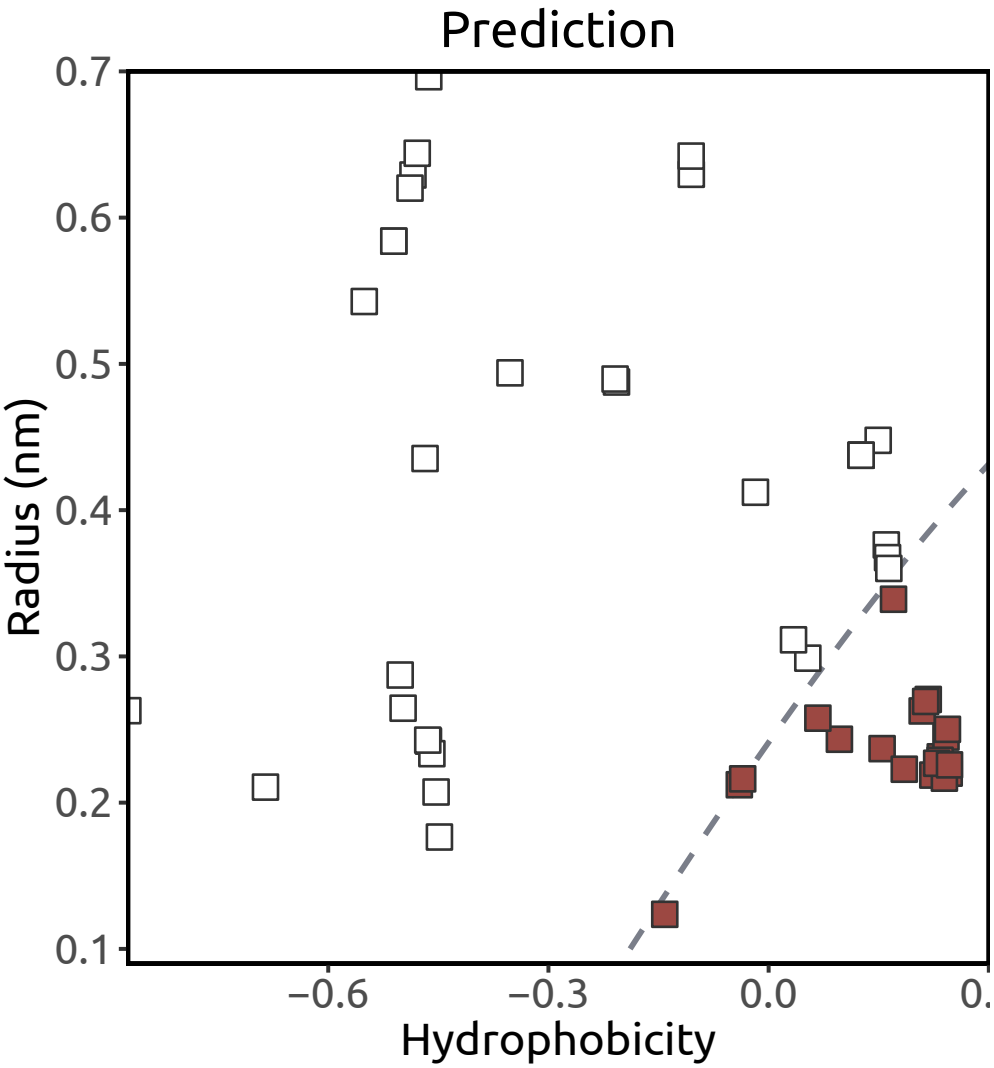
barrier to water

Nav1.4 (PDB ID: 5XSY)

Electrophorus electricus
cryo–EM (4 Å)

Yan et al., 2017





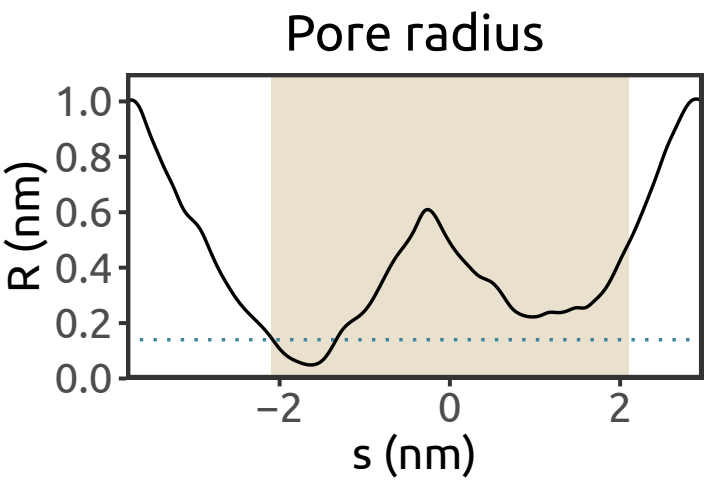
Heuristic score:
2.04 (n = 21)

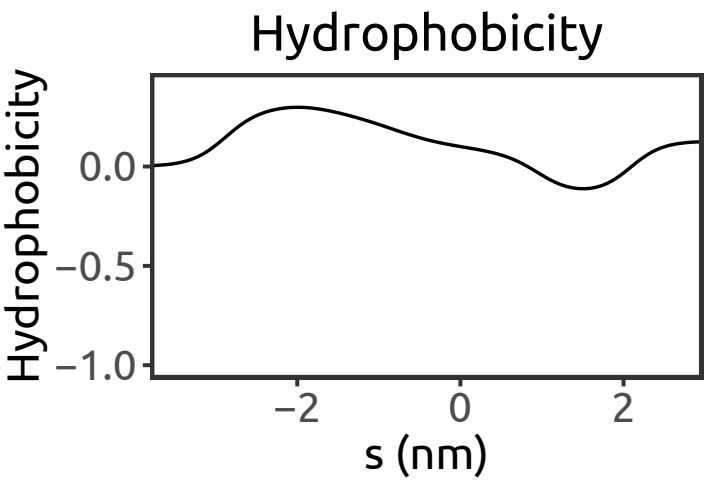
Simulation result:
barrier to water

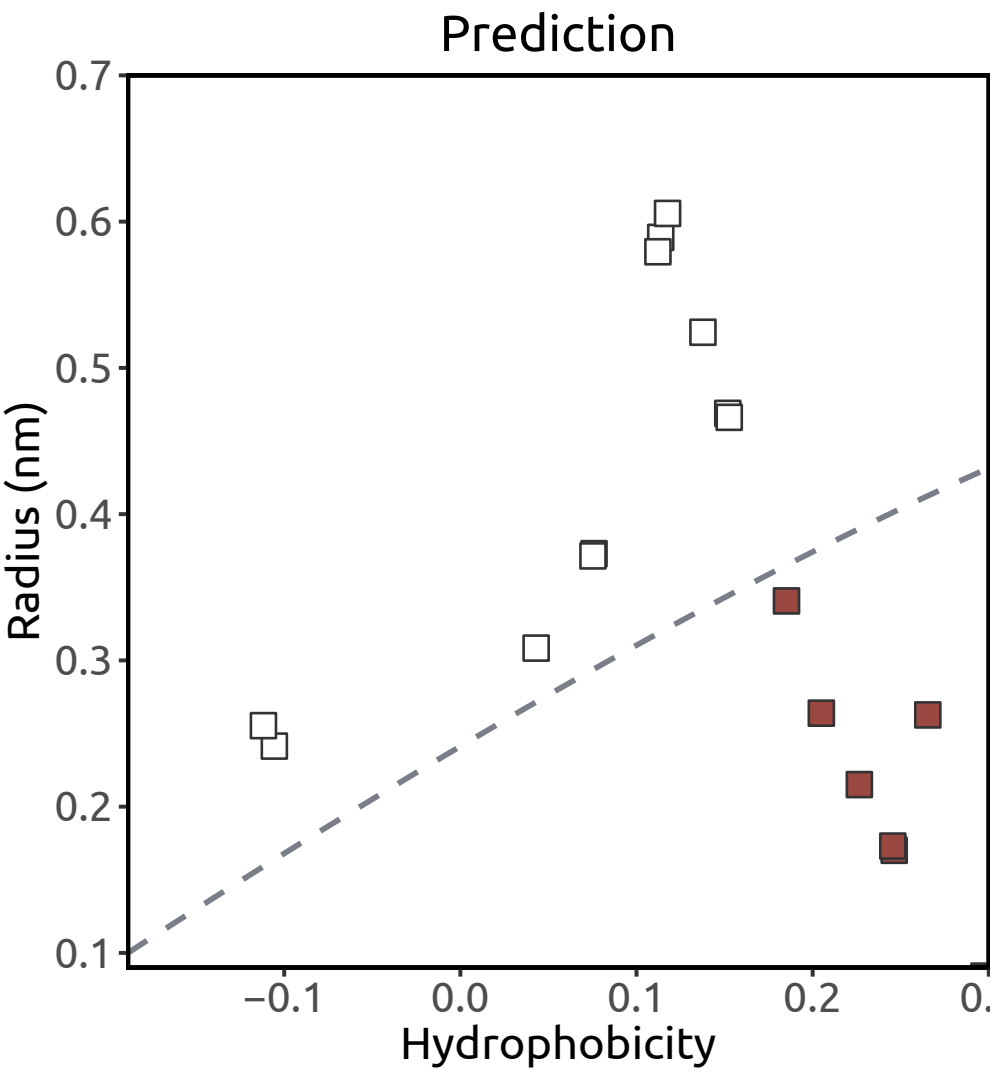
NavAb (PDB ID: 4EKW)

Arcobacter butzleri
X–ray (3.21 Å)

Payandeh et al., 2012







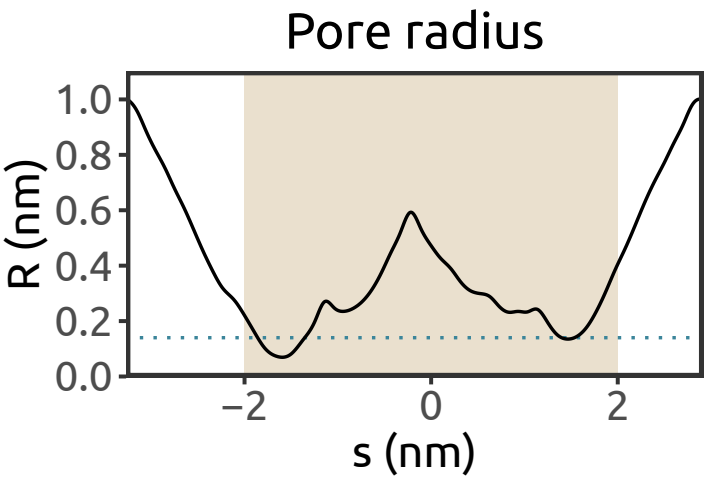
Heuristic score:
1.72 (n = 9)

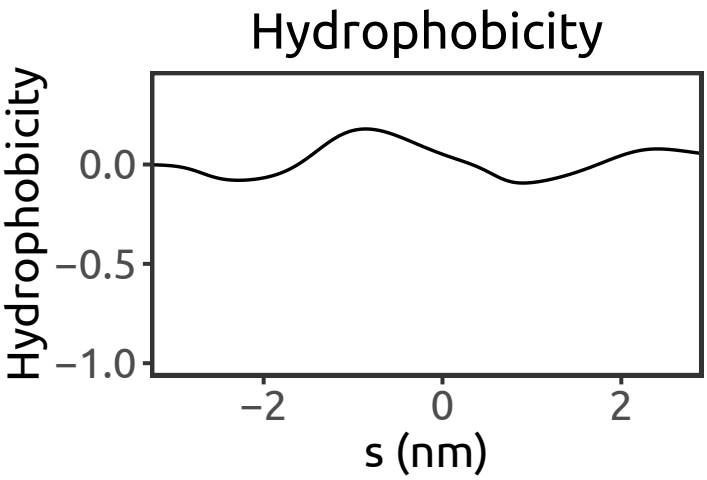
Simulation result:
barrier to water

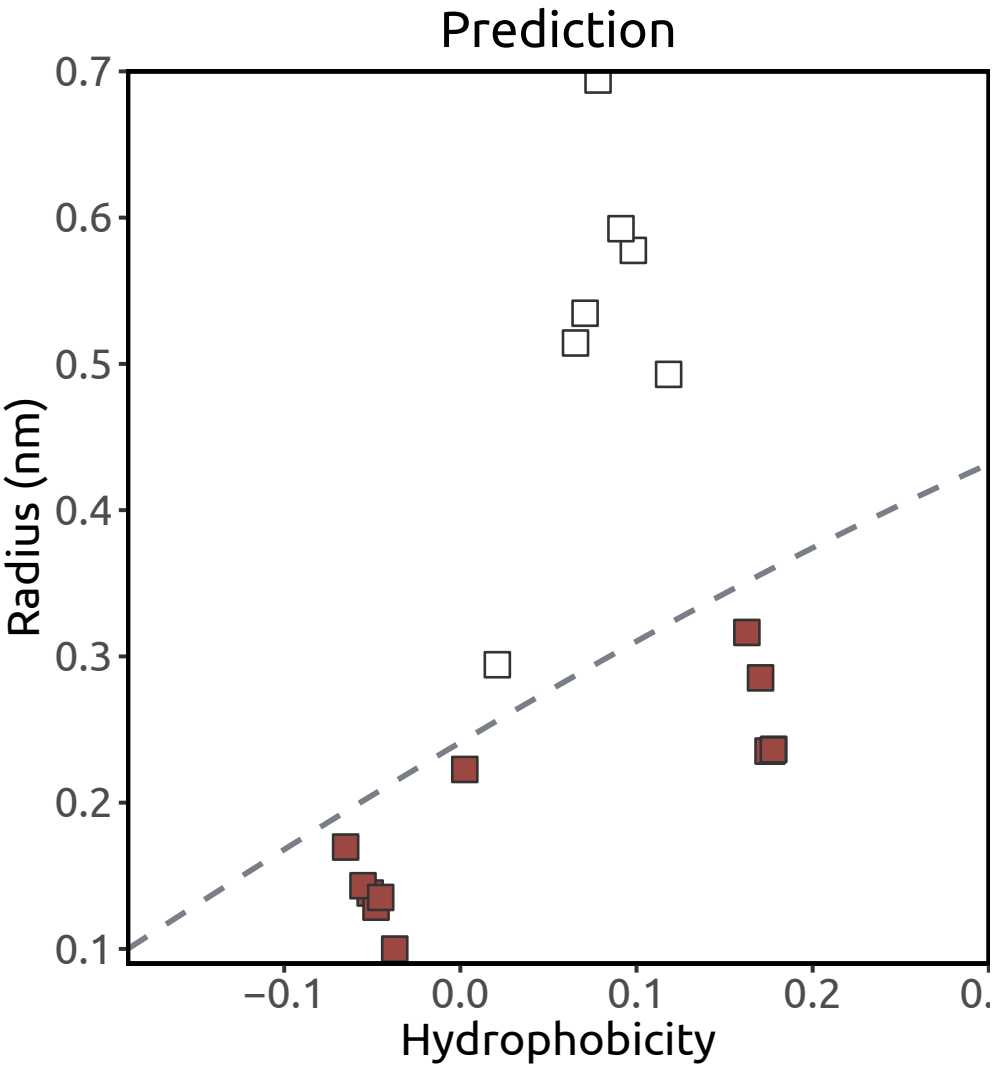
NavAb (PDB ID: 4MW8)

Arcobacter butzleri
X–ray (3.26 Å)

Tang et al., 2014







Heuristic score:
1.11 (n = 15)

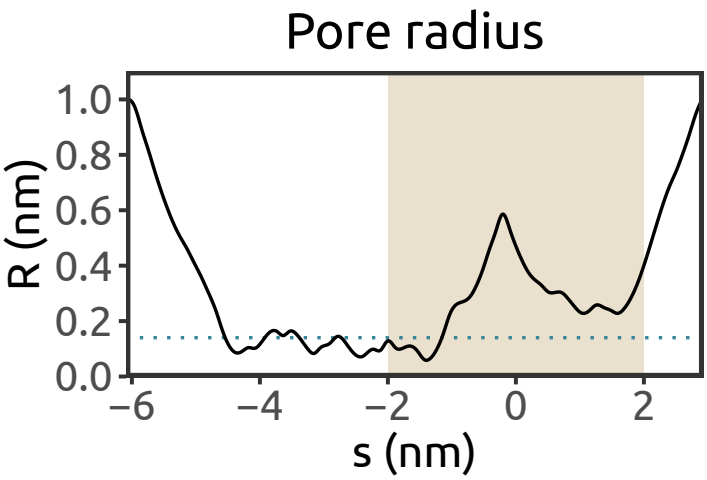
Simulation result:
hydrated channel

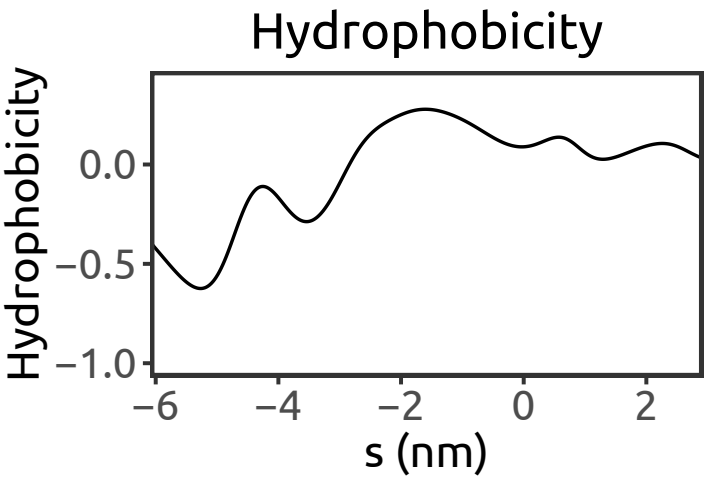
NavAb (PDB ID: 5EK0)

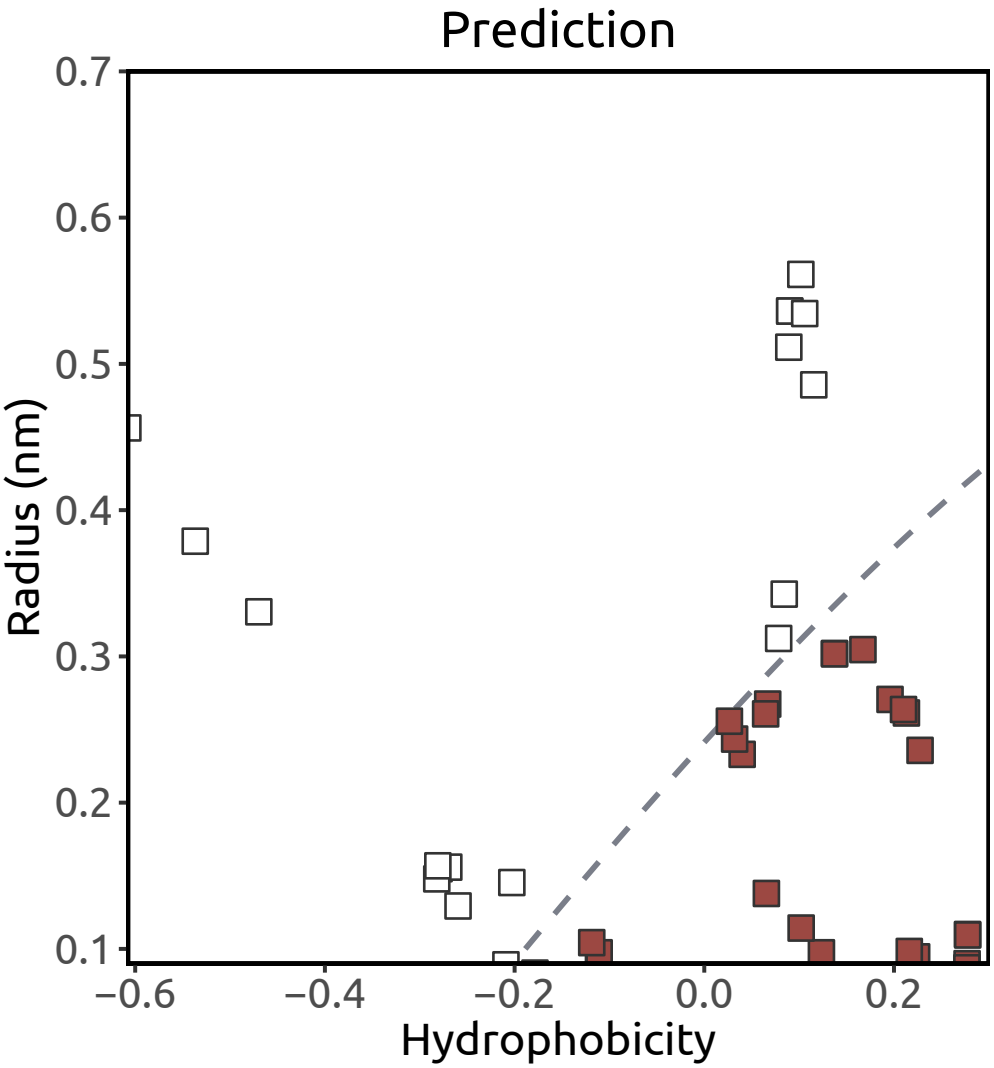
Arcobacter butzleri

X–ray (3.53 Å)

Ahuja et al., 2015







Heuristic score:

3.4 (n = 28)

Simulation result:

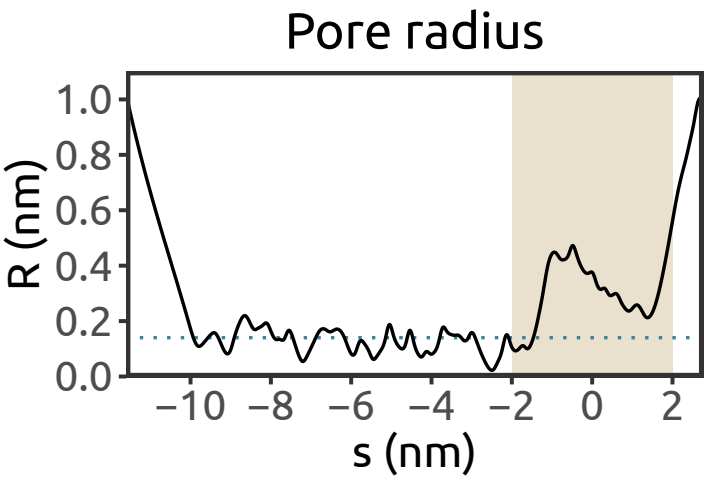
barrier to water

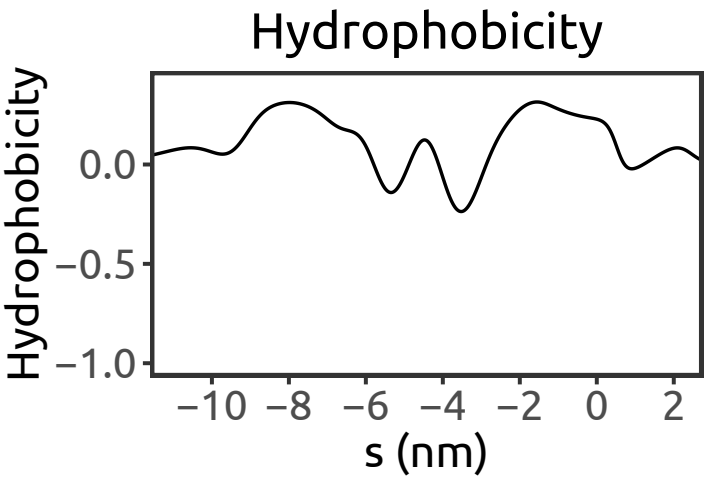
NavAb (PDB ID: 5VB2)

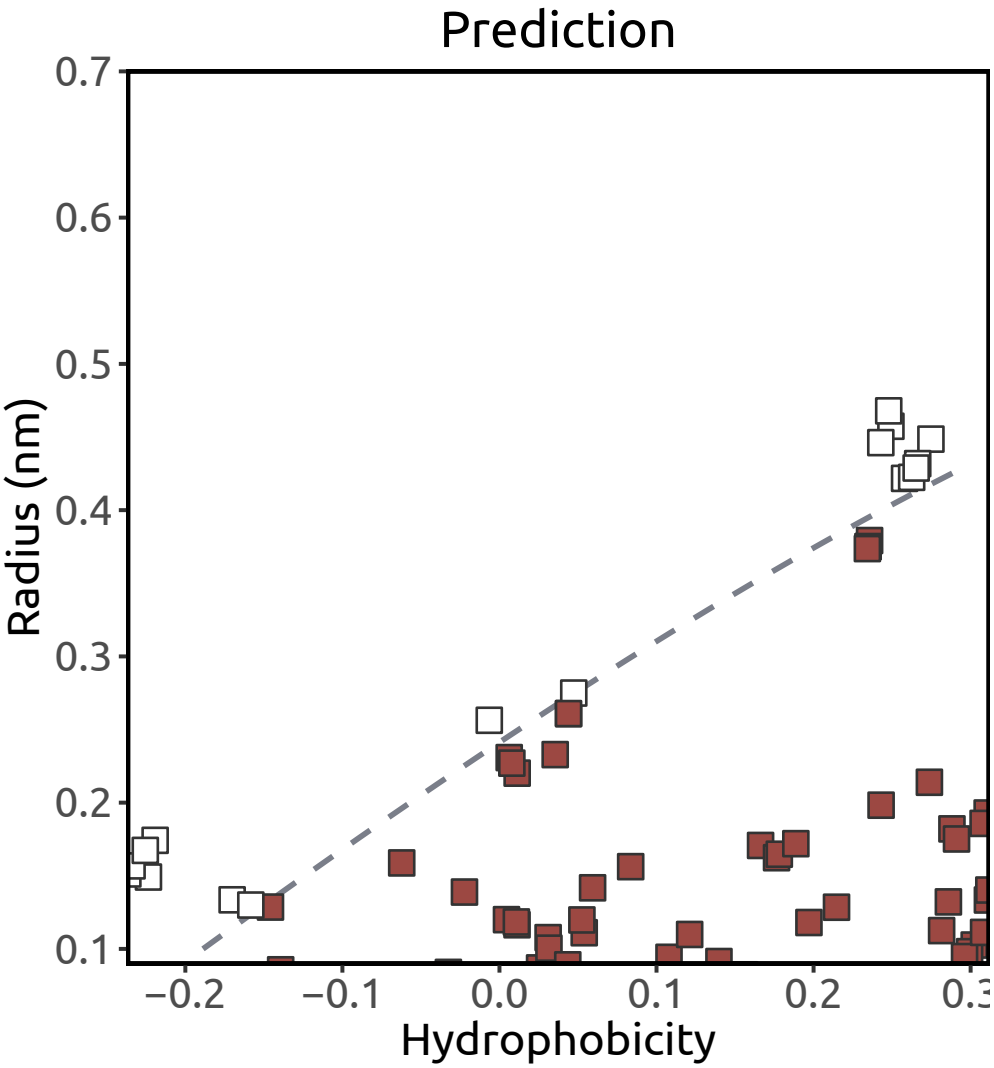
Arcobacter butzleri

X–ray (3.2 Å)

Lenaeus et al., 2017







Heuristic score:

9.06 (n = 61)

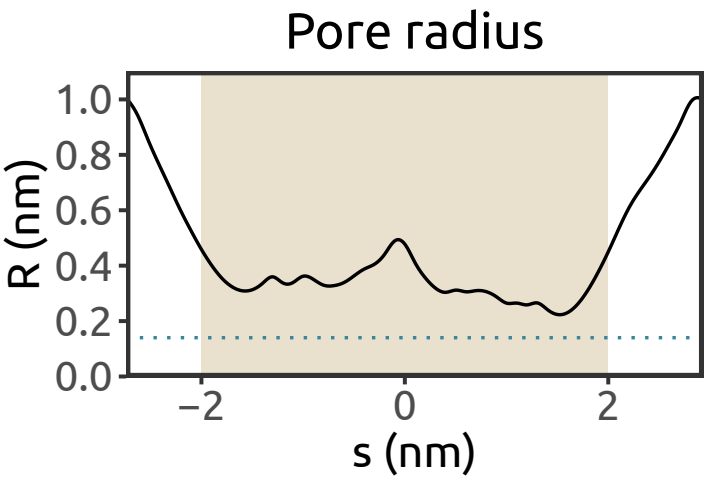
Simulation result:

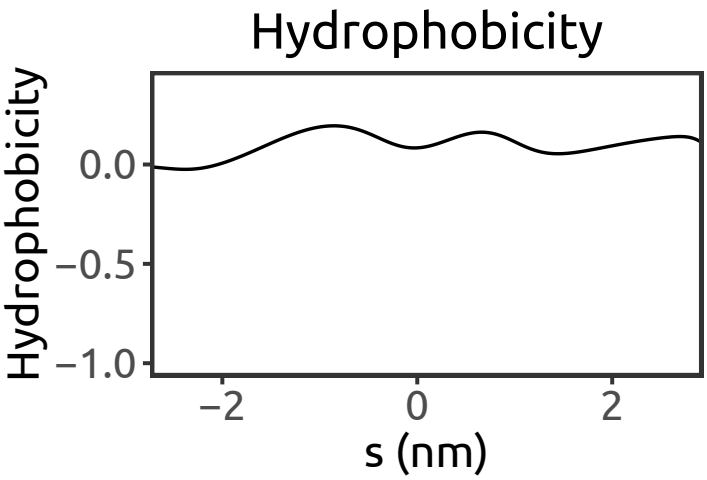
barrier to water

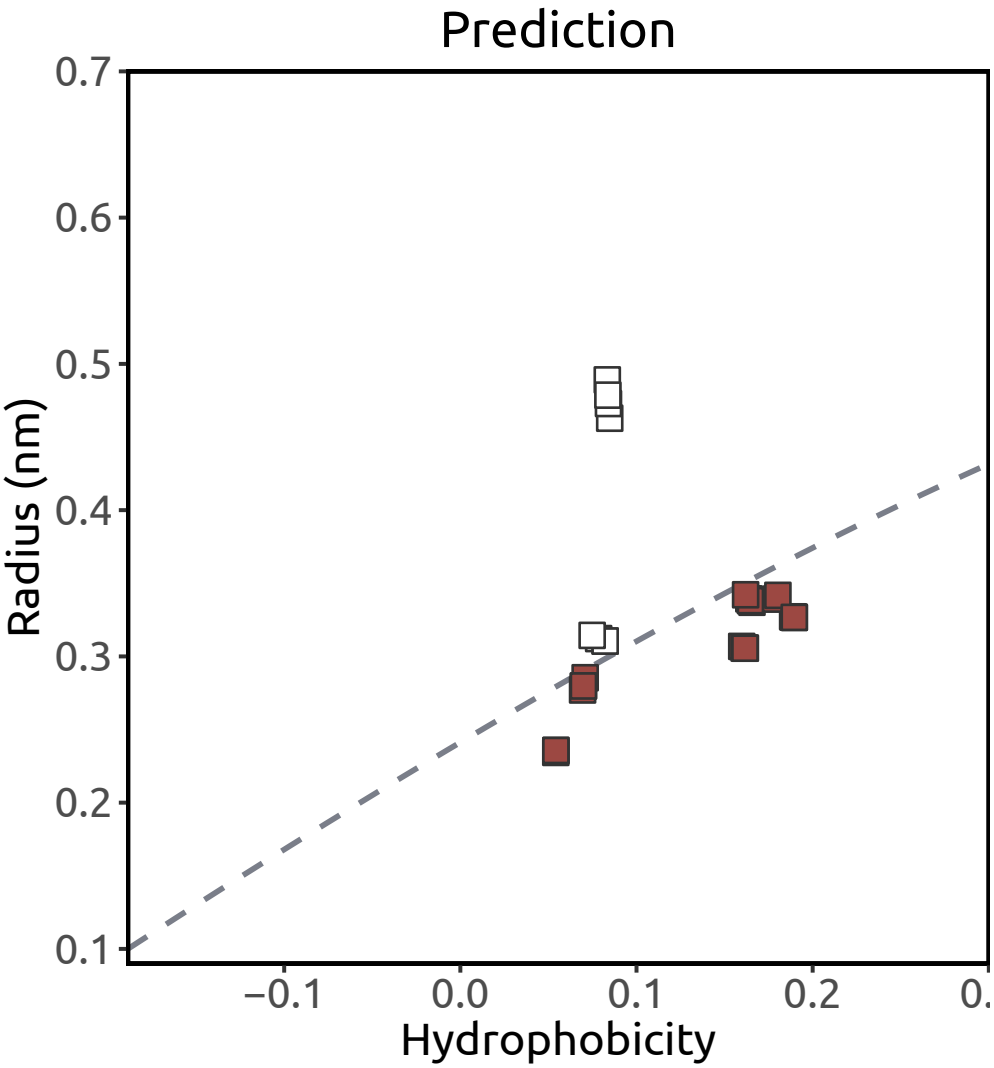
NavAb (PDB ID: 5VB8)

Arcobacter butzleri
X–ray (2.85 Å)

Lenaeus et al., 2017







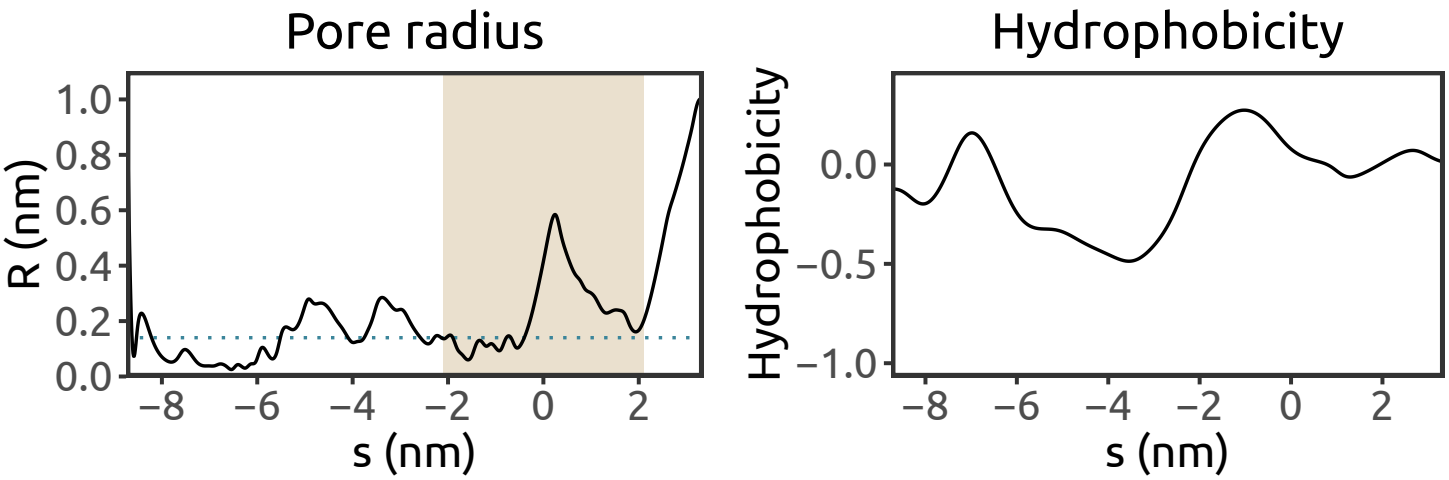
Heuristic score:
0.51 (n = 21)

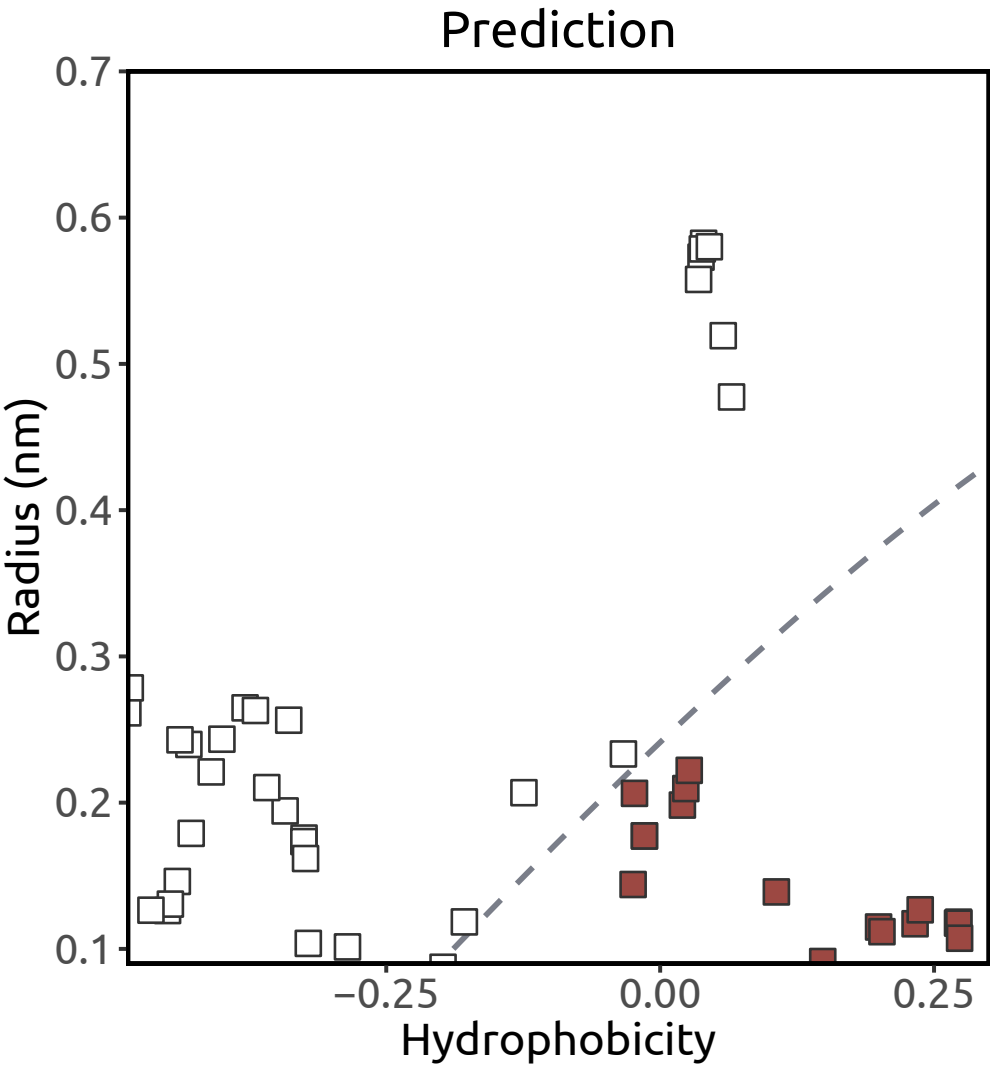
Simulation result:
barrier to water

NavAe1 (PDB ID: 4LTO)

Alkalilimnicola ehrlichii
X–ray (3.46 Å)

Shaya et al., 2014





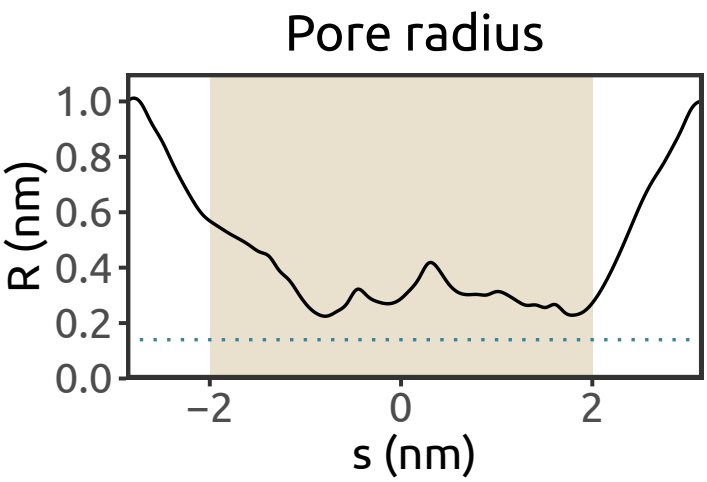
Heuristic score:
3.76 (n = 24)

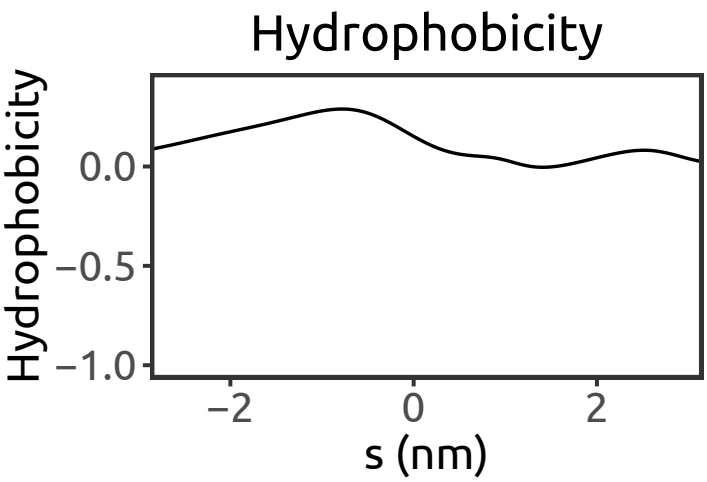
Simulation result:
barrier to water

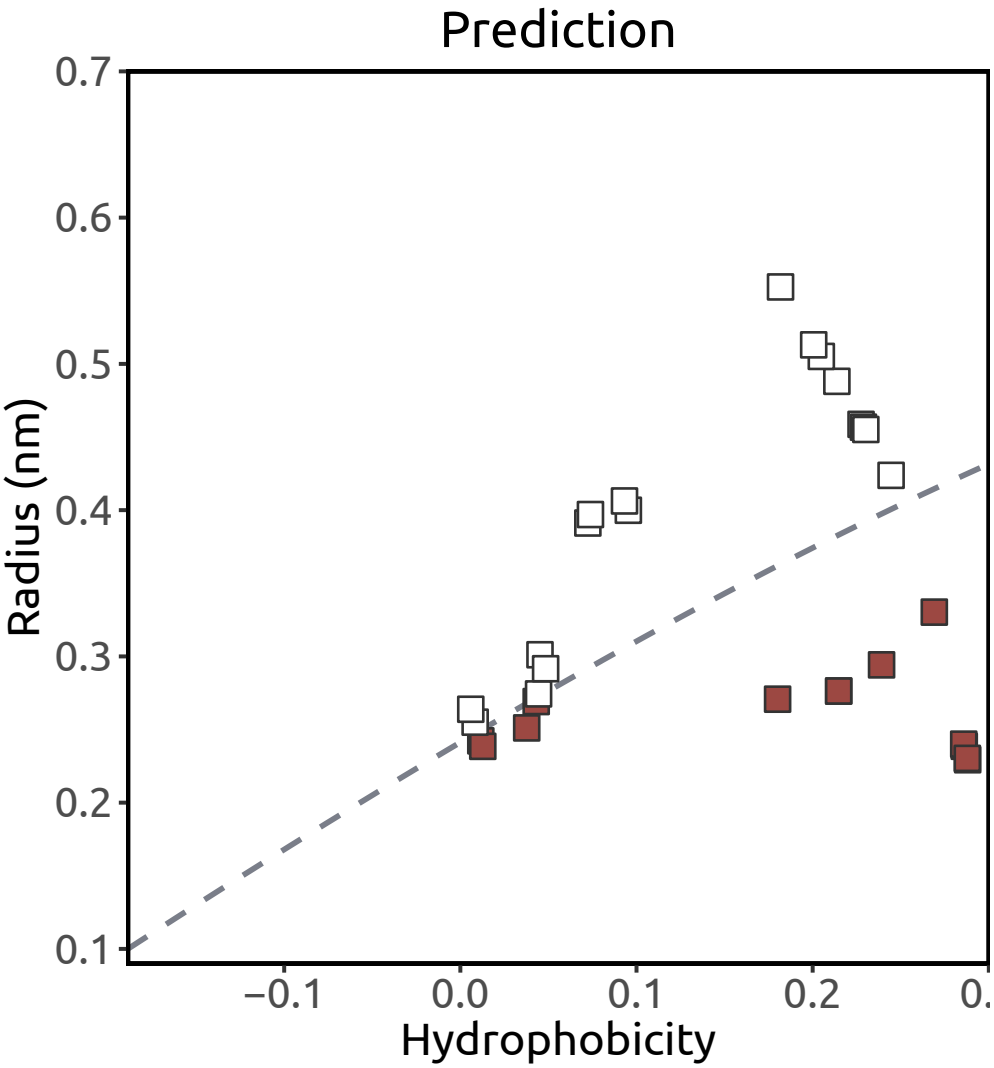
NavMm (PDB ID: 4CBC)

Magnetococcus marinus
X–ray (2.66 Å)

Bagnéris et al., 2014







Heuristic score:
1.11 (n = 13)

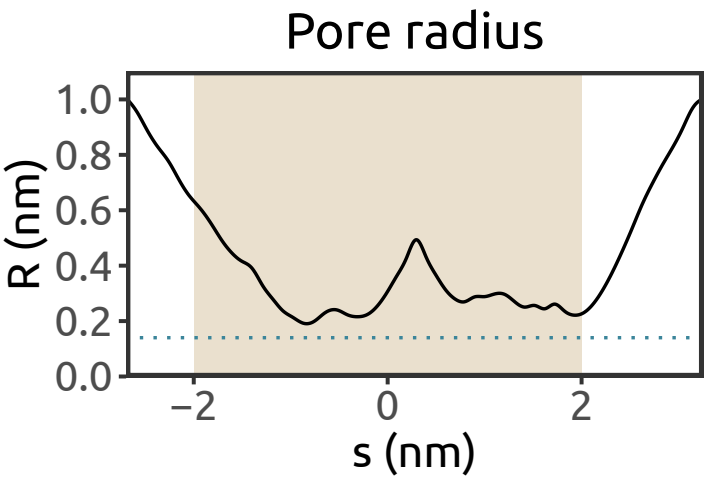
Simulation result:
barrier to water

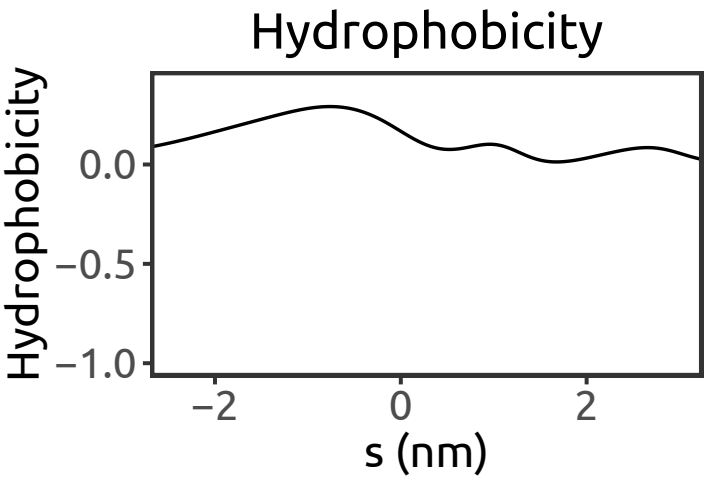
NavMm (PDB ID: 4OXS)

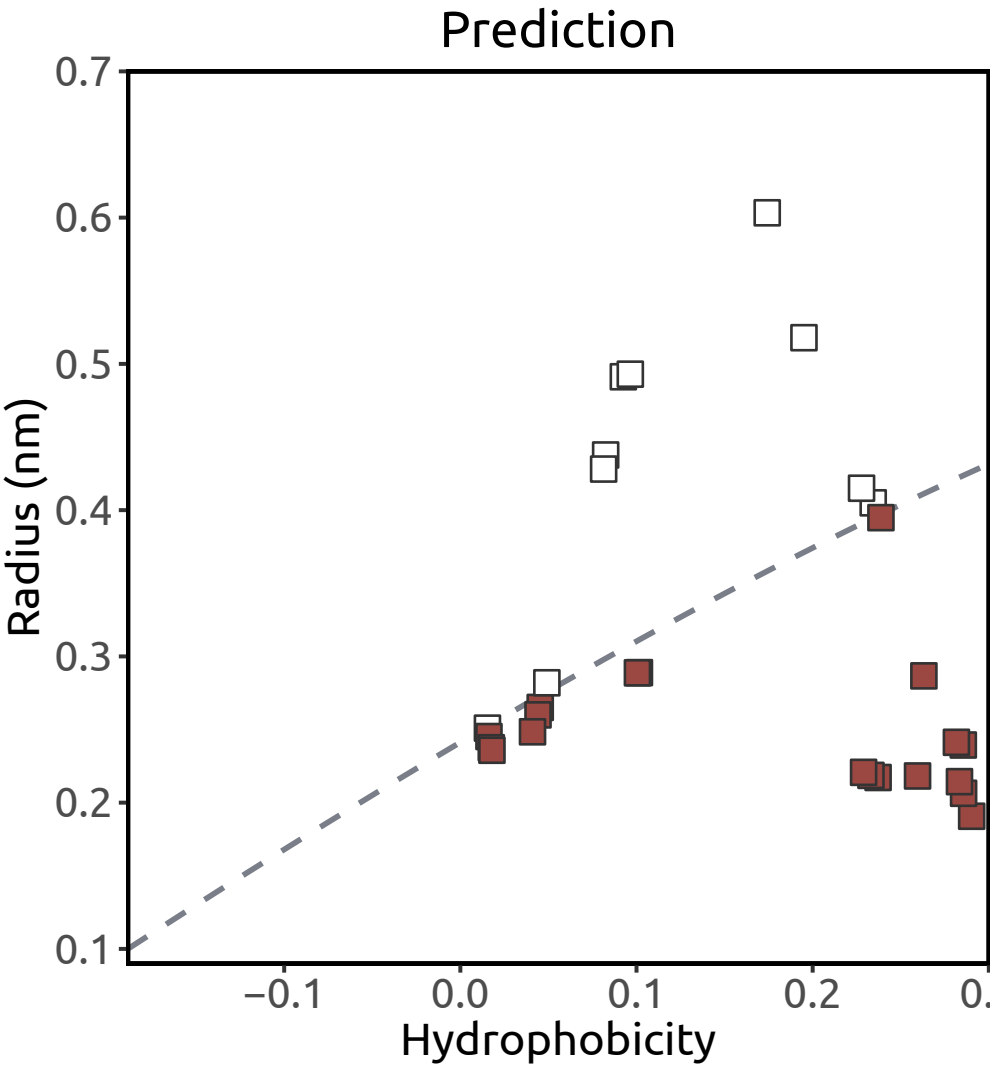
Magnetococcus marinus

X–ray (2.8 Å)

Bagnéris et al., 2014







Heuristic score:

1.72 (n = 19)

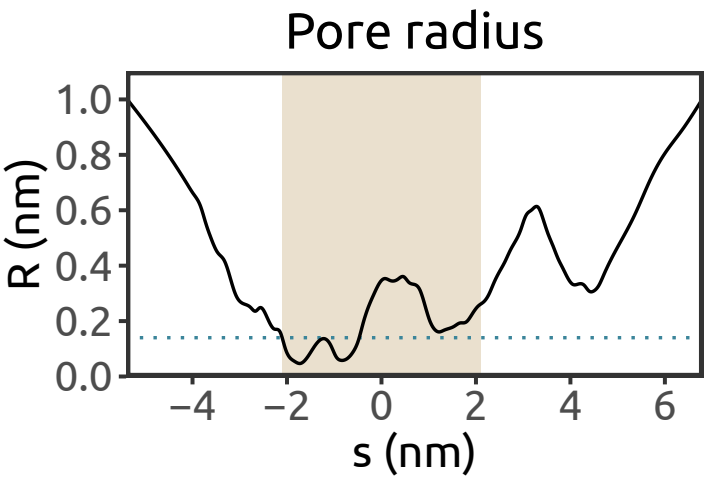
Simulation result:

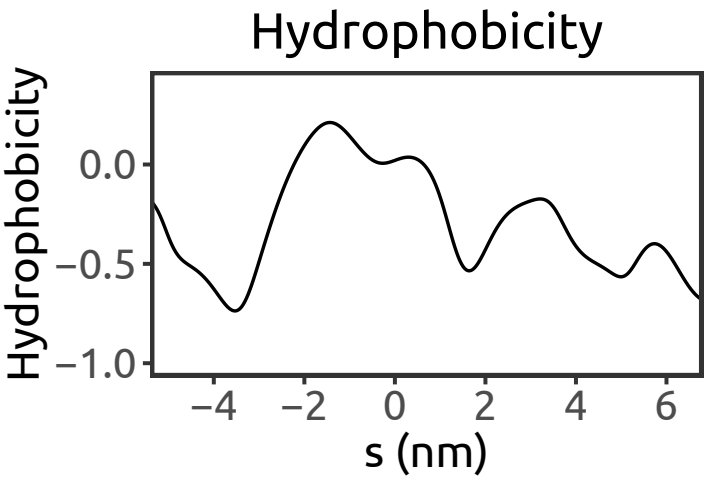
barrier to water

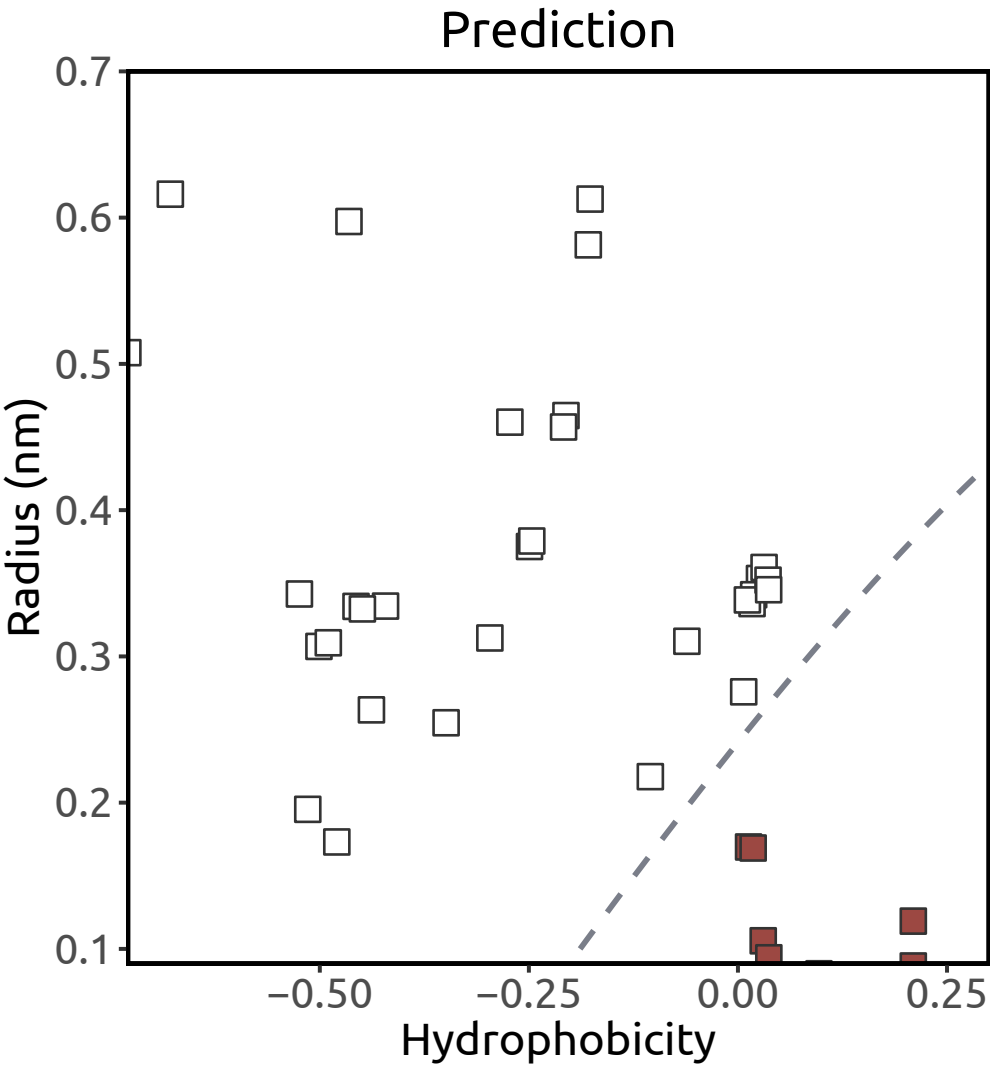
NavPa (PDB ID: 5X0M)

Periplaneta americana
cryo–EM (3.8 Å)

Shen et al., 2017







Heuristic score:
1.91 (n = 11)

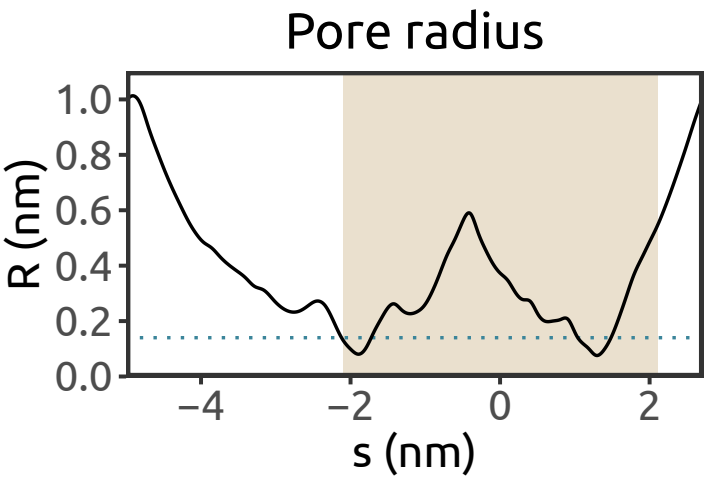
Simulation result:
barrier to water

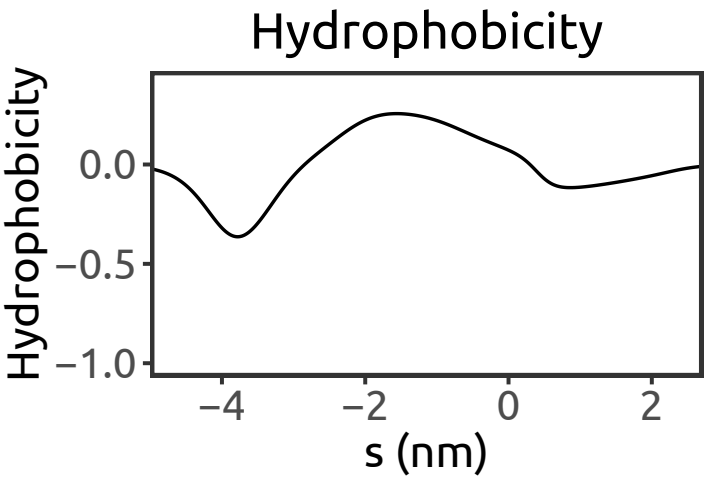
NavRh (PDB ID: 4DXW)

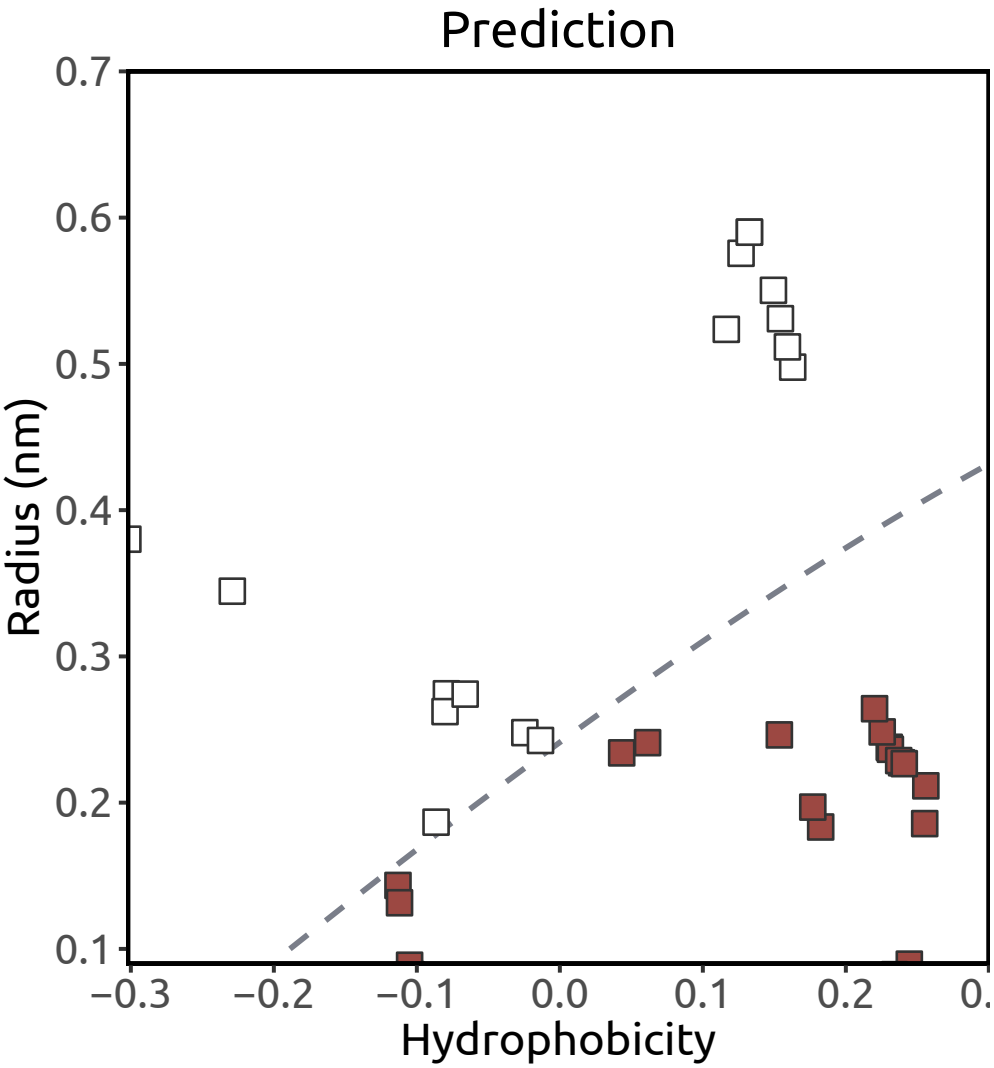
Rickettsiales sp. HIMB114

X–ray (3.05 Å)

Zhang et al., 2012







Heuristic score:

2.67 (n = 21)

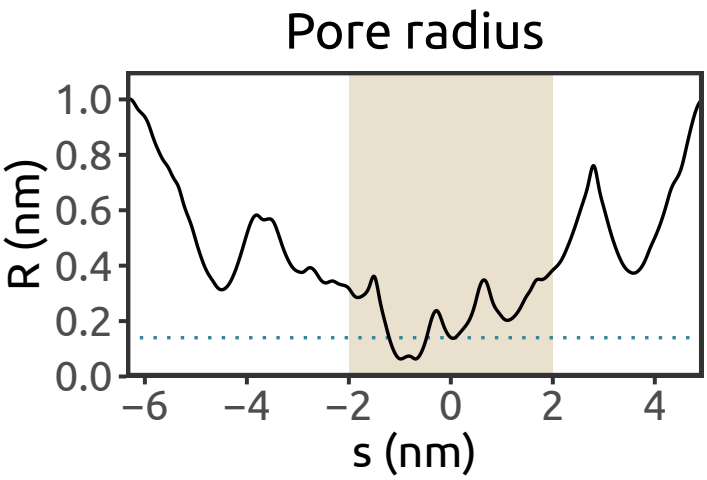
Simulation result:

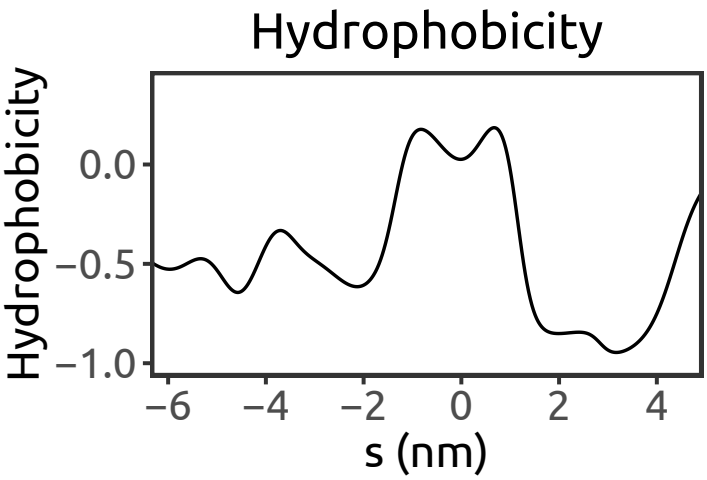
barrier to water

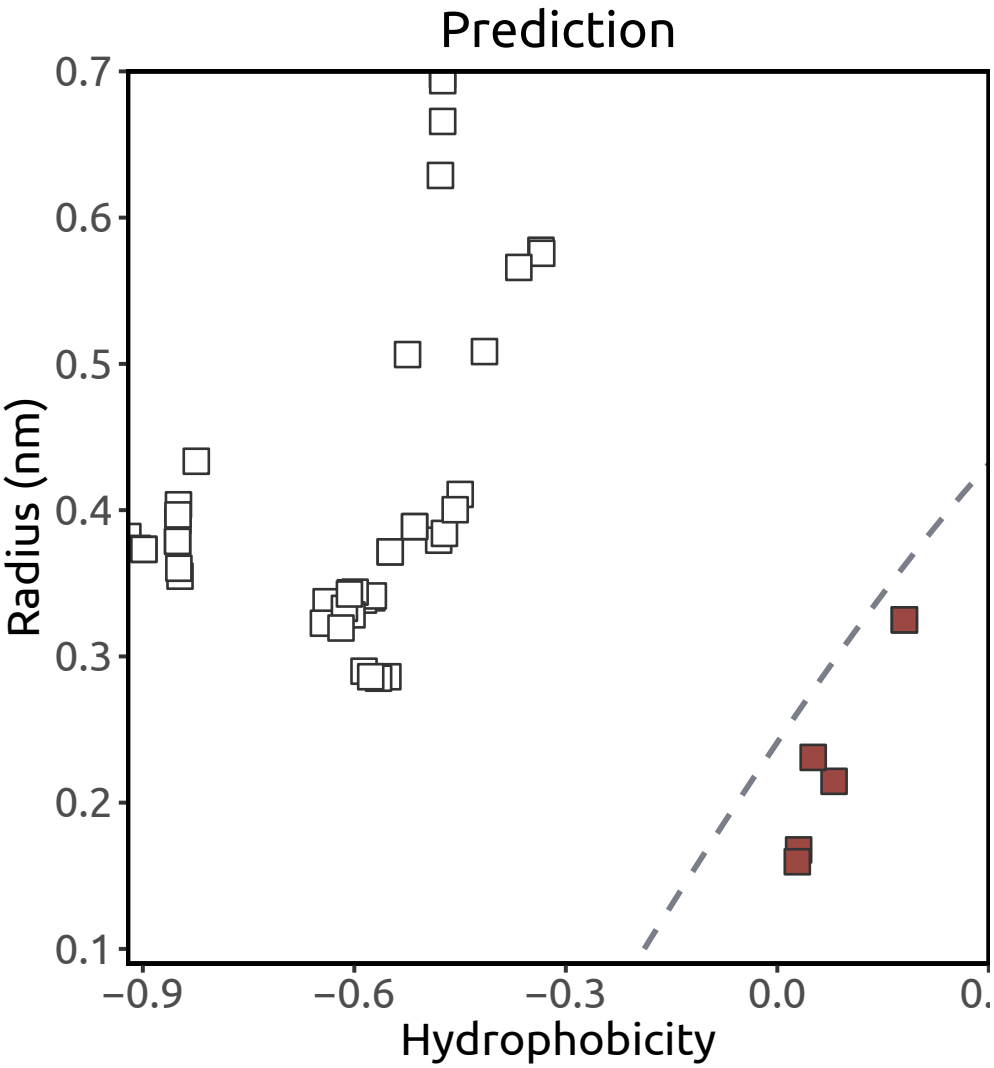
RyR1 (PDB ID: 3J8H)

Oryctolagus cuniculus
cryo–EM (3.8 Å)

Yan et al., 2015







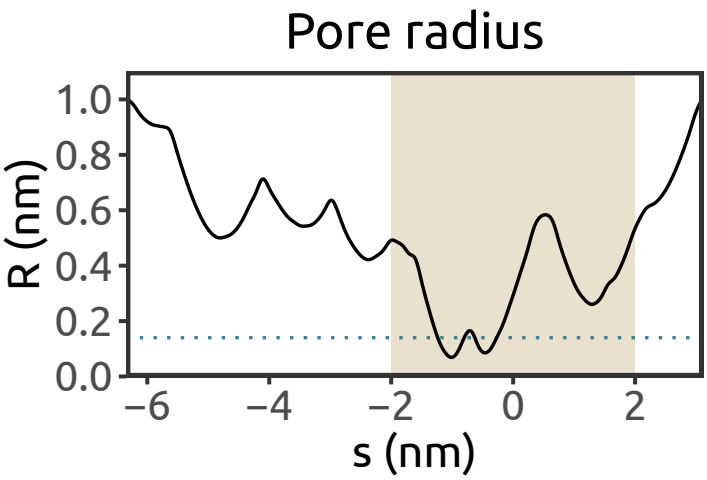
Heuristic score:
1.29 (n = 10)

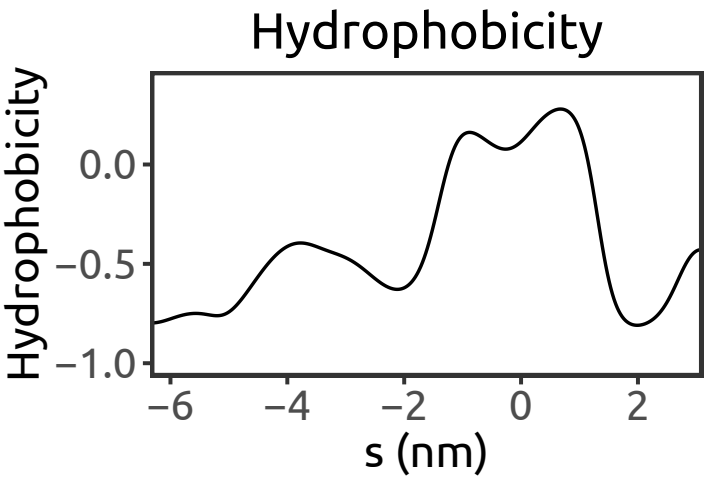
Simulation result:
barrier to water

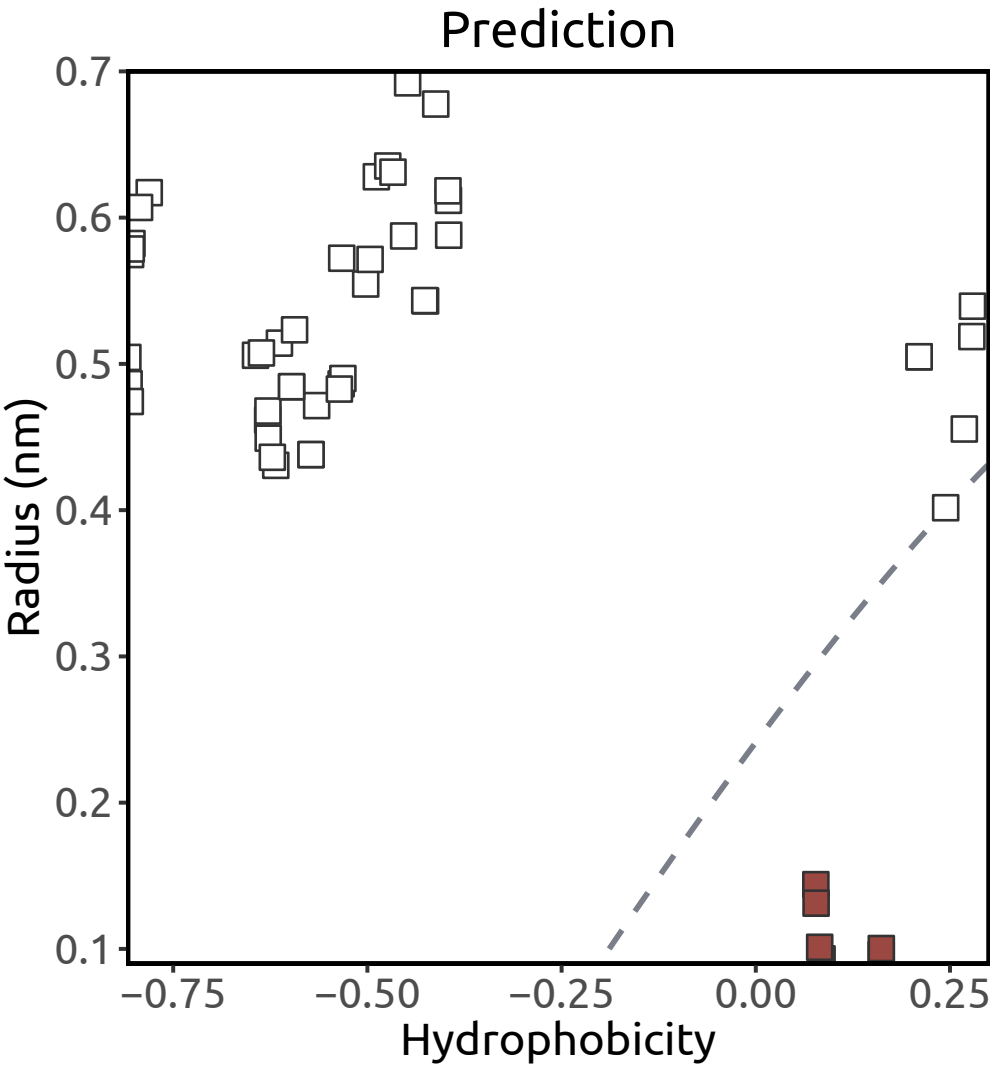
RyR1 (PDB ID: 5TB0)

Oryctolagus cuniculus
cryo–EM (4.4 Å)

des et al., 2016







Heuristic score:
1.46 (n = 8)

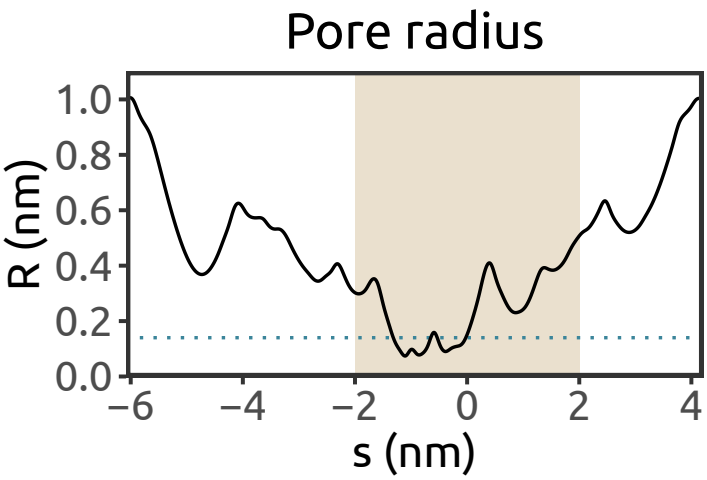
Simulation result:
barrier to water

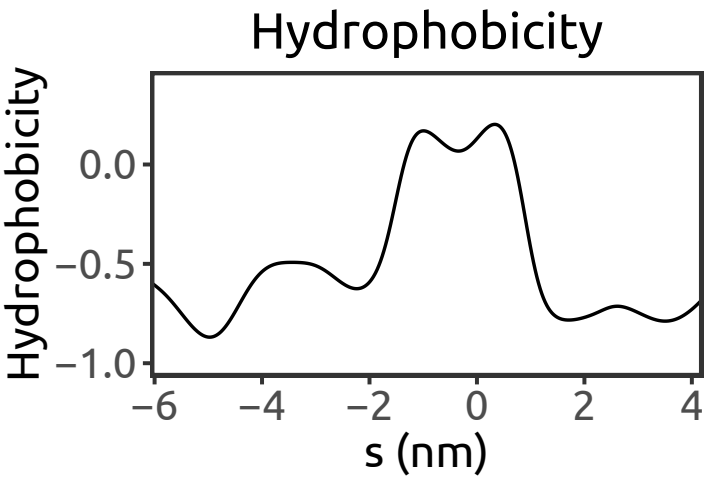
RyR2 (PDB ID: 5GO9)

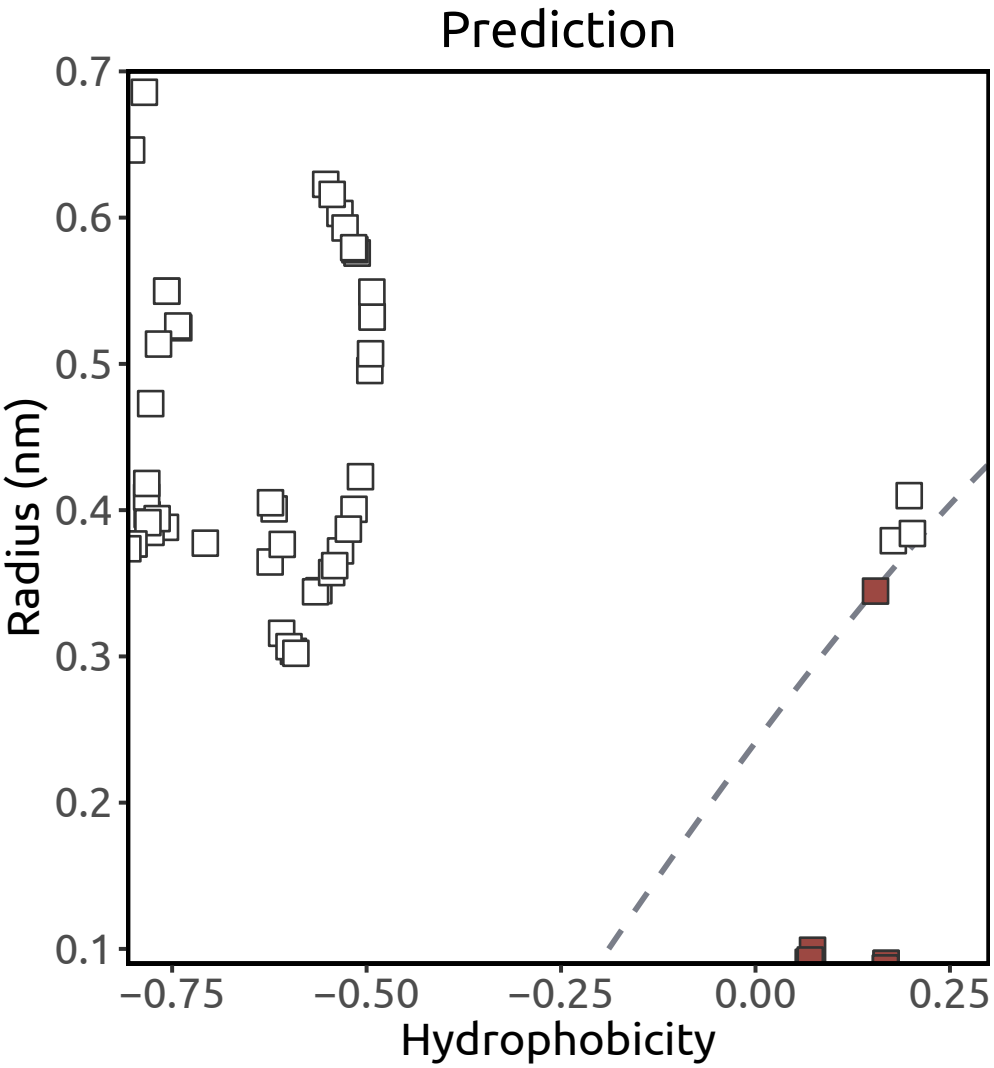
Sus scrofa

cryo–EM (4.4 Å)

Peng et al., 2016







Heuristic score:

1.53 (n = 9)

Simulation result:

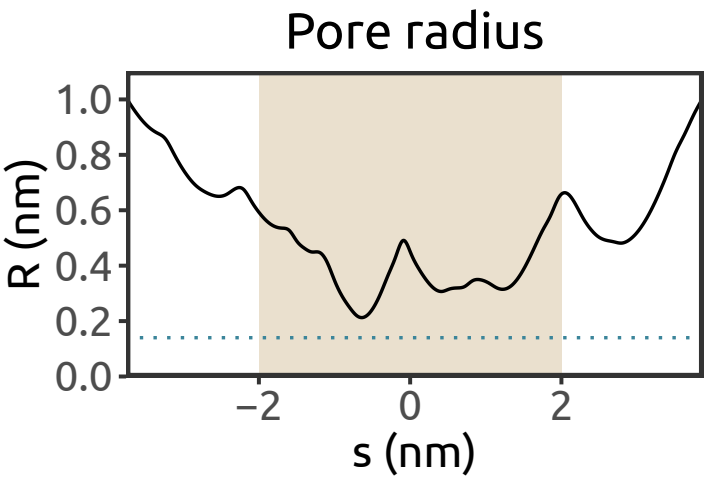
barrier to water

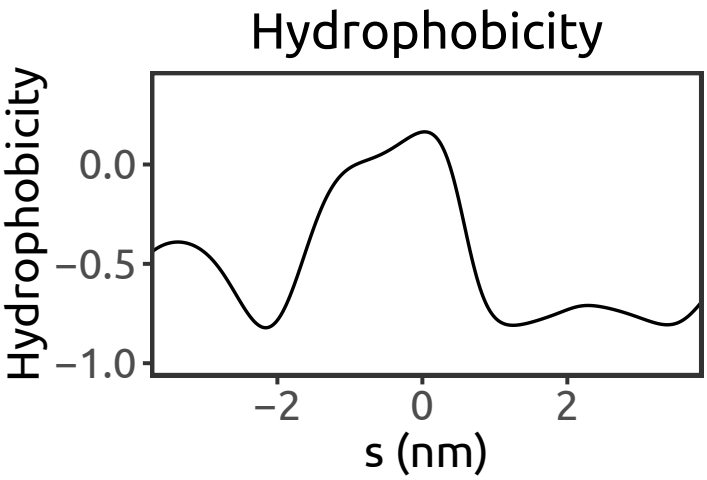
RyR2 (PDB ID: 5GOA)

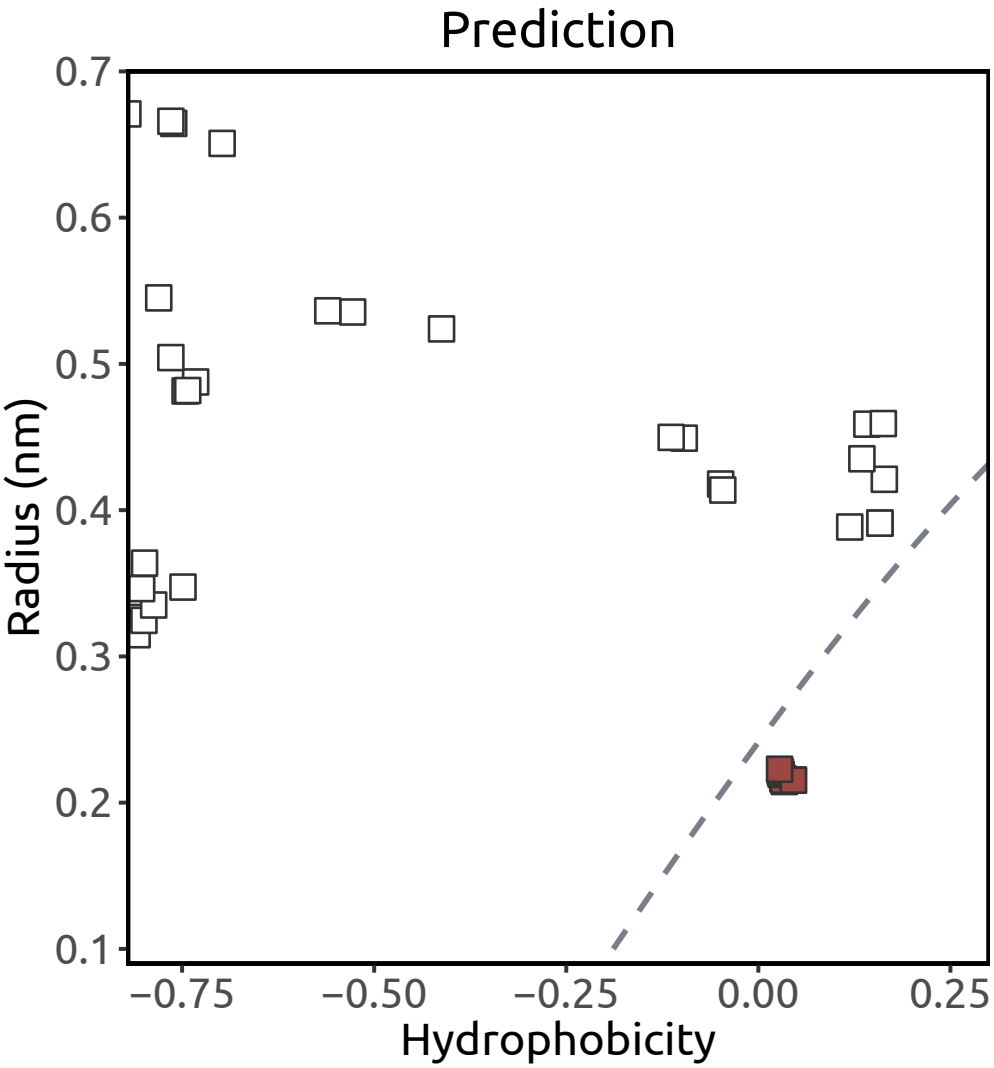
Sus scrofa

cryo–EM (4.2 Å)

Peng et al., 2016







Heuristic score:

0.32 (n = 8)

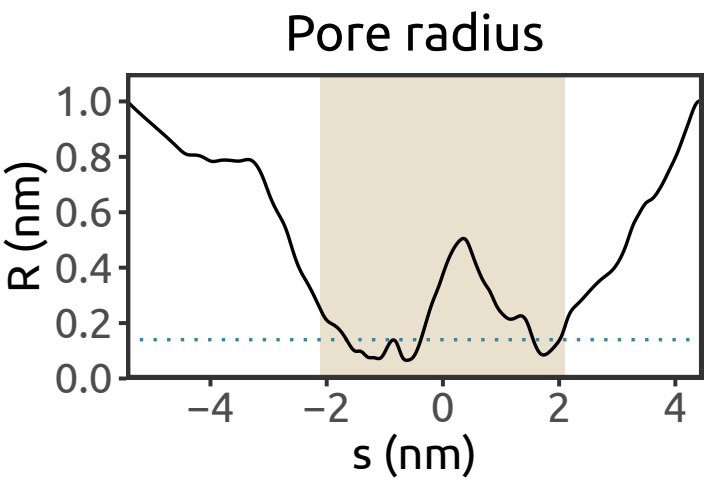
Simulation result:

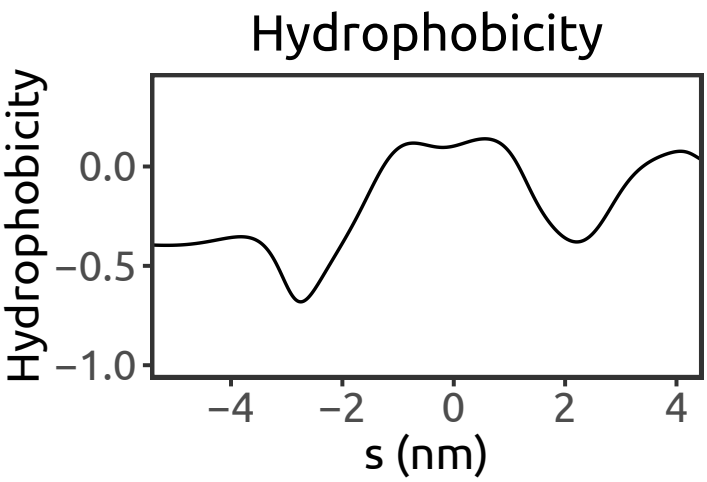
hydrated channel

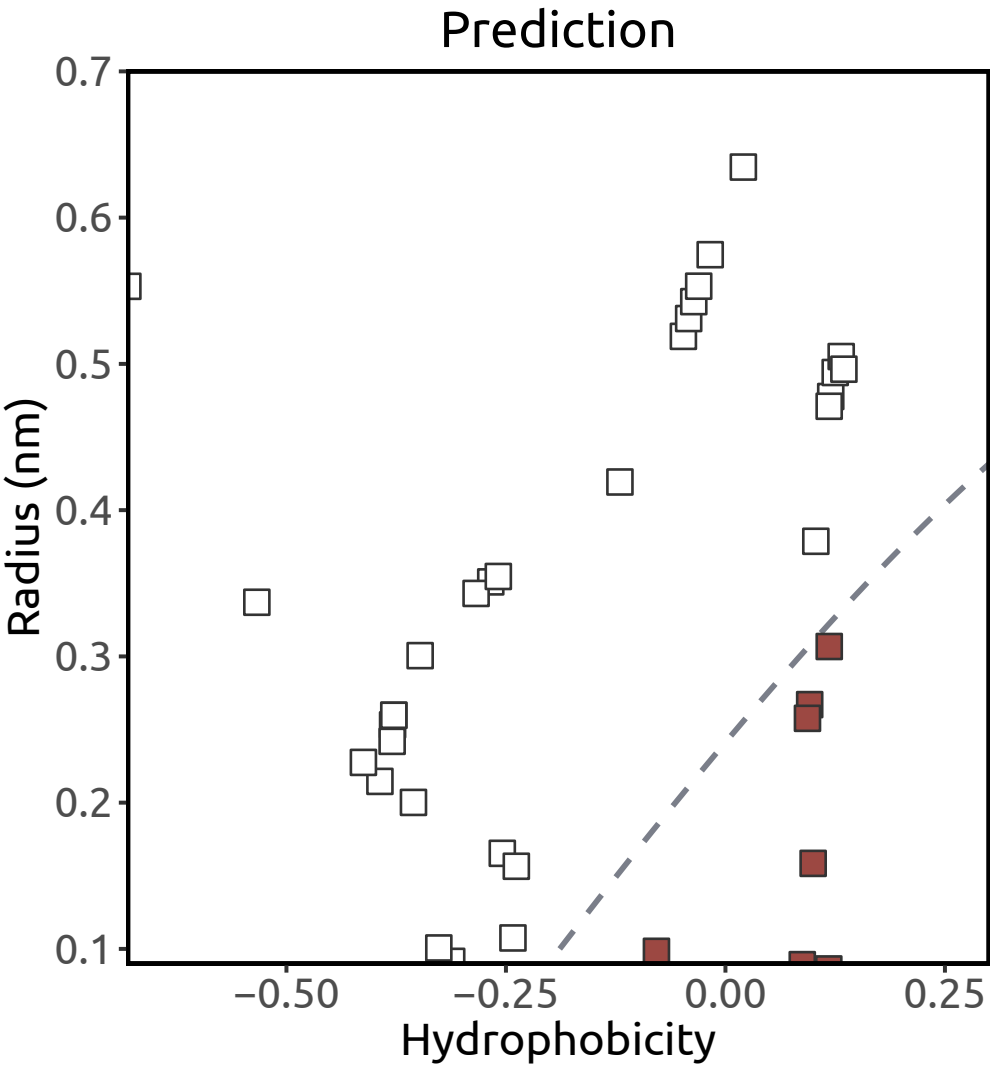
TPC1 (PDB ID: 5DQQ)

Arabidopsis thaliana
X–ray (2.87 Å)

Kintzer & Stroud, 2016







Heuristic score:
1.56 (n = 12)

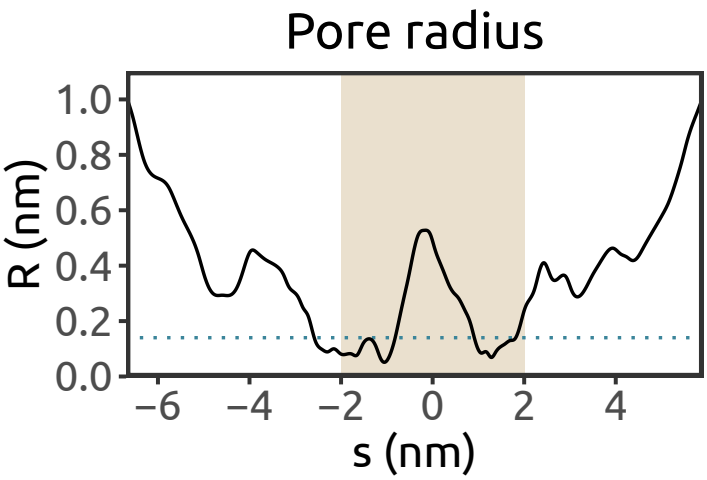
Simulation result:
barrier to water

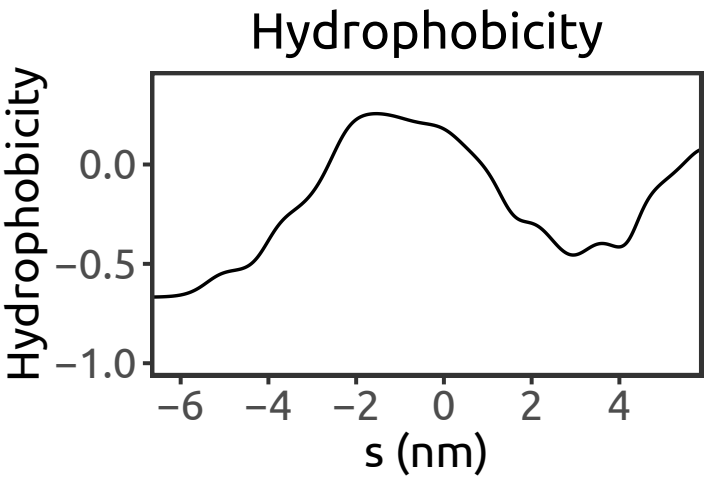
TPC1 (PDB ID: 6C96)

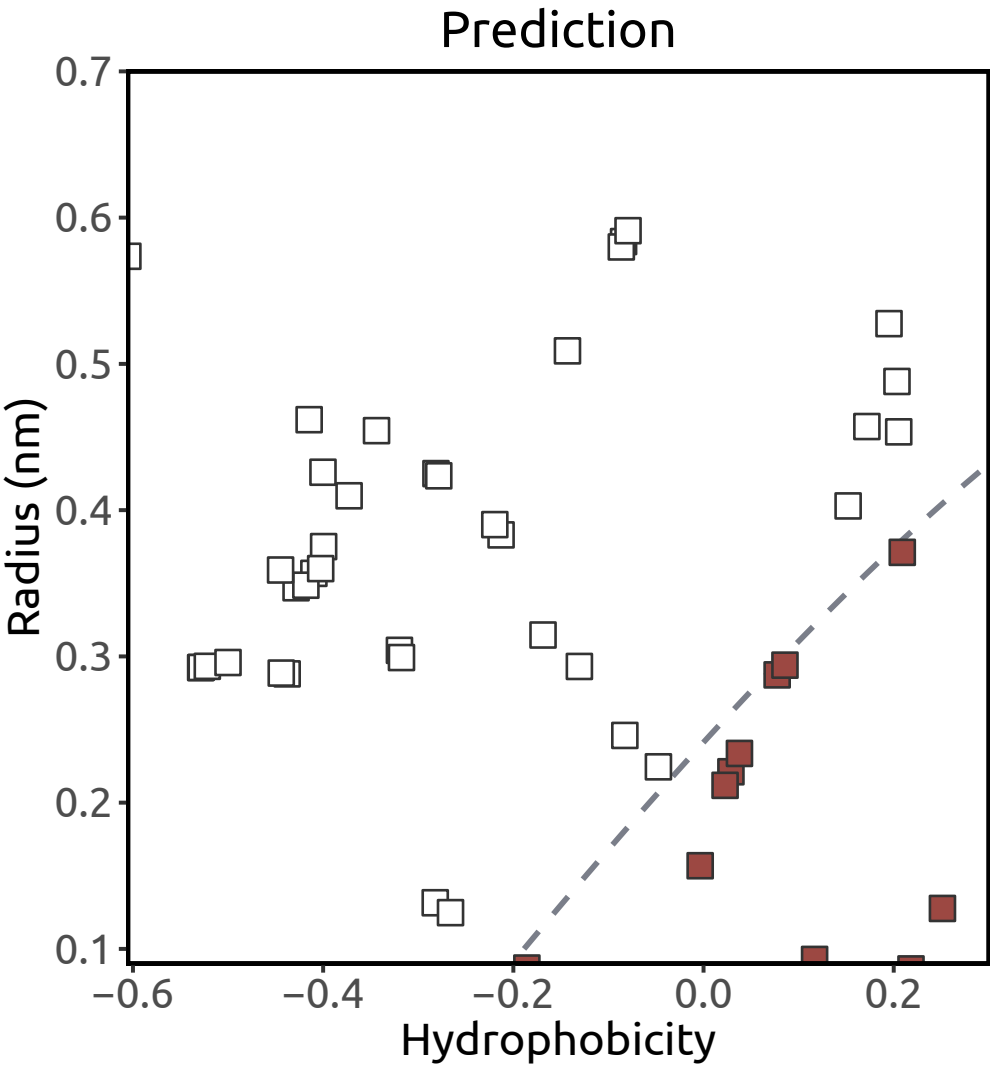
Mus musculus

cryo–EM (3.4 Å)

She et al., 2018







Heuristic score:

2.55 (n = 17)

Simulation result:

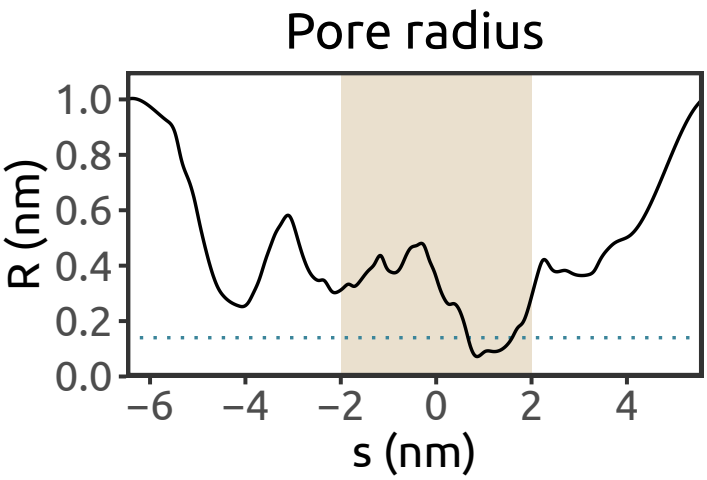
barrier to water

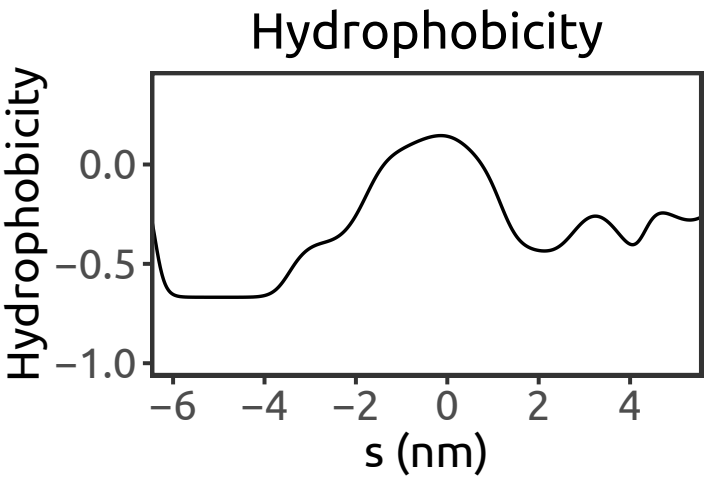
TPC1 (PDB ID: 6C9A)

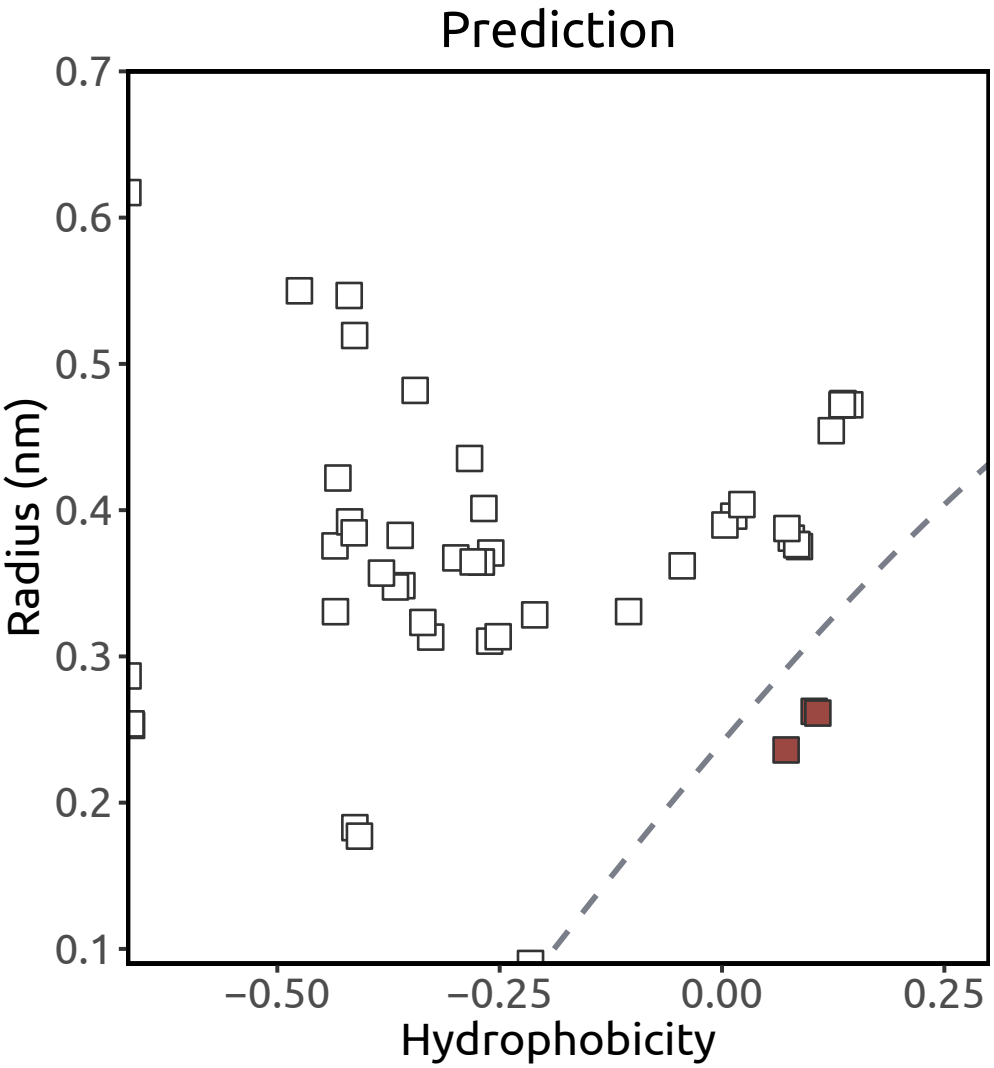
Mus musculus

cryo–EM (3.2 Å)

She et al., 2018







Heuristic score:

0.25 (n = 4)

Simulation result:

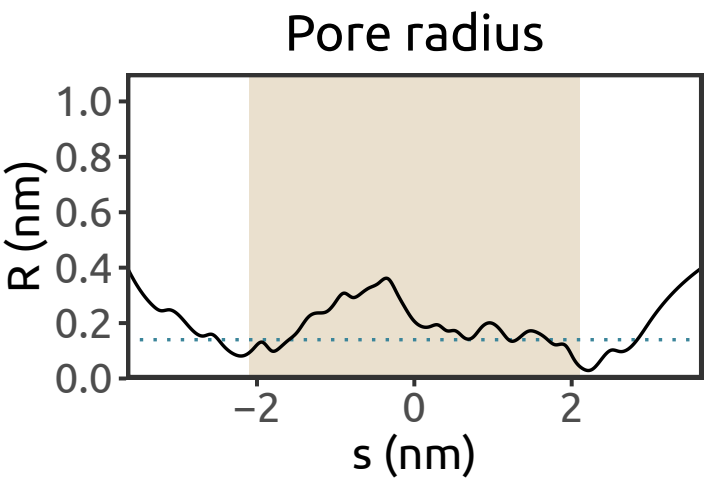
hydrated channel

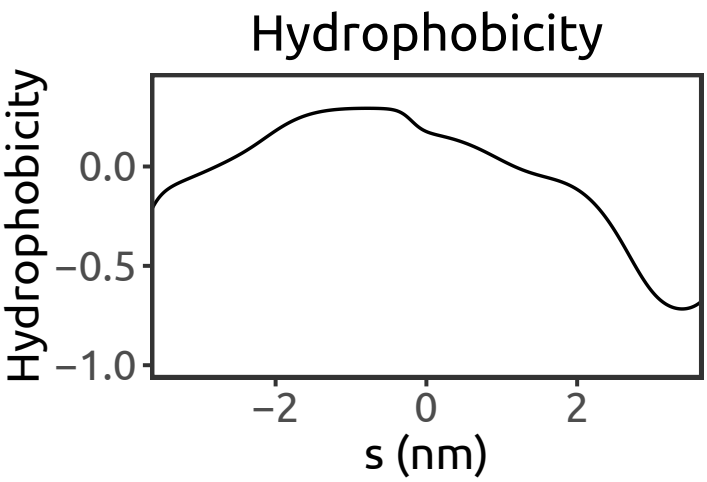
ASIC1 (PDB ID: 2QTS)

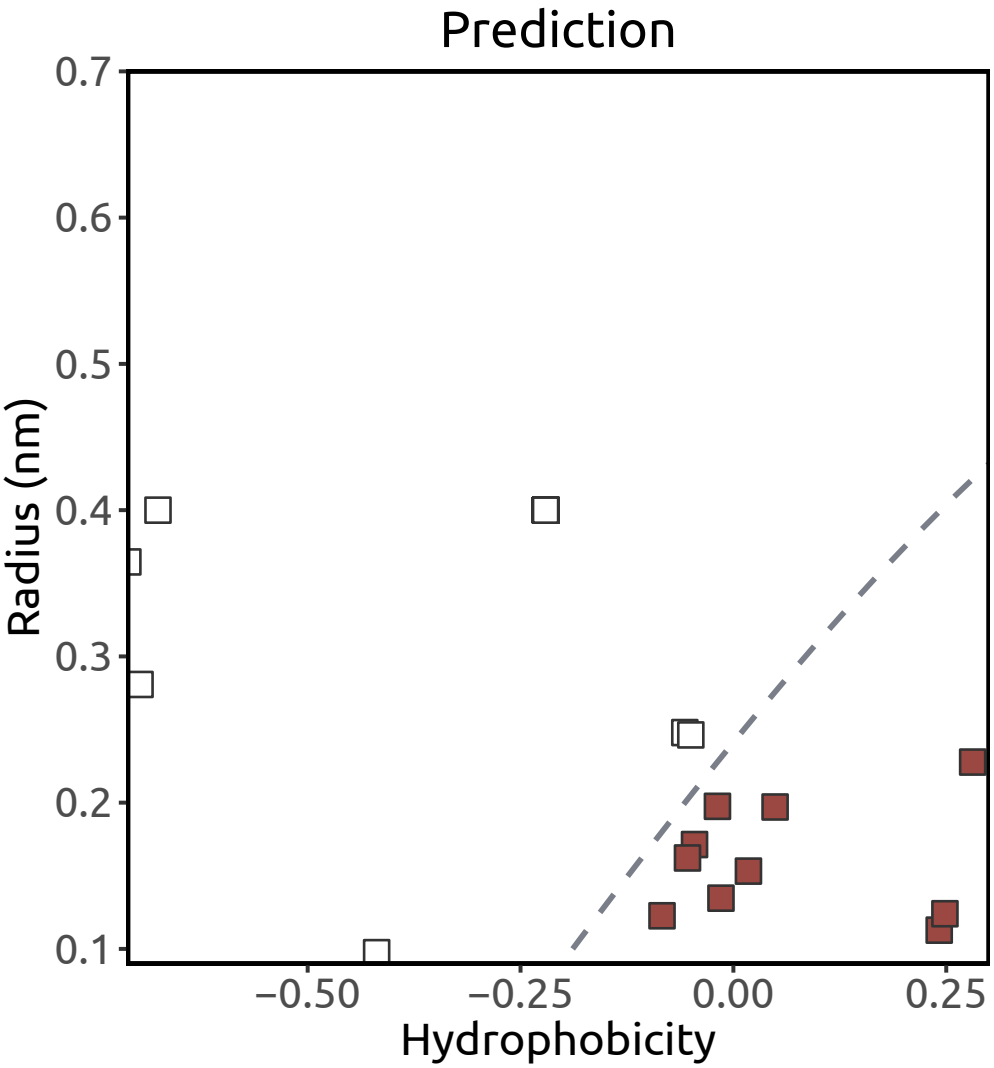
Gallus gallus

X–ray (1.9 Å)

Jasti et al., 2007







Heuristic score:

1.35 (n = 13)

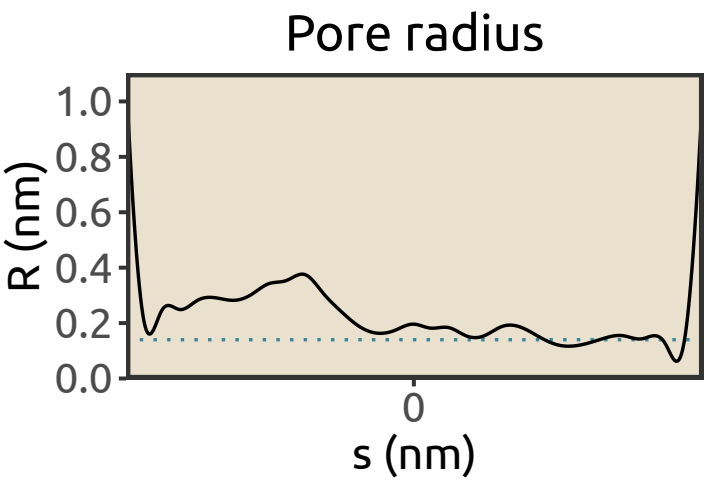
Simulation result:

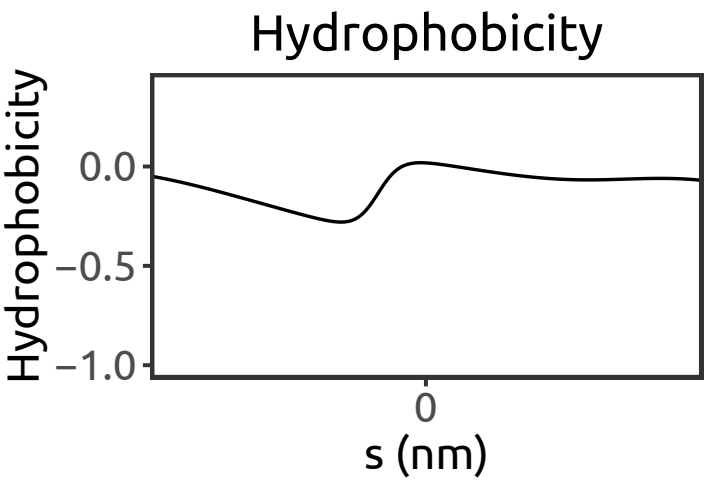
barrier to water

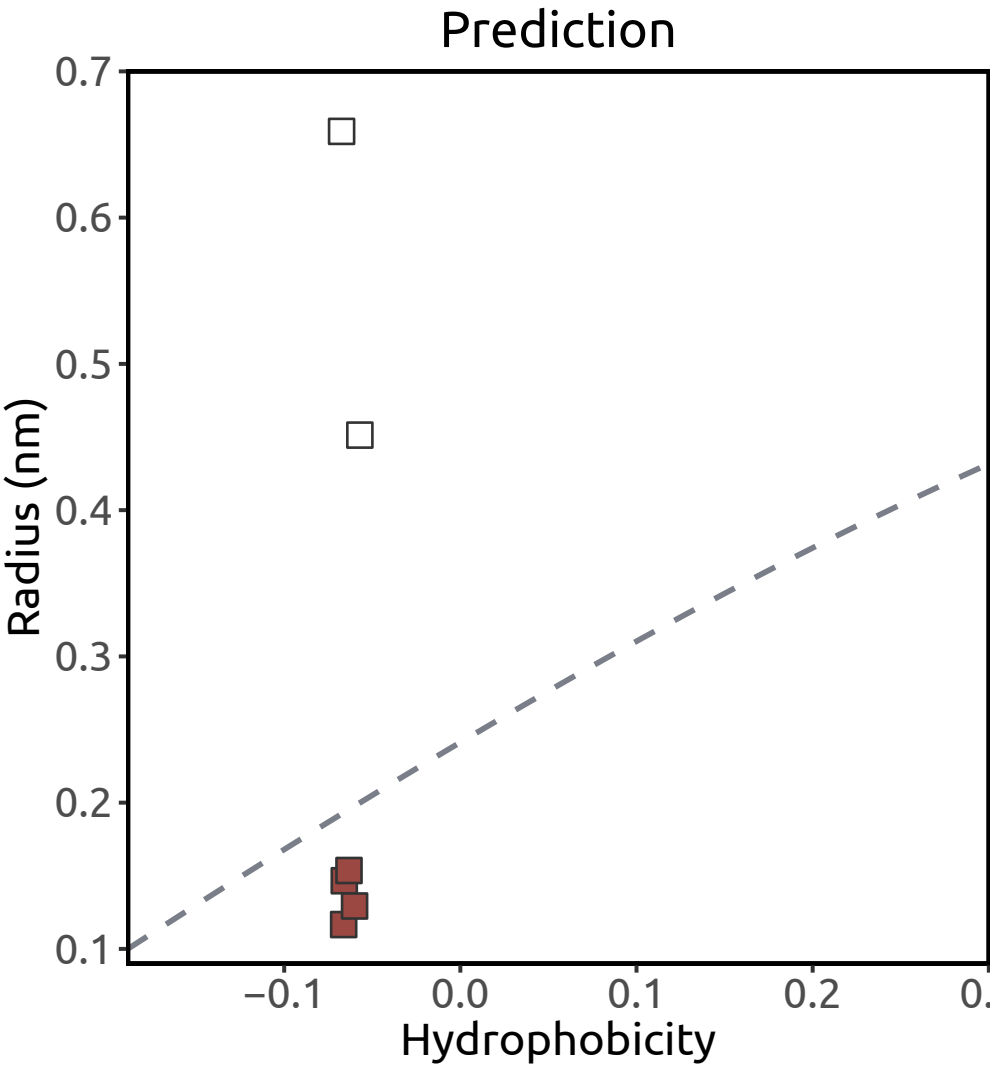
ASIC1 (PDB ID: 3S3W)

Gallus gallus
X–ray (2.6 Å)

Dawson et al., 2012







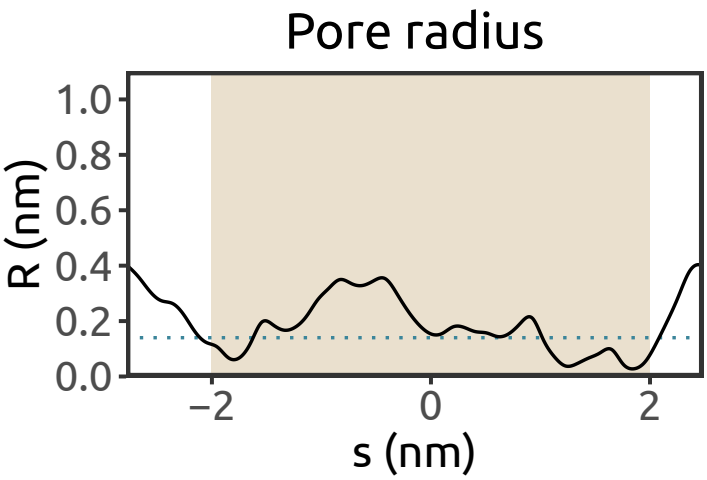
Heuristic score:
0.19 (n = 4)

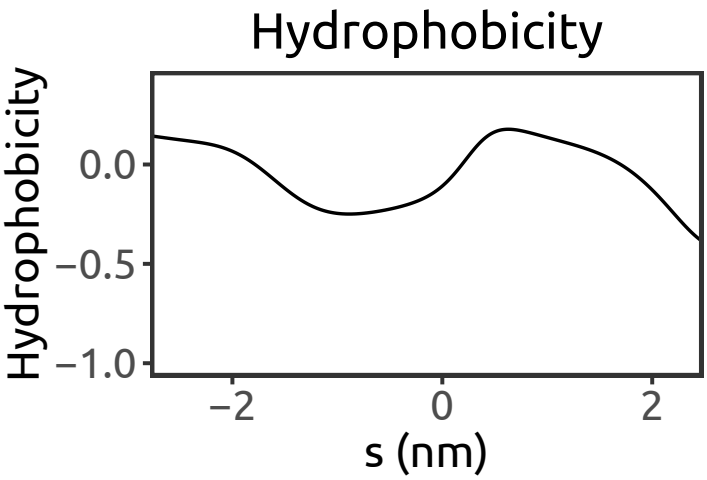
Simulation result:
barrier to water

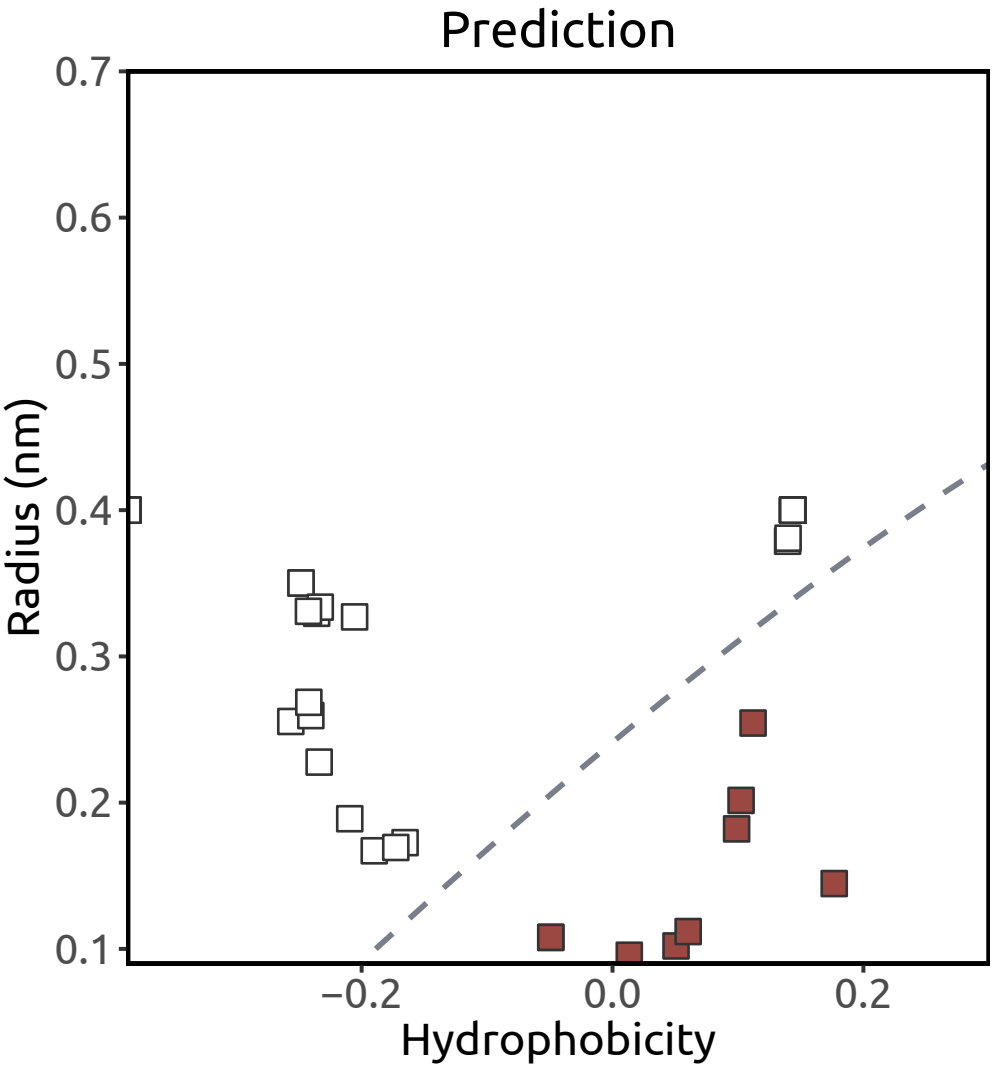
ASIC1 (PDB ID: 4NTW)

Gallus gallus
X–ray (2.07 Å)

Baconguis et al., 2014







Heuristic score:
2.35 (n = 17)

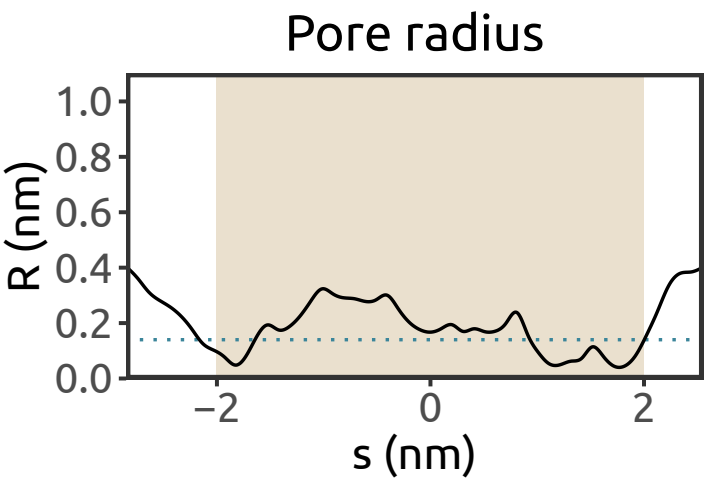
Simulation result:
hydrated channel

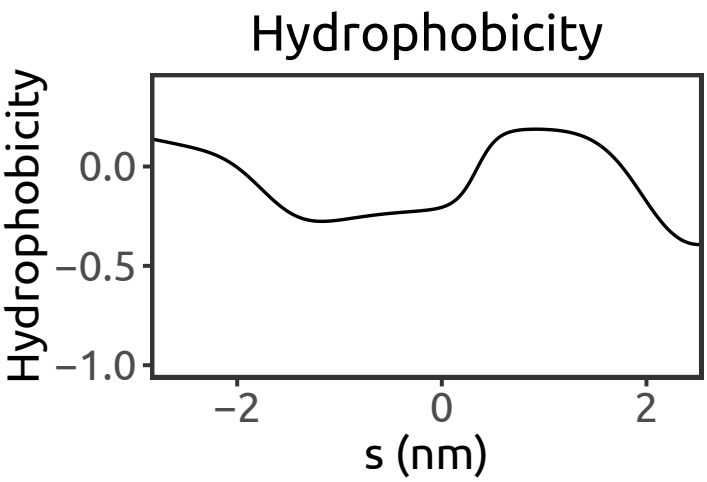
ASIC1 (PDB ID: 4NTY)

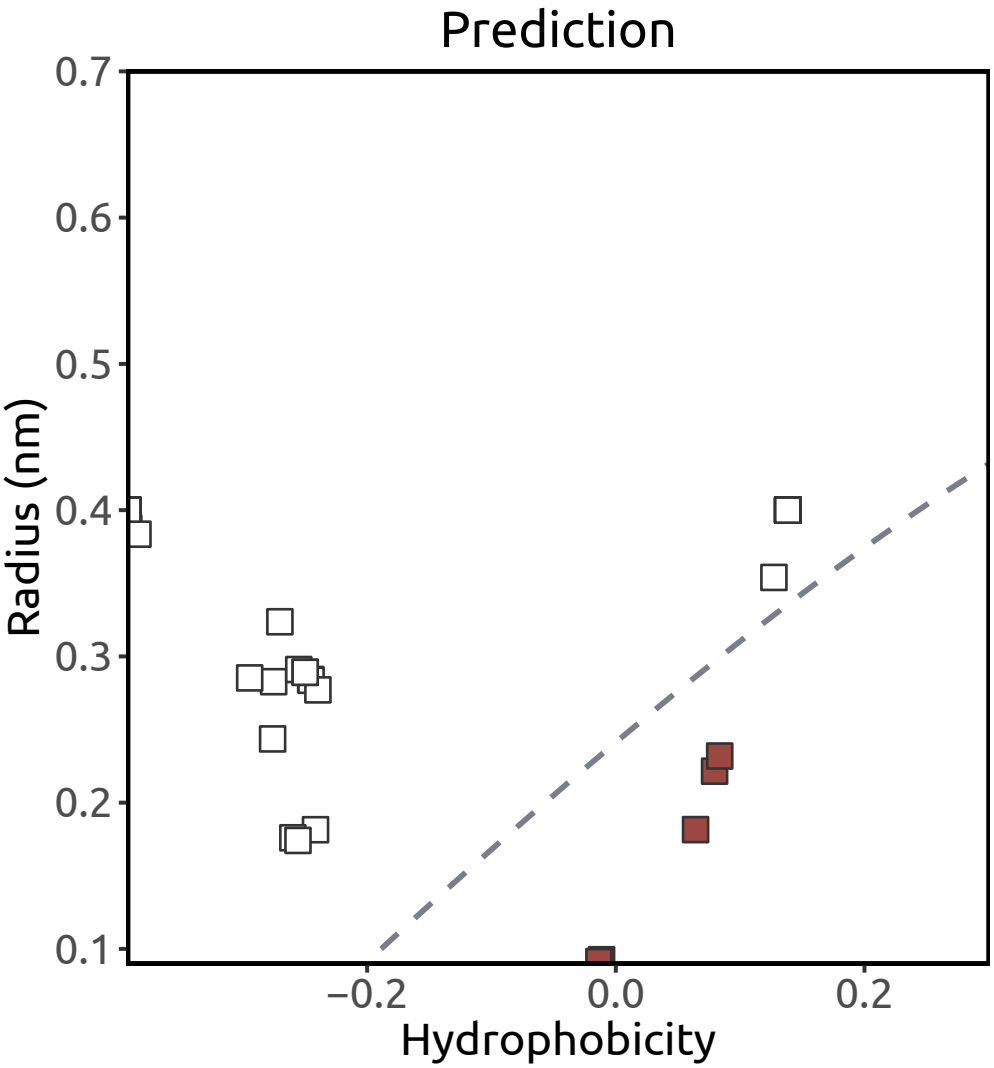
Gallus gallus

X–ray (2.65 Å)

Baconguis et al., 2014







Heuristic score:

1.83 (n = 12)

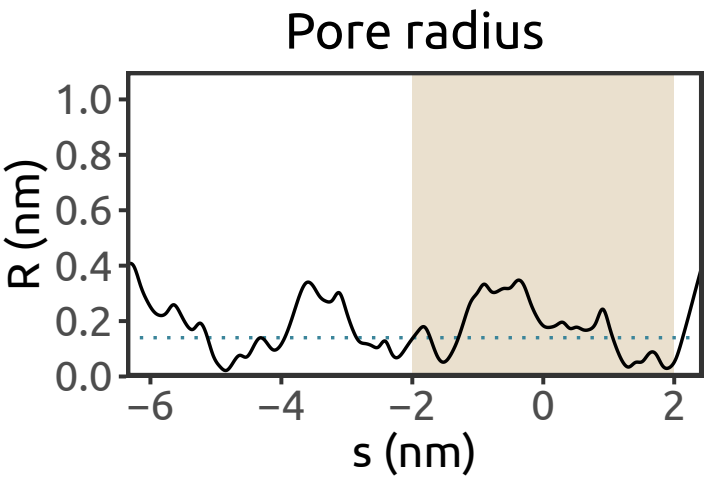
Simulation result:

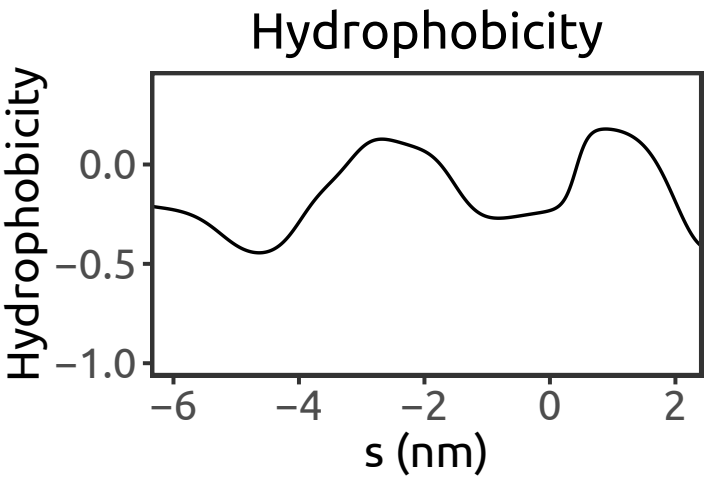
hydrated channel

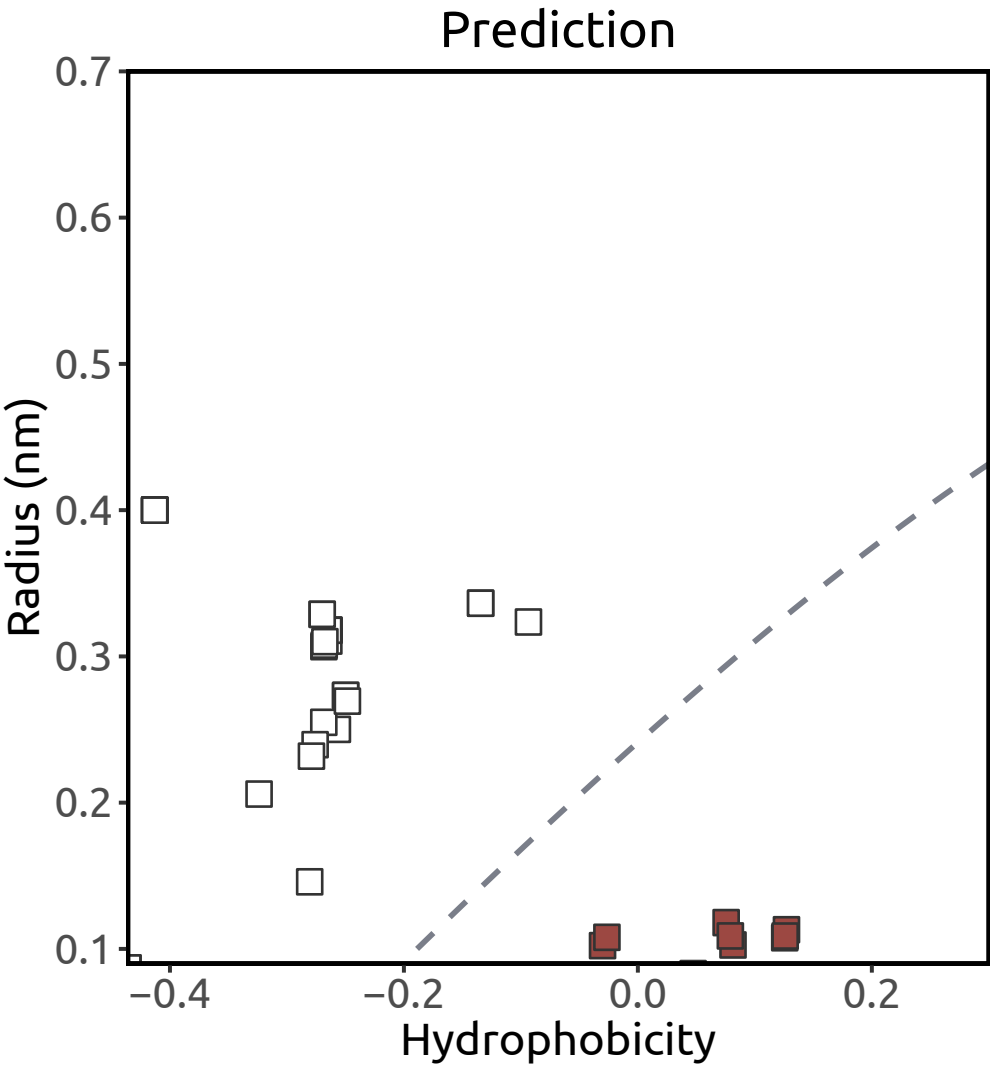
ASIC1 (PDB ID: 4NYK)

Gallus gallus
X–ray (3 Å)

Gonzales et al., 2009







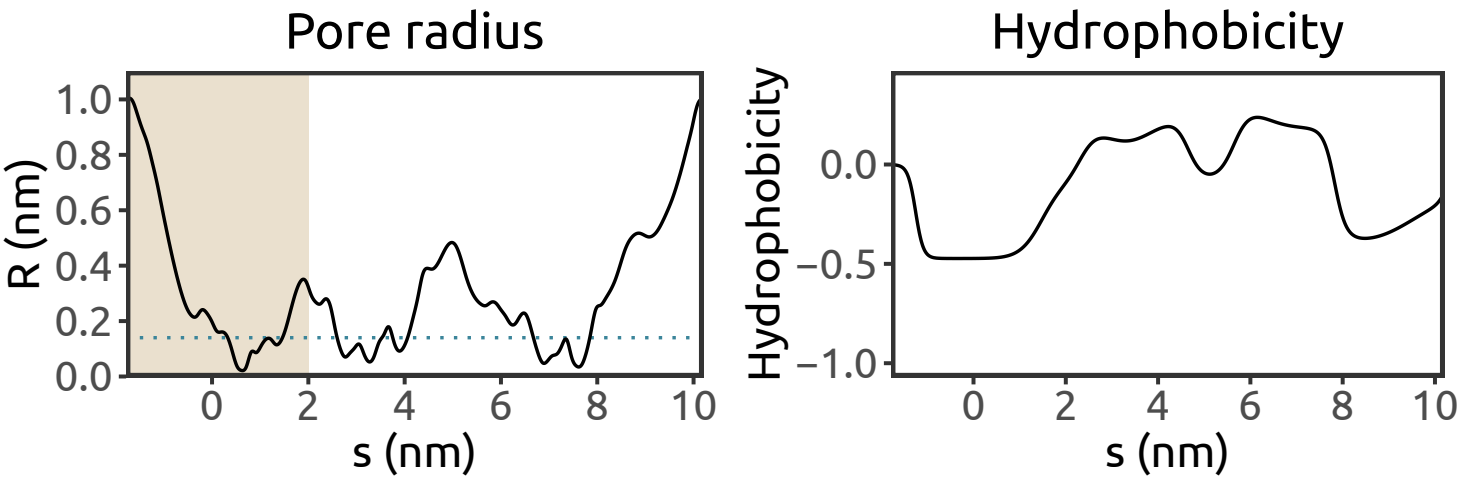
Heuristic score:
2.43 (n = 15)

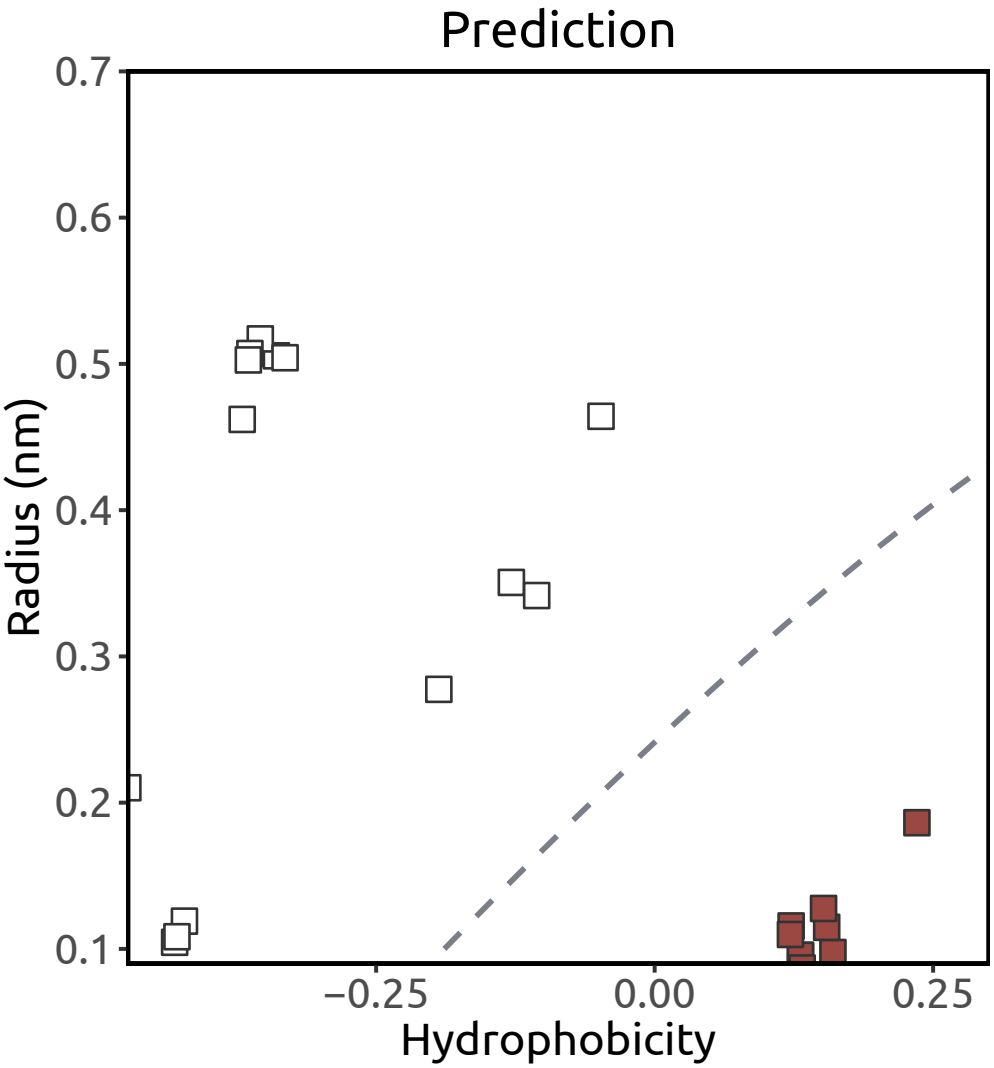
Simulation result:
barrier to water

ASIC1 (PDB ID: 5WKU)

Gallus gallus
X–ray (2.95 Å)

Yoder et al., 2018





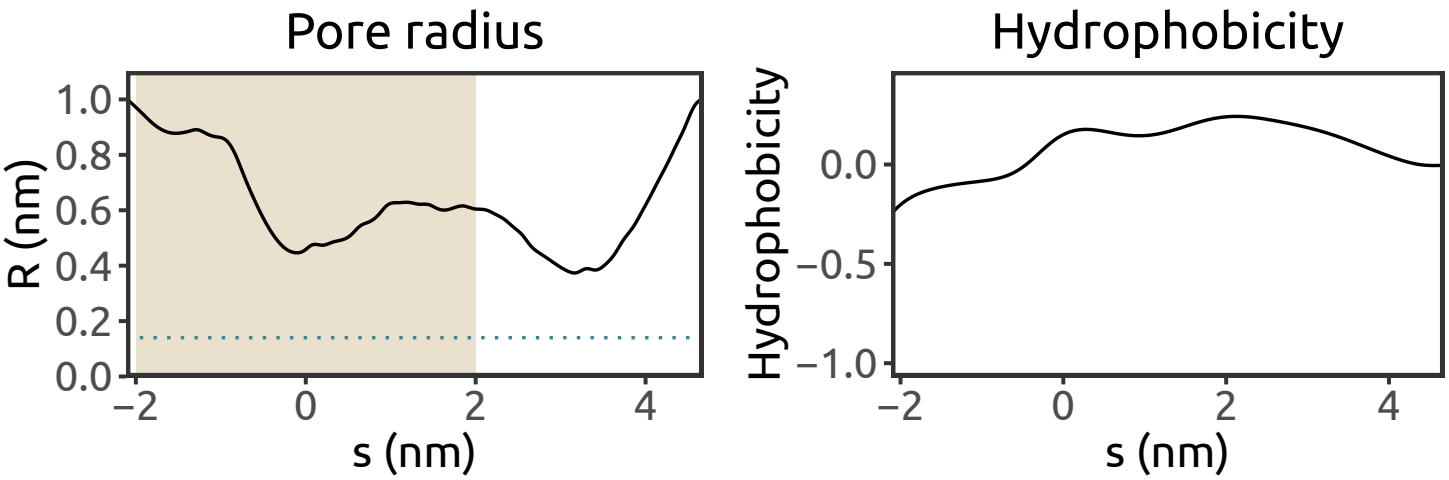
Heuristic score:
2.67 (n = 13)

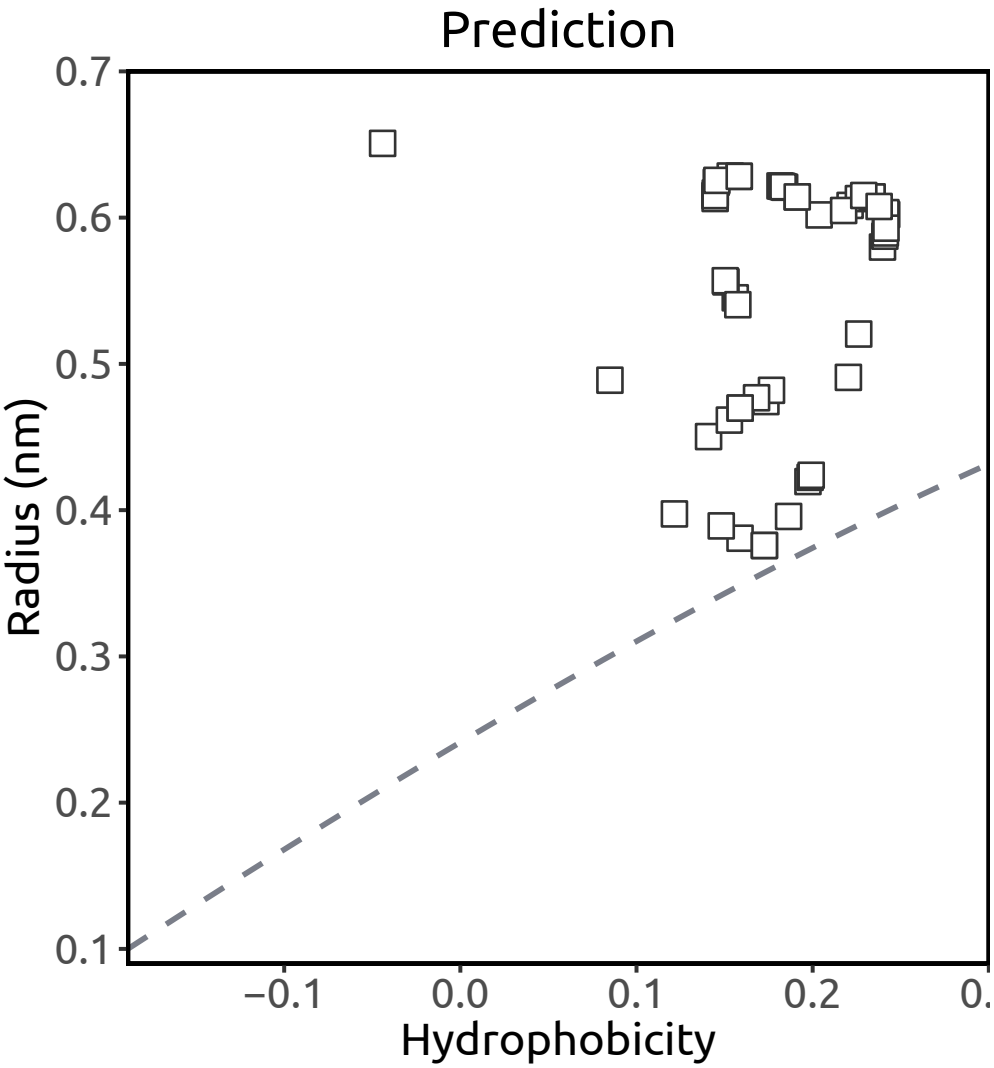
Simulation result:
barrier to water

ExbBExbD (PDB ID: 5SV0)

Escherichia coli
X–ray (2.6 Å)

Celia et al., 2016





Heuristic score:
0 (n = 0)

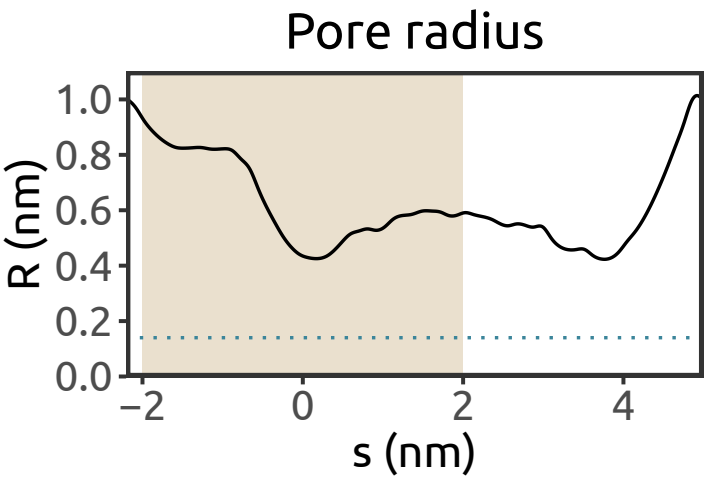
Simulation result:
hydrated channel

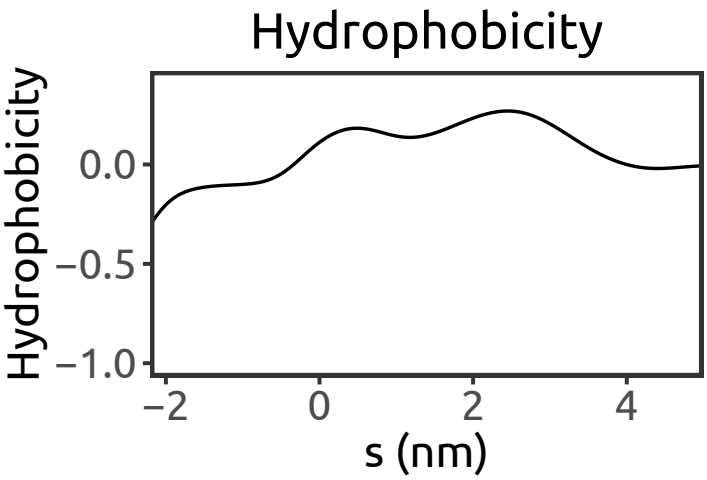
ExbBExbD (PDB ID: 5SV1)

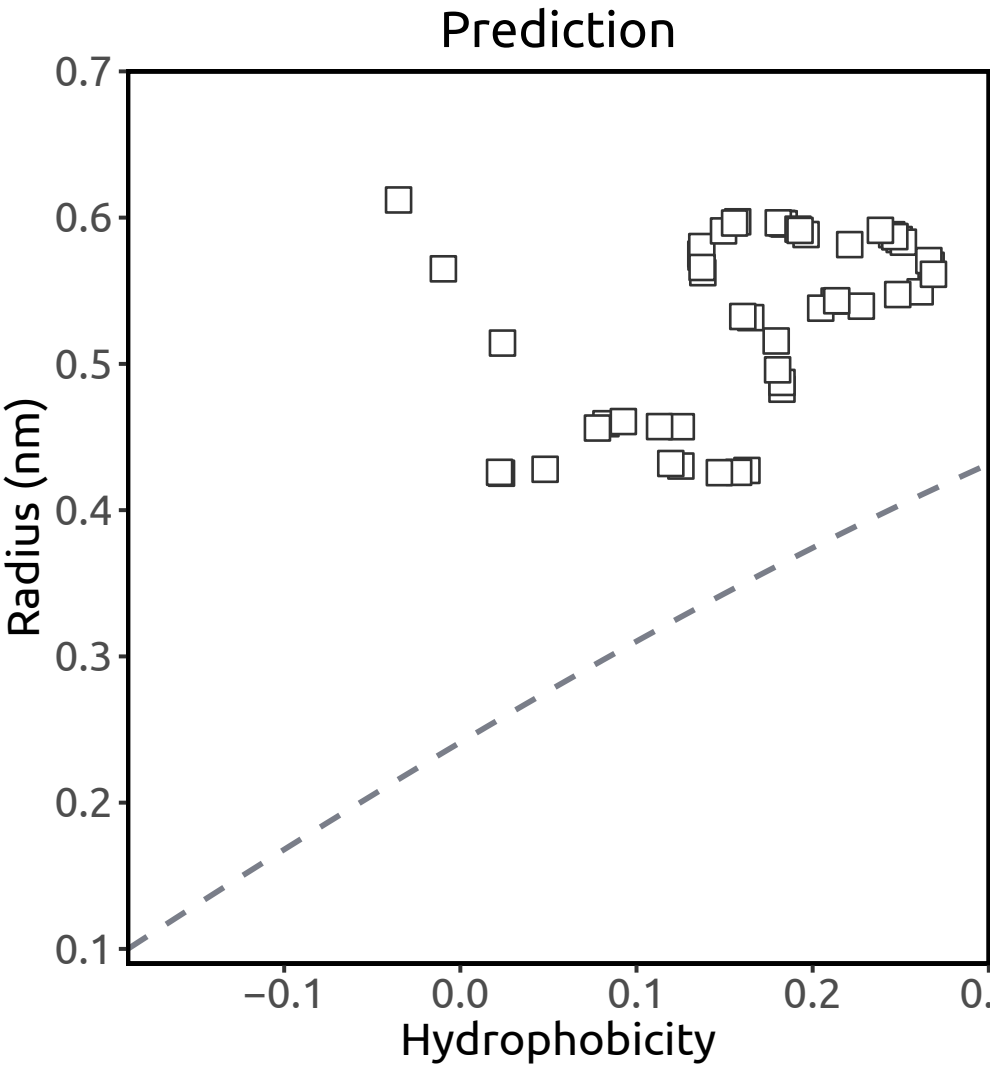
Escherichia coli

X–ray (3.5 Å)

Celia et al., 2016







Heuristic score:

0 (n = 0)

Simulation result:

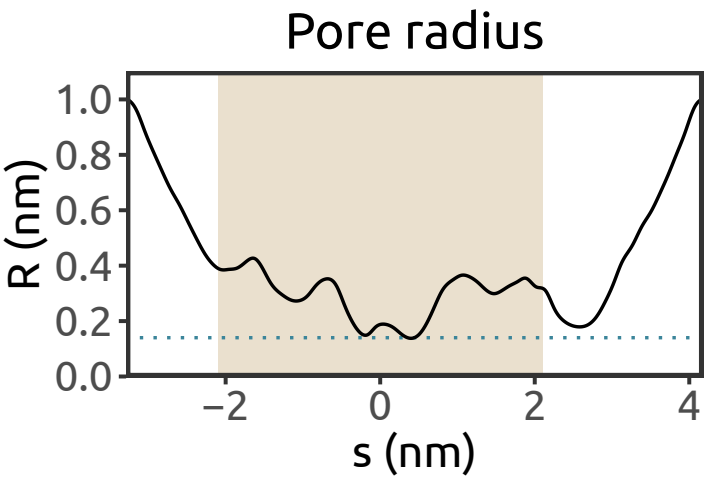
hydrated channel

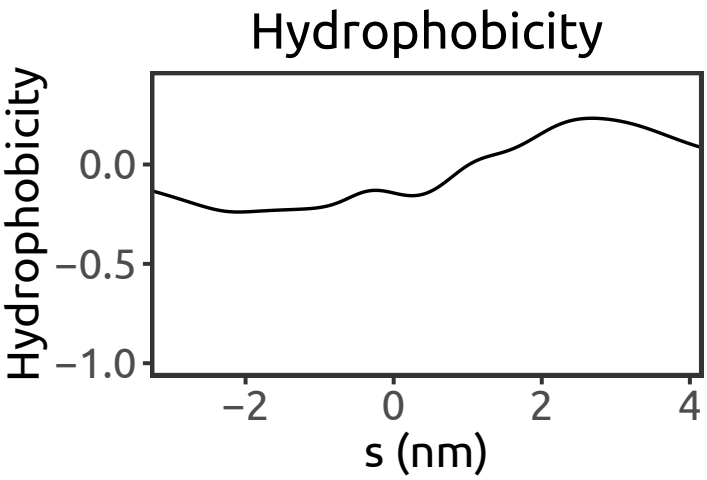
M2 (PDB ID: 2KIX)

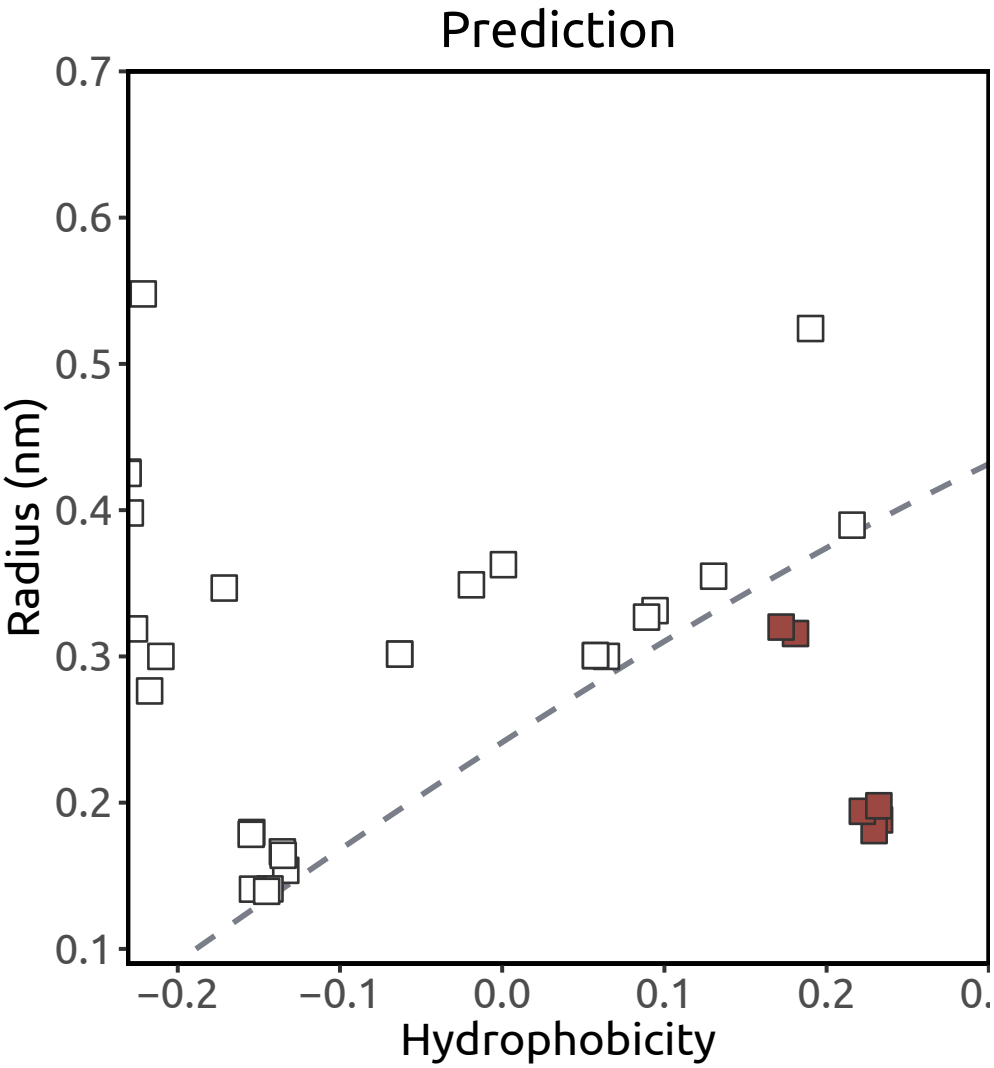
Influenza B

aq NMR

Wang et al., 2009







Heuristic score:

0.76 (n = 6)

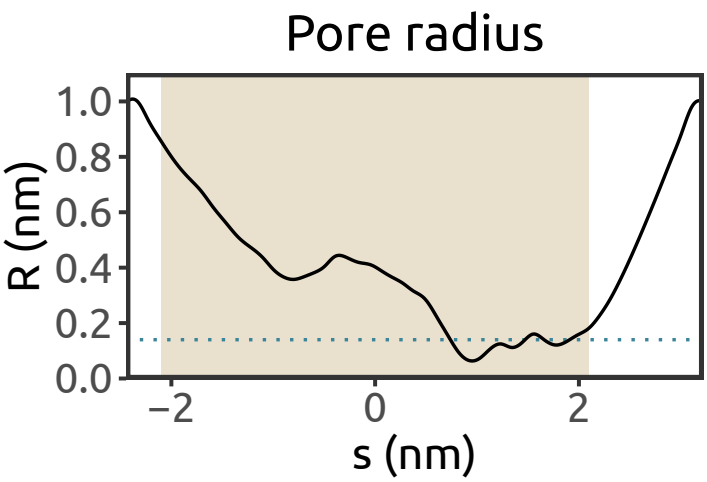
Simulation result:

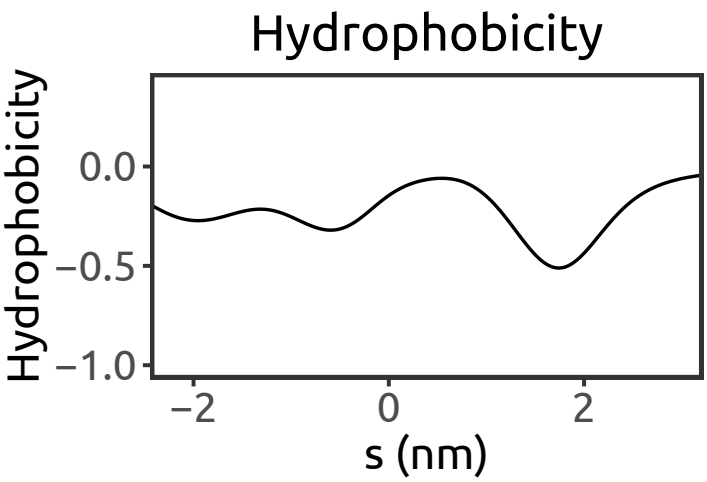
barrier to water

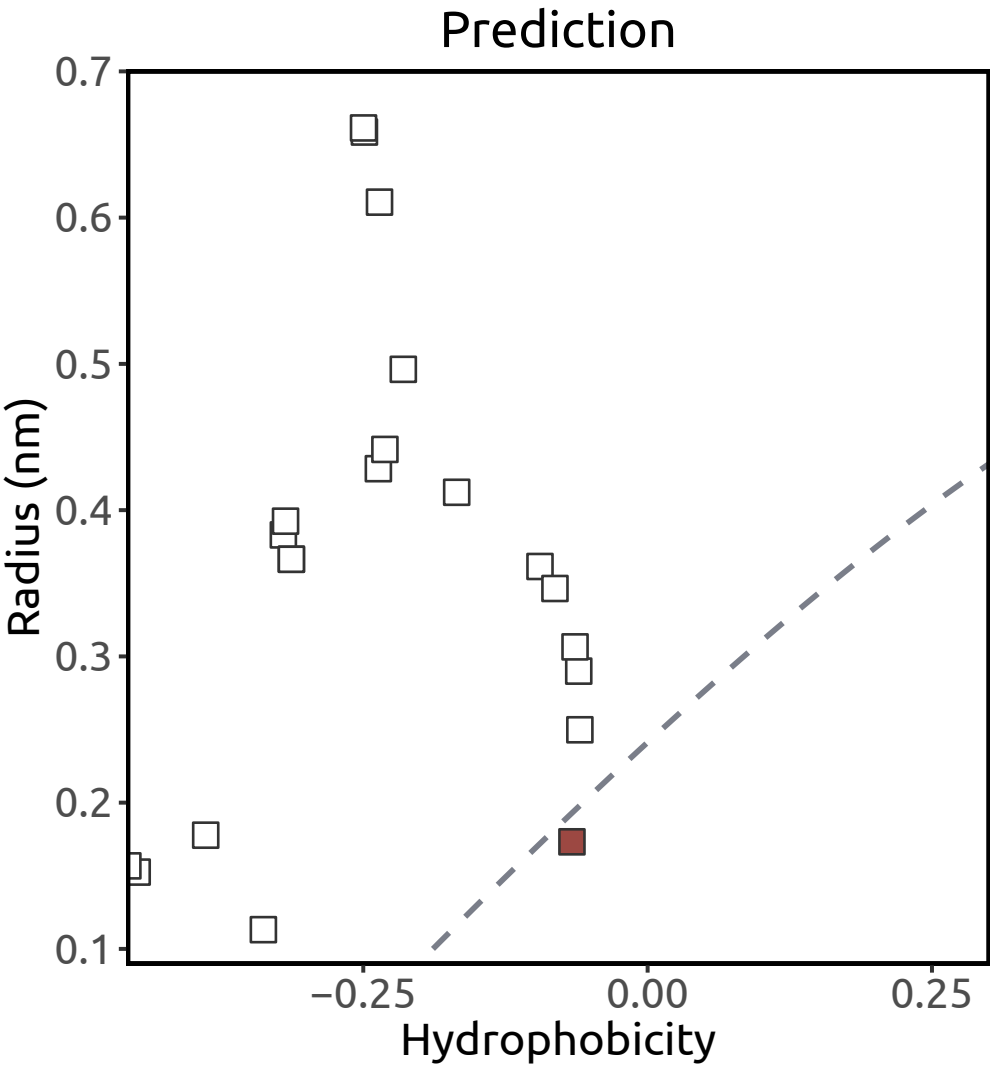
M2 (PDB ID: 3BKD)

Influenza A
X–ray (2.05 Å)

Stouffer et al., 2008







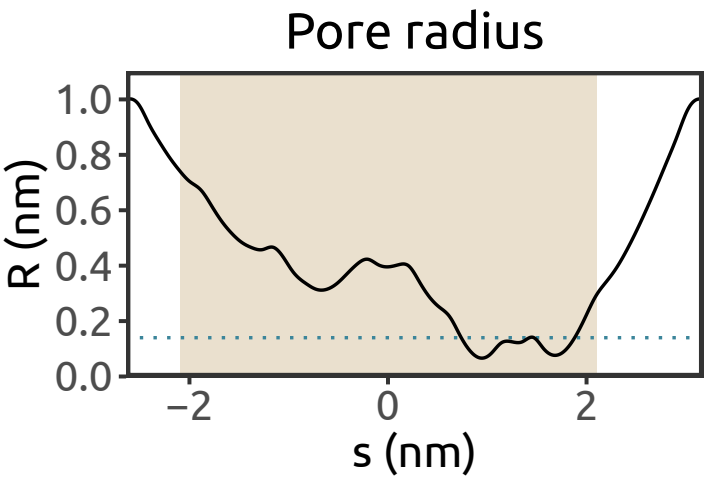
Heuristic score:
0.27 (n = 5)

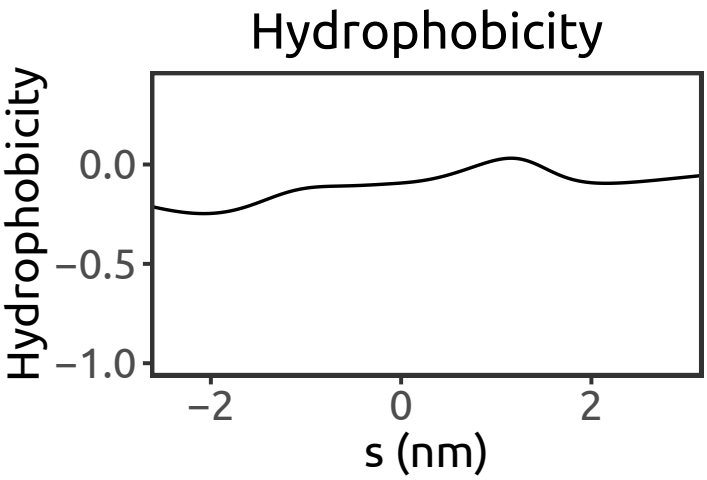
Simulation result:
barrier to water

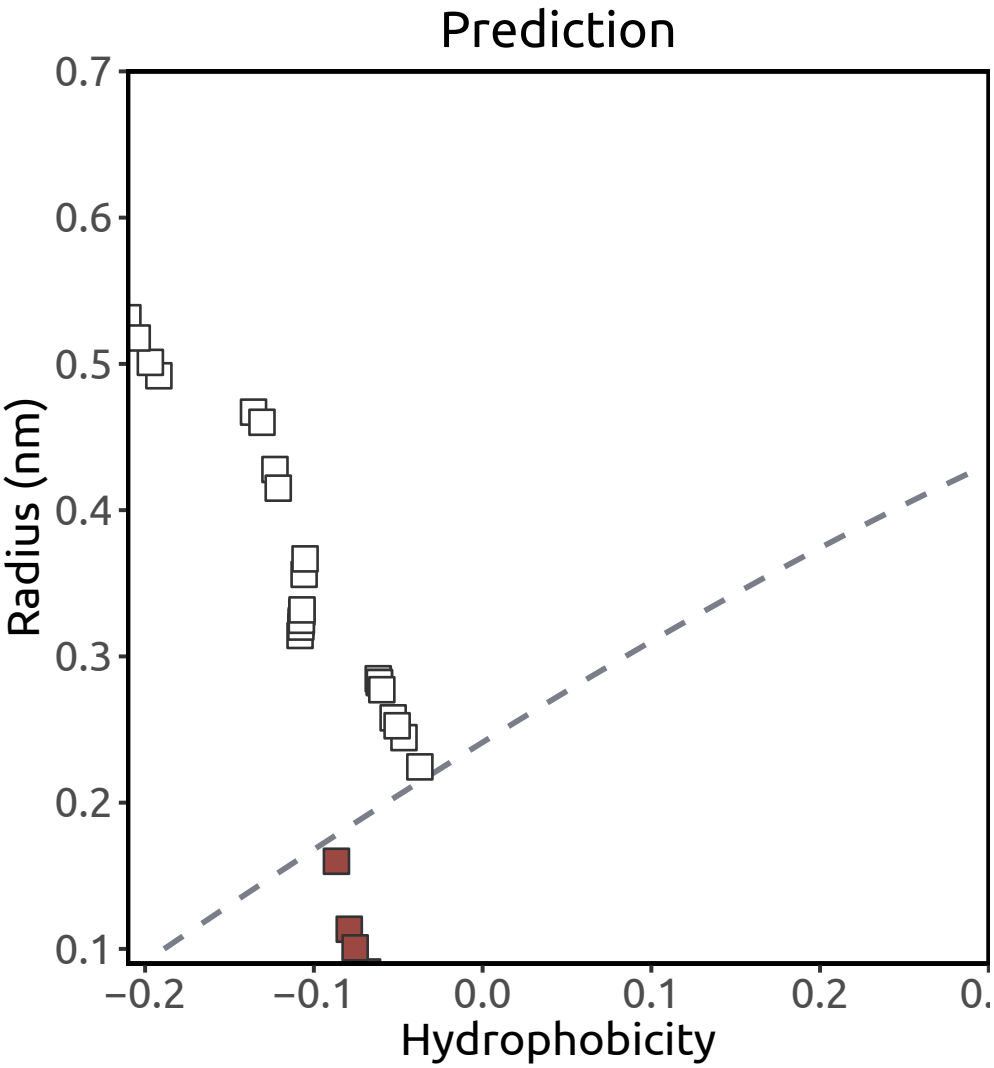
M2 (PDB ID: 4QKC)

Influenza A
X–ray (1.1 Å)

Thomaston et al., 2015







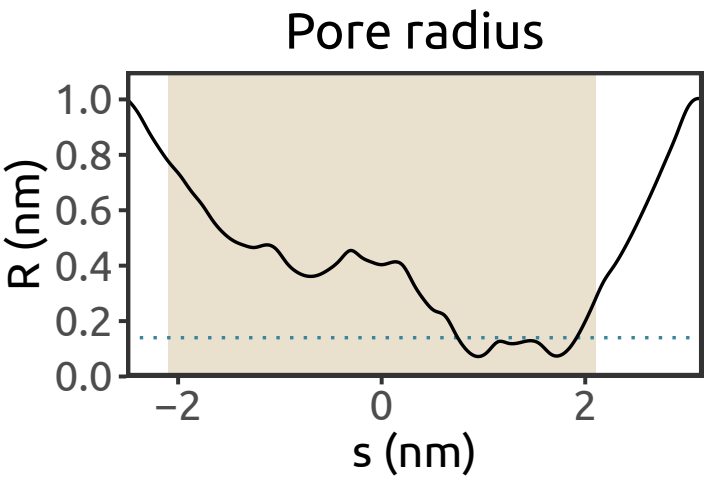
Heuristic score:
0.82 (n = 8)

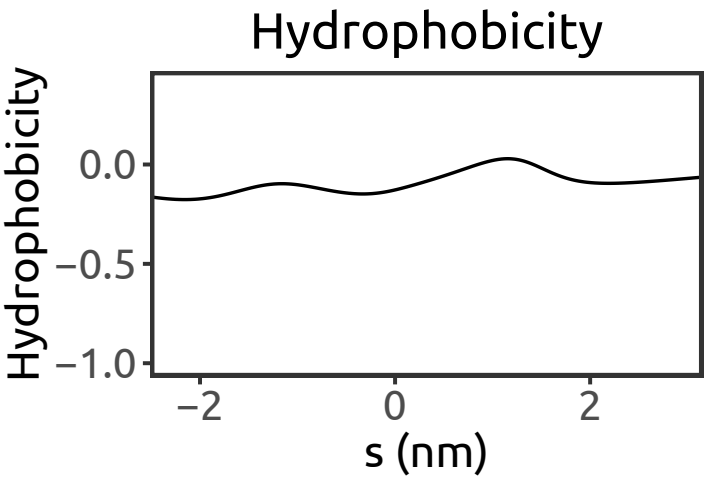
Simulation result:
barrier to water

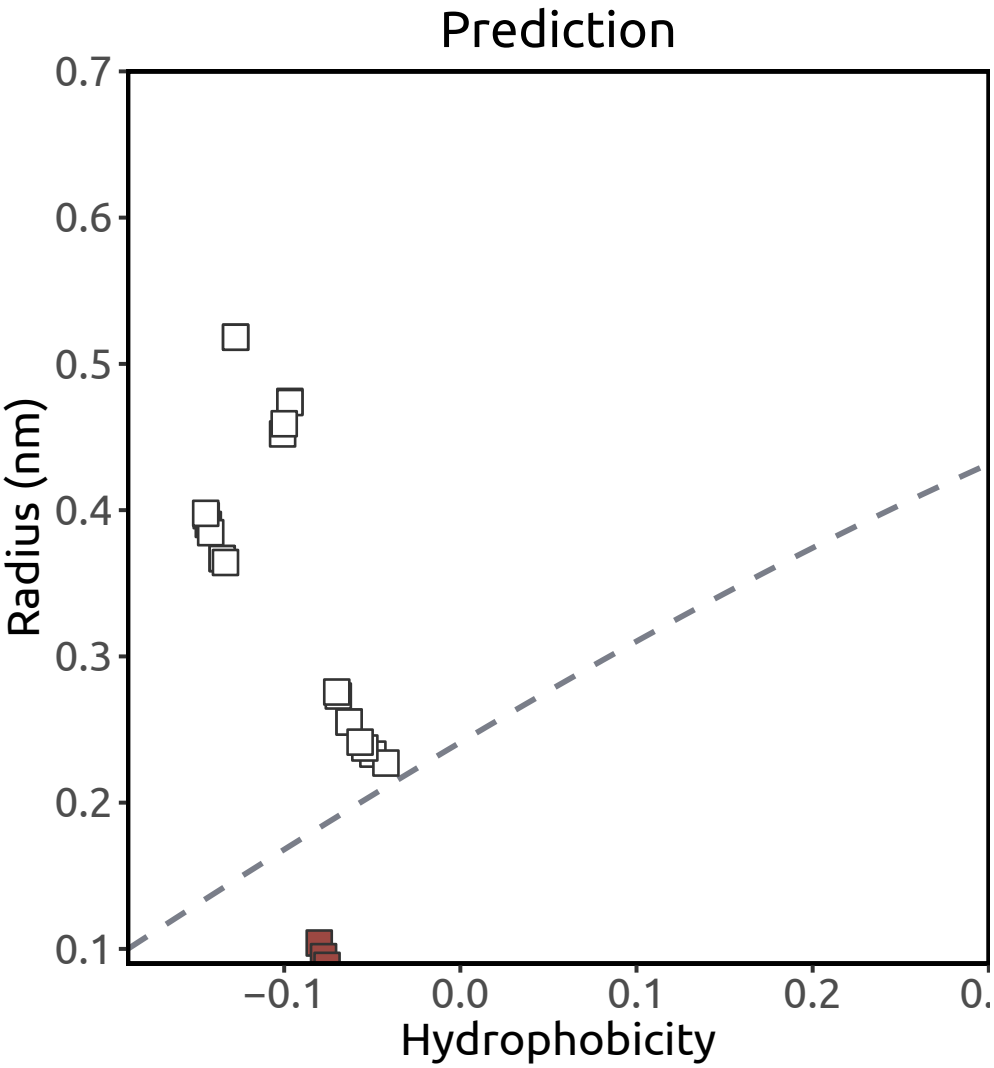
M2 (PDB ID: 5JOO)

Influenza A
X–ray (1.41 Å)

Thomaston et al., 2017







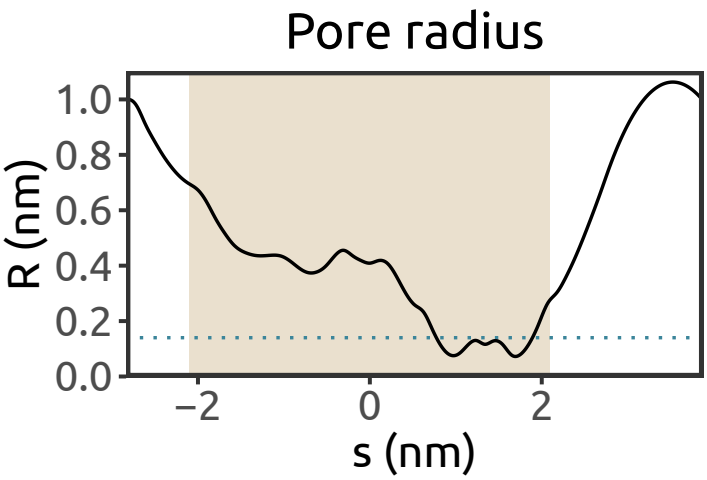
Heuristic score:
0.88 (n = 8)

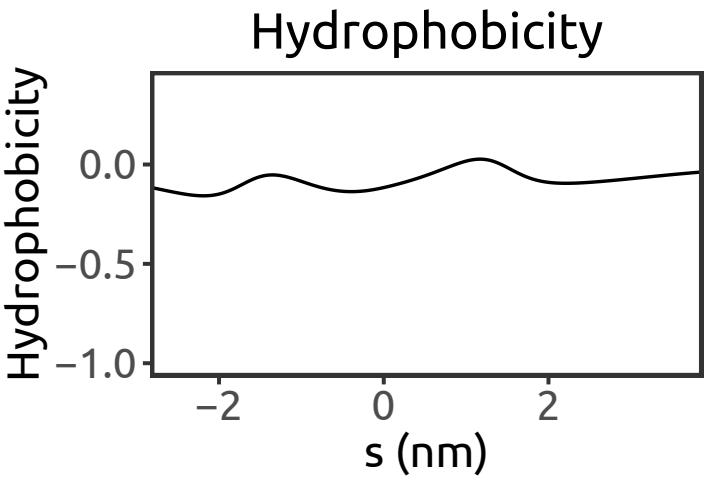
Simulation result:
barrier to water

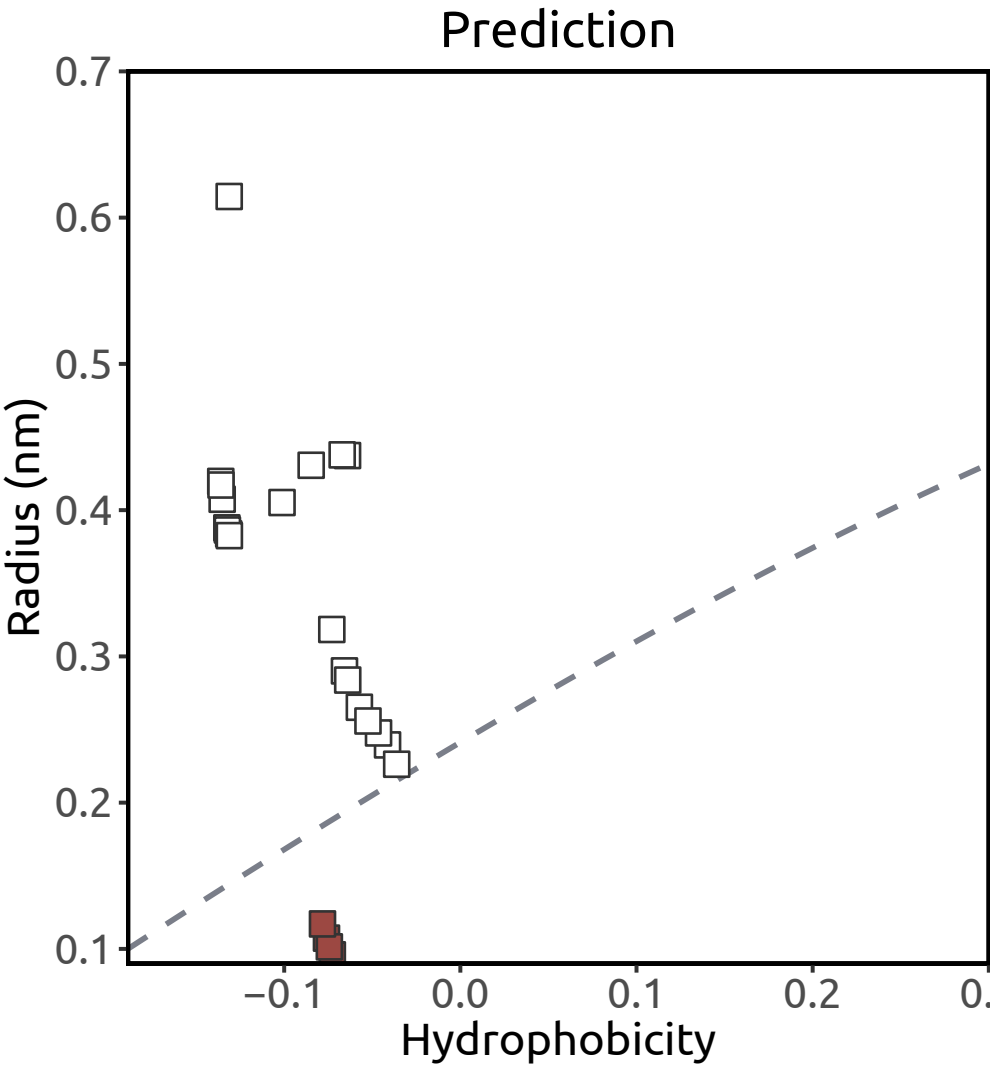
M2 (PDB ID: 5TTC)

Influenza A
X–ray (1.4 Å)

Thomaston et al., 2017







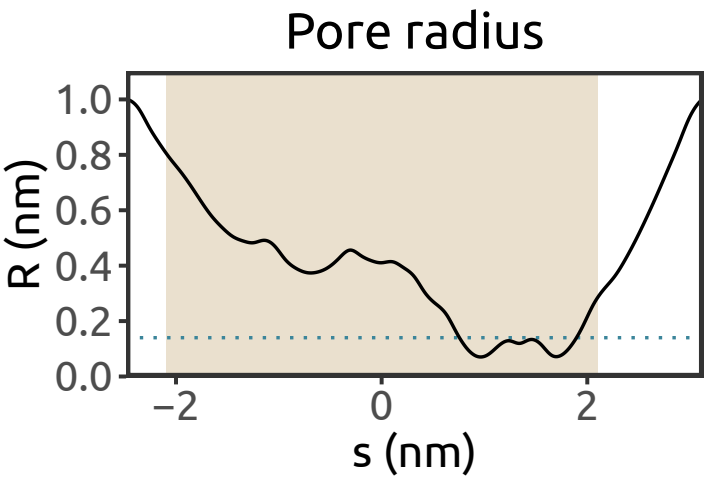
Heuristic score:
0.83 (n = 8)

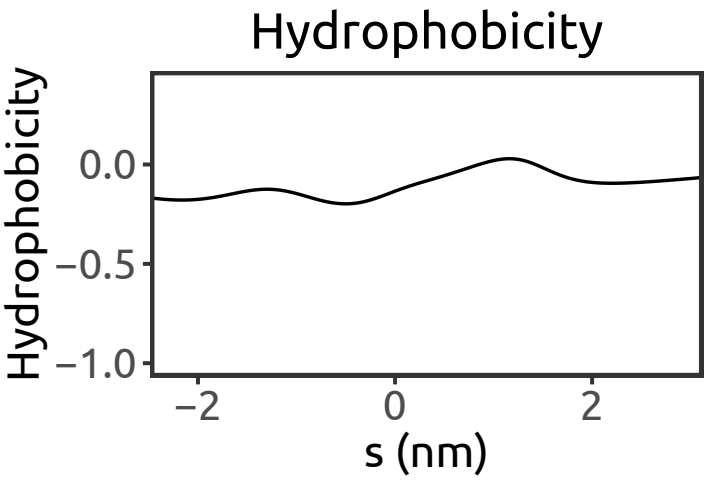
Simulation result:
barrier to water

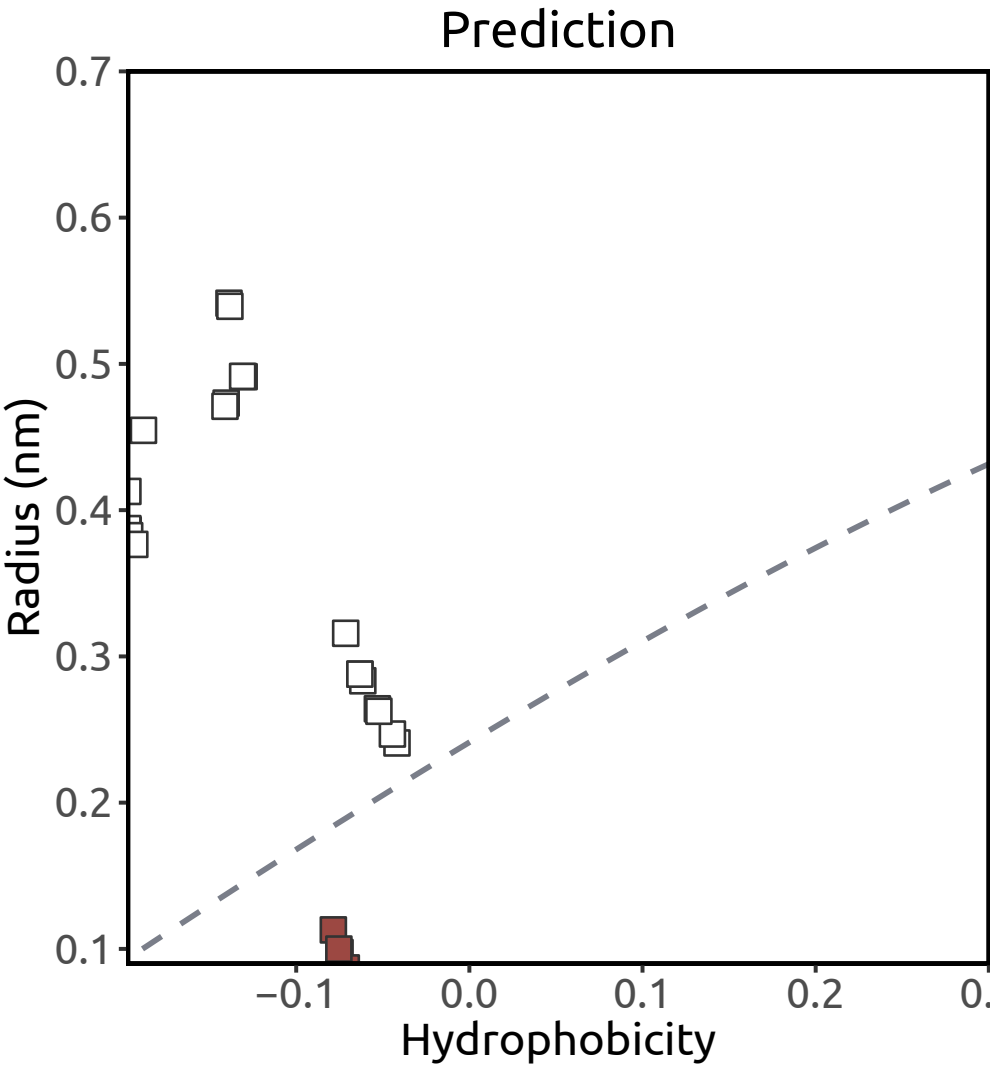
M2 (PDB ID: 5UM1)

Influenza A
X–ray (1.45 Å)

Thomaston et al., 2017







Heuristic score:
0.87 (n = 8)

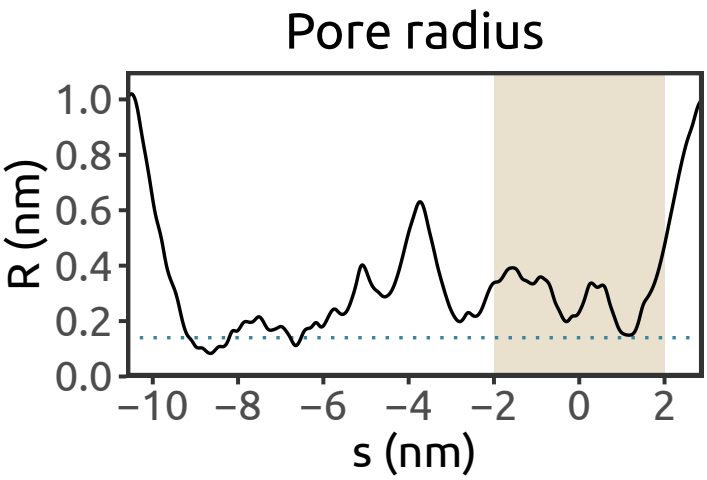
Simulation result:
barrier to water

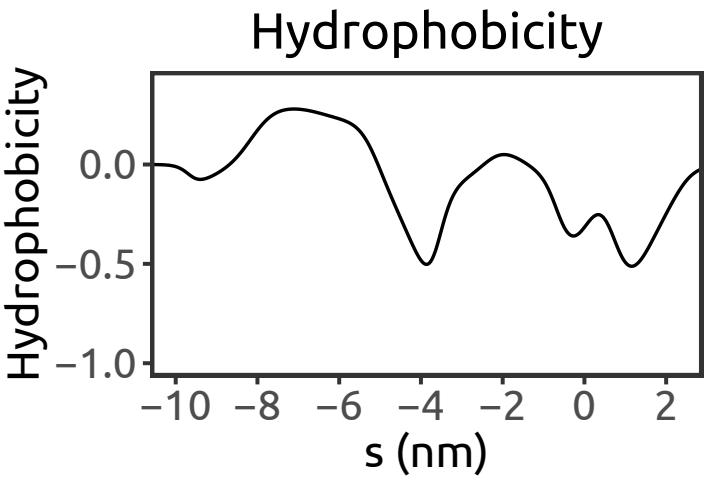
MCU (PDB ID: 5ID3)

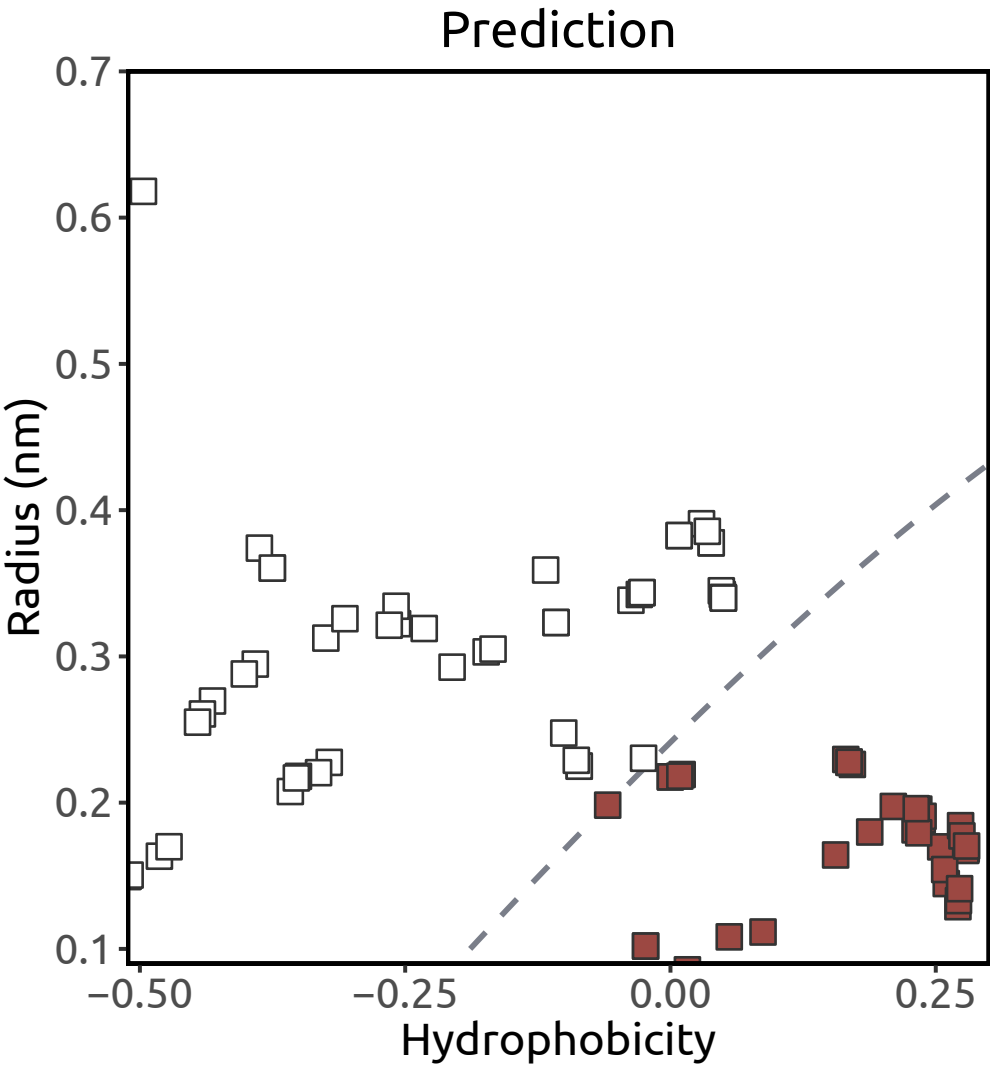
Caenorhabditis elegans

aq NMR

Oxenoid et al., 2016







Heuristic score:

5.2 (n = 35)

Simulation result:

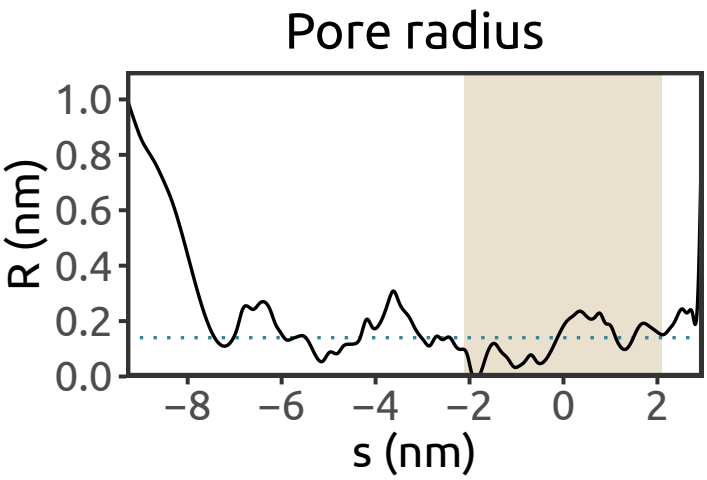
barrier to water

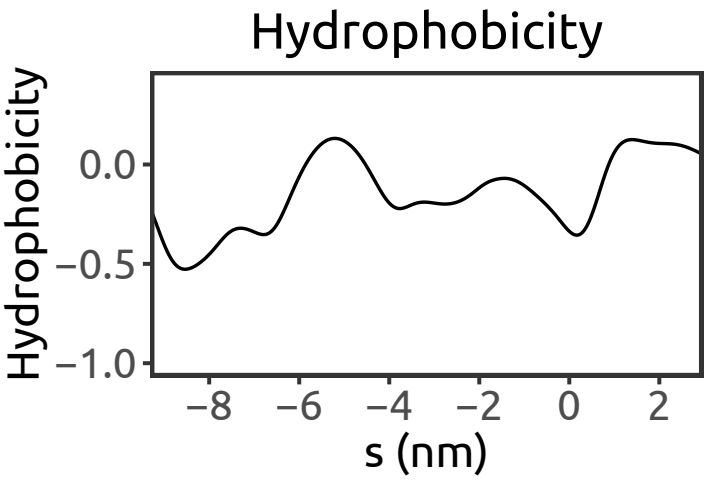
MgtE (PDB ID: 2ZY9)

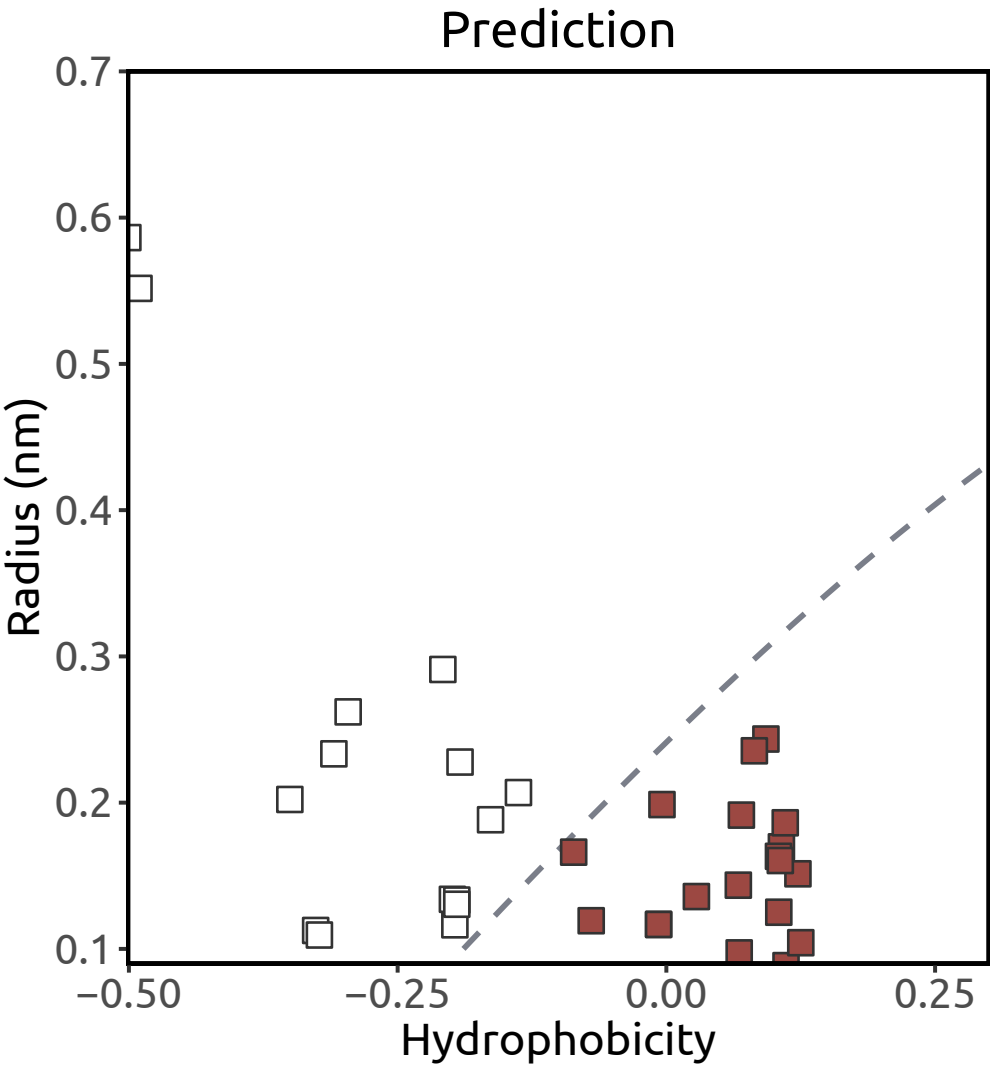
Thermus thermophilus

X–ray (2.94 Å)

Hattori et al., 2009







Heuristic score:

2.58 (n = 23)

Simulation result:

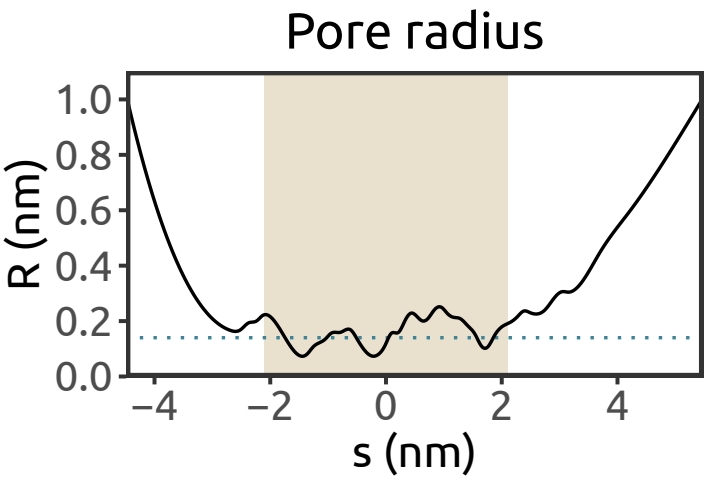
barrier to water

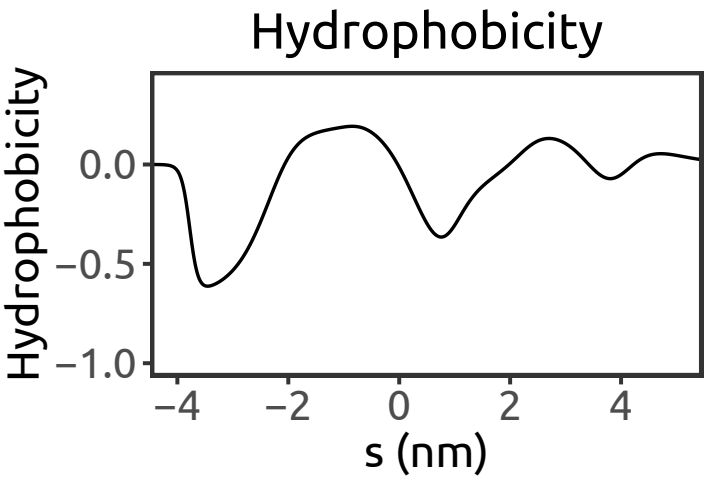
MgtE (PDB ID: 4U9N)

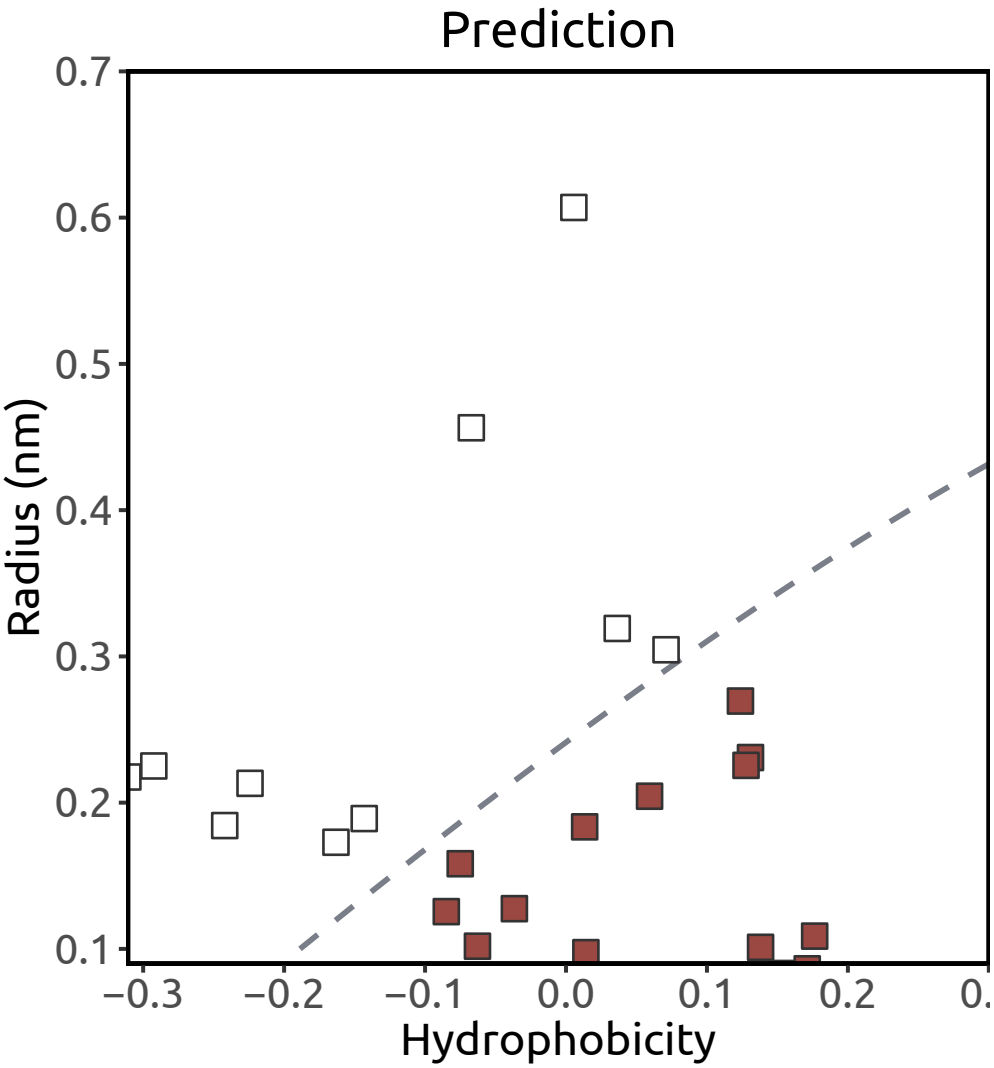
Thermus thermophilus

X–ray (2.2 Å)

Takeda et al., 2014







Heuristic score:

1.94 (n = 16)

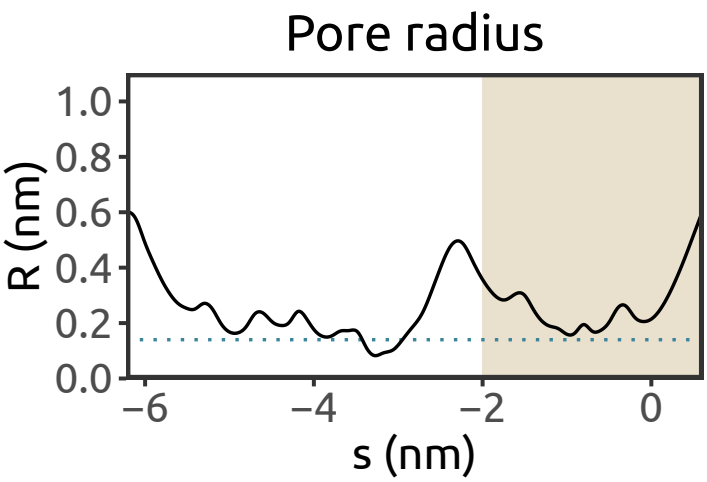
Simulation result:

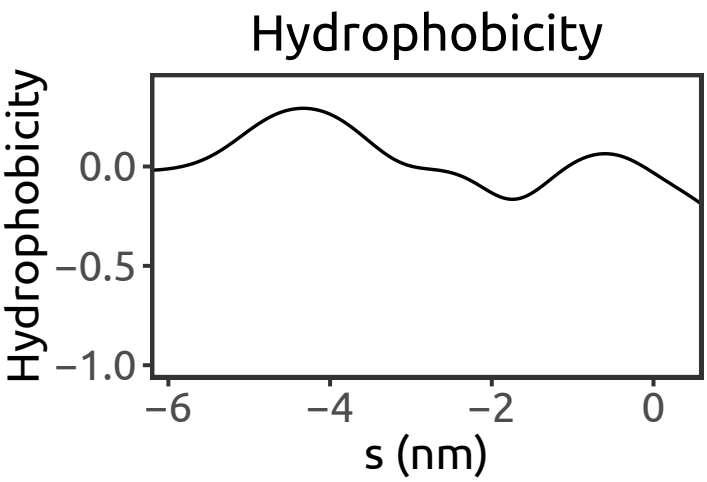
barrier to water

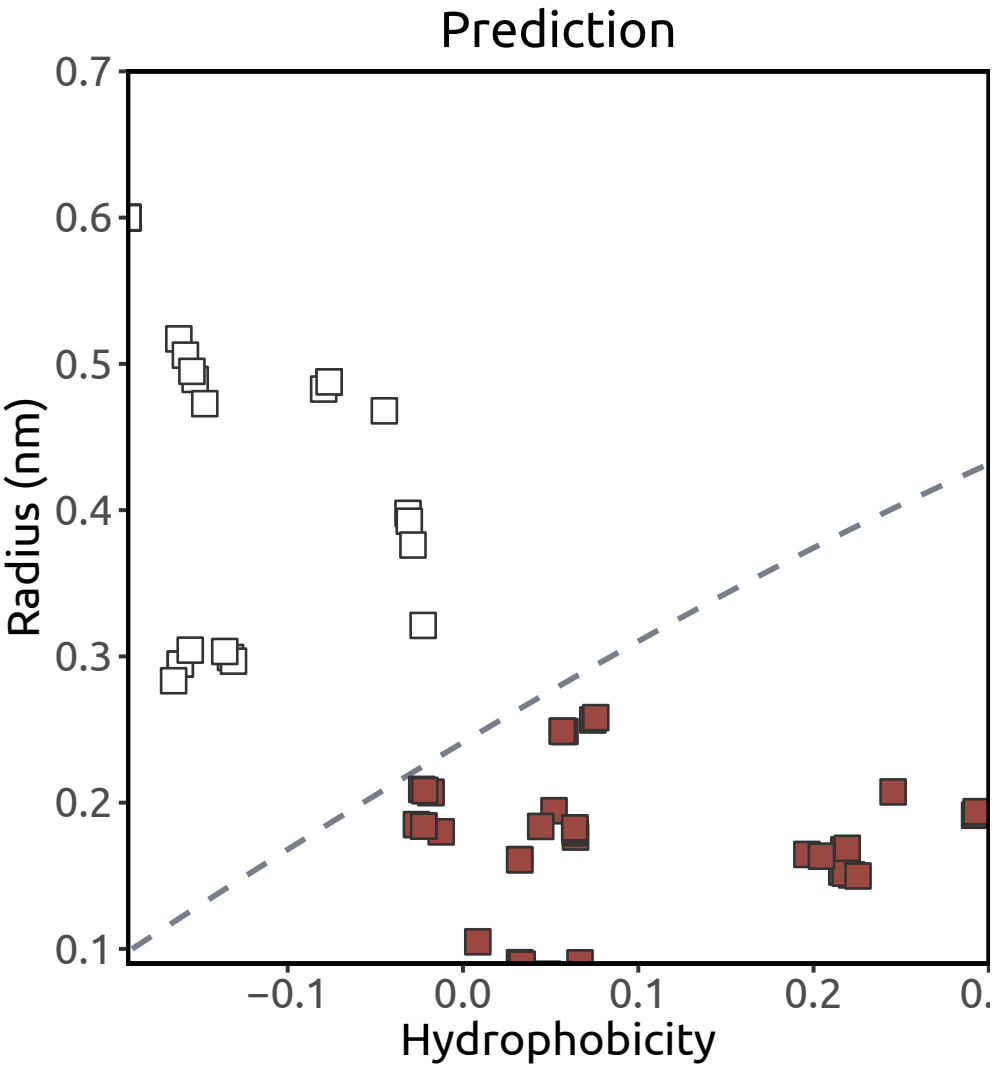
MscL (PDB ID: 2OAR)

Mycobacterium tuberculosis
X–ray (3.5 Å)

Chang et al., 1998







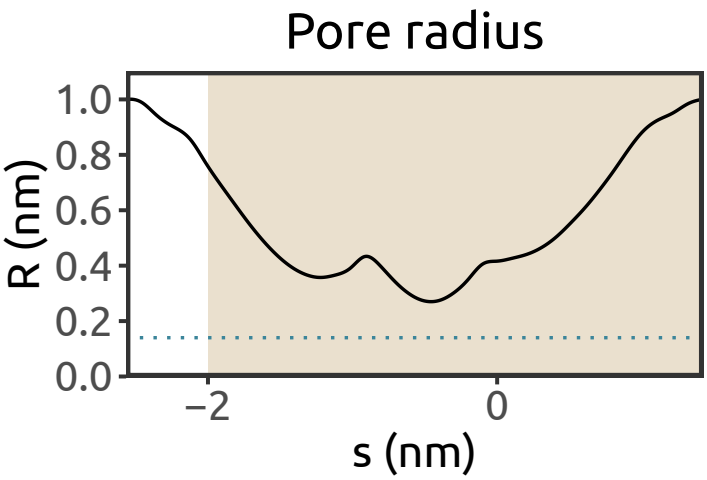
Heuristic score:
4.73 (n = 44)

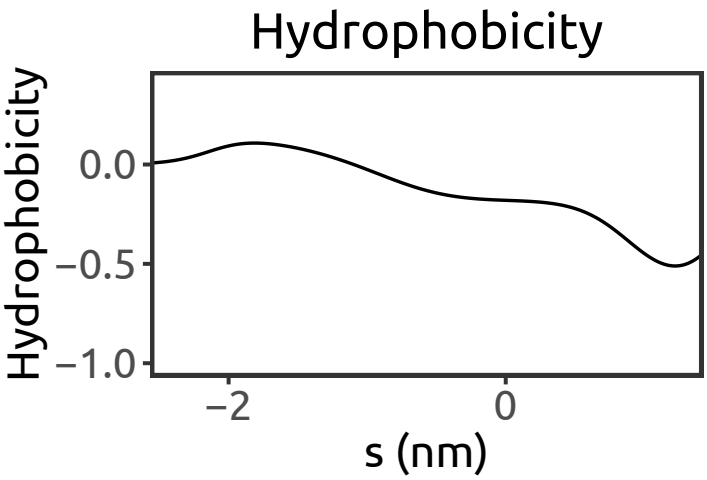
Simulation result:
barrier to water

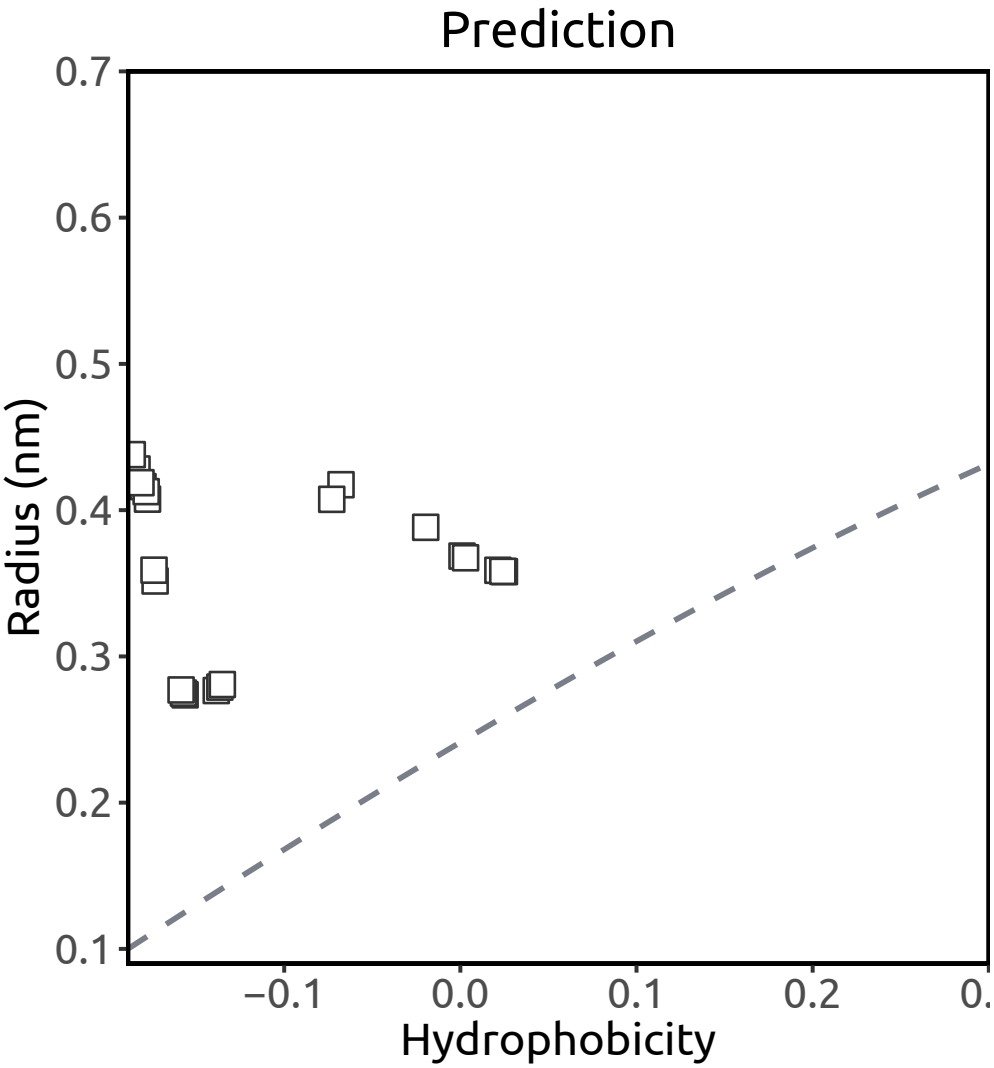
MscL (PDB ID: 3HZQ)

Staphylococcus aureus
X–ray (3.82 Å)

Liu et al., 2009







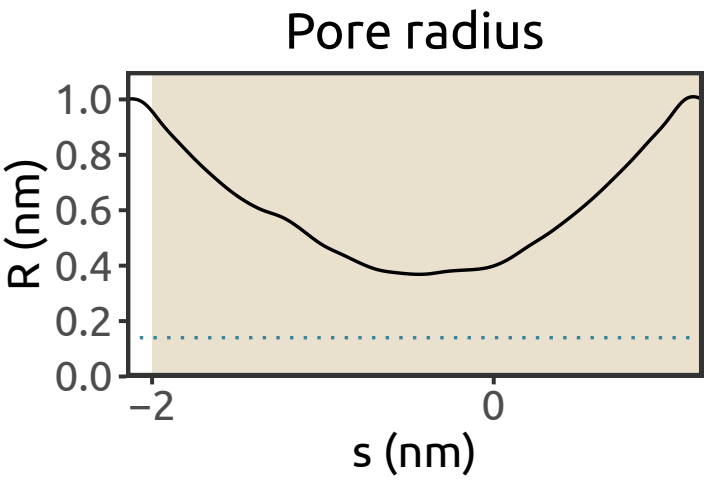
Heuristic score:
0 (n = 0)

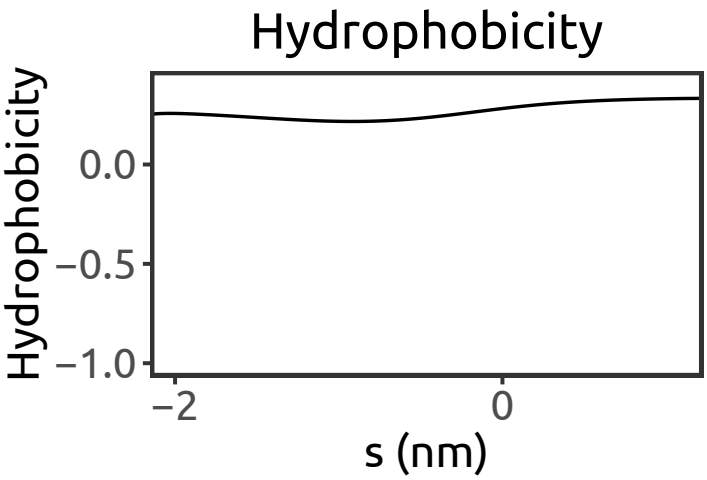
Simulation result:
hydrated channel

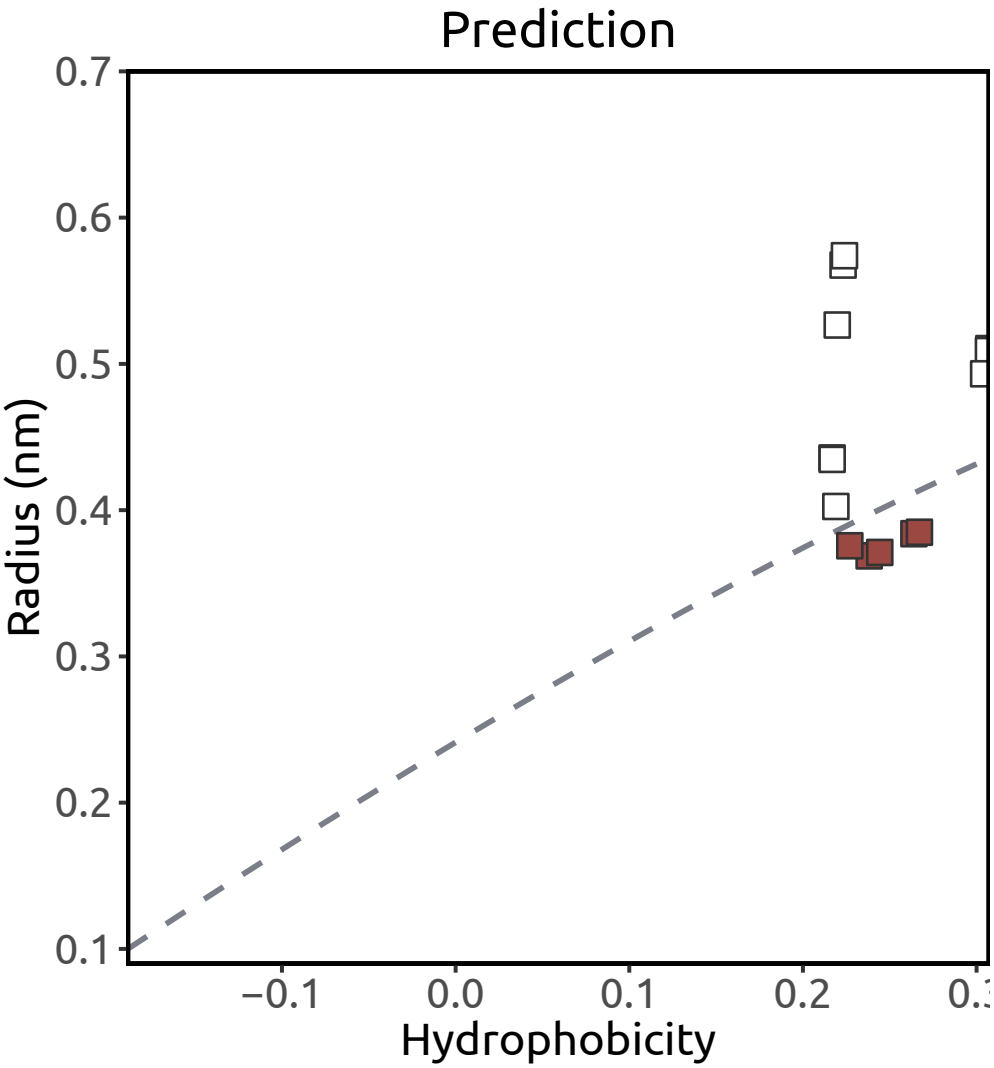
MscL (PDB ID: 4Y7J)

Methanosarcina acetivorans
X−ray (4.1 Å)

Li et al., 2015







Heuristic score:
0.11 (n = 5)

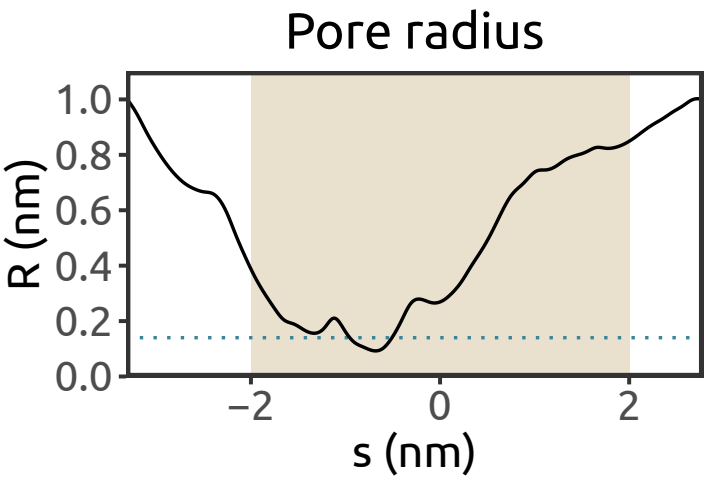
Simulation result:
hydrated channel

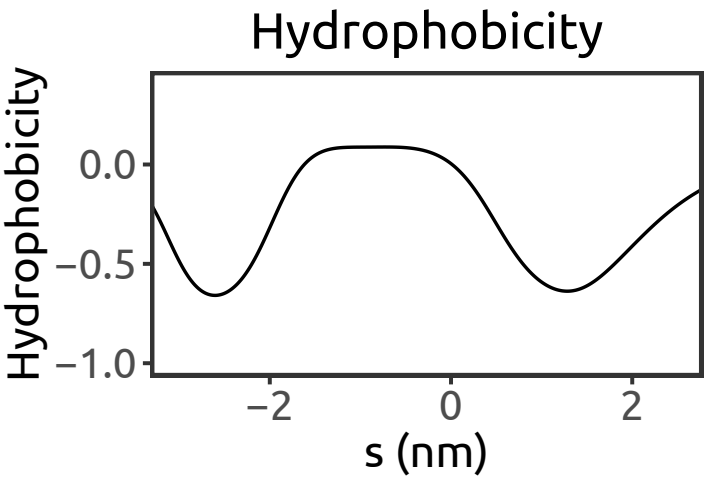
MscL (PDB ID: 4Y7K)

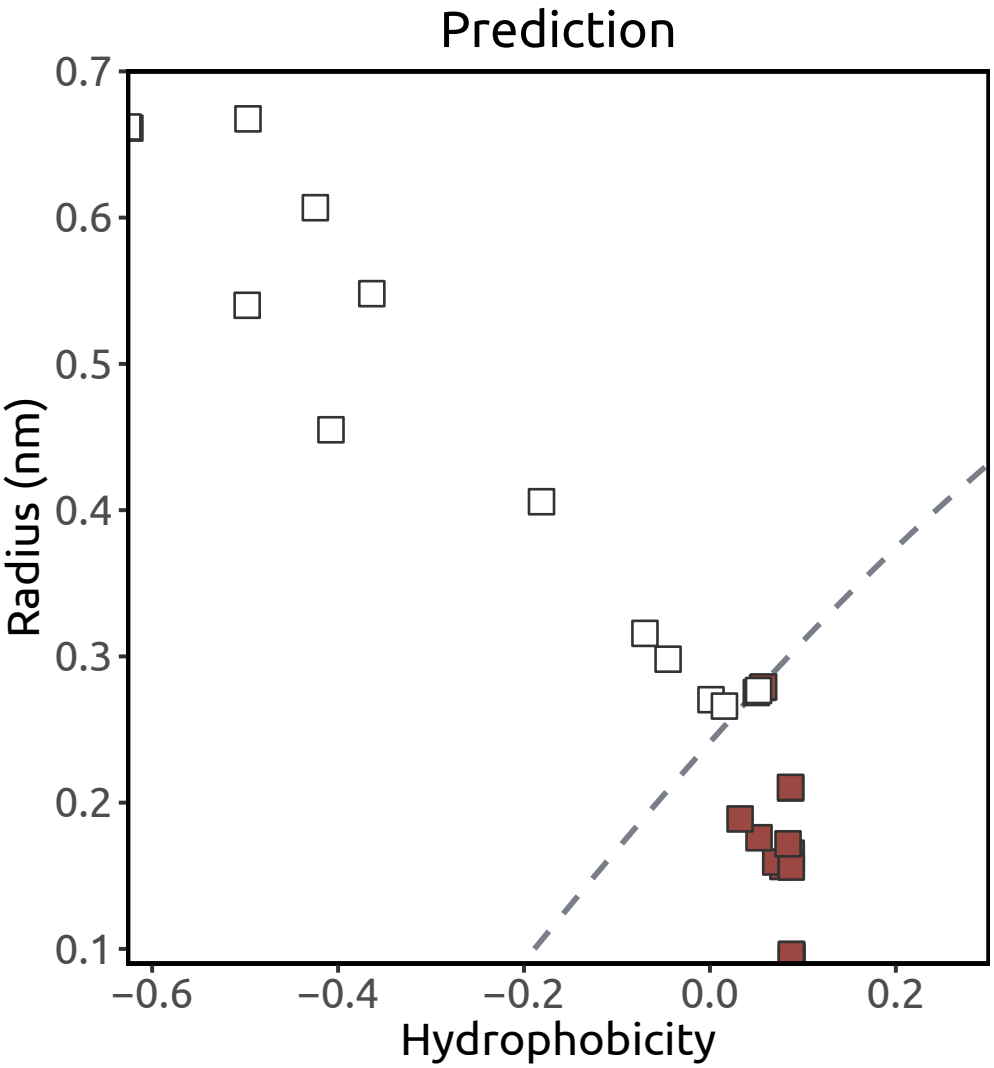
Methanosarcina acetivorans

X–ray (3.5 Å)

Li et al., 2015







Heuristic score:

1.83 (n = 17)

Simulation result:

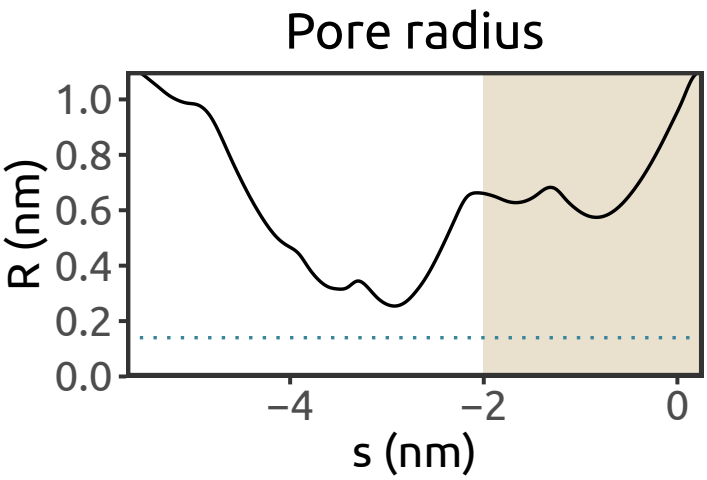
barrier to water

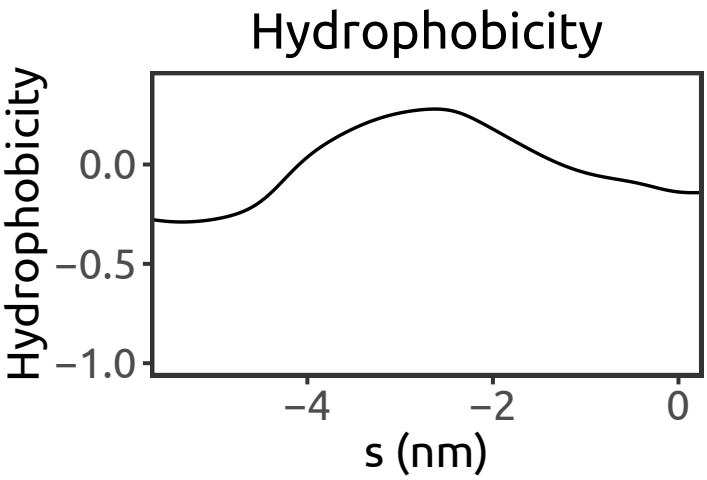
MscS (PDB ID: 2OAU)

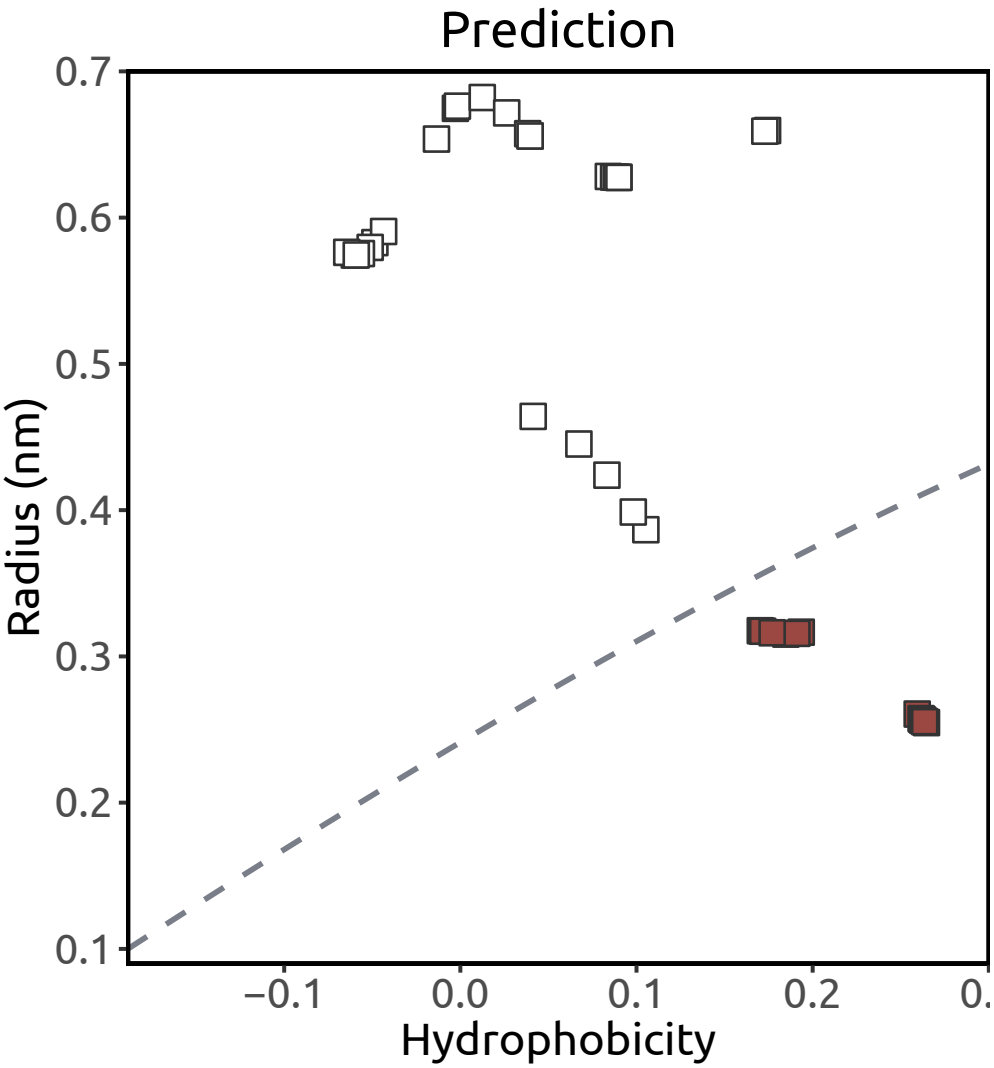
Escherichia coli

X–ray (3.7 Å)

Bass et al., 2002







Heuristic score:

1.03 (n = 12)

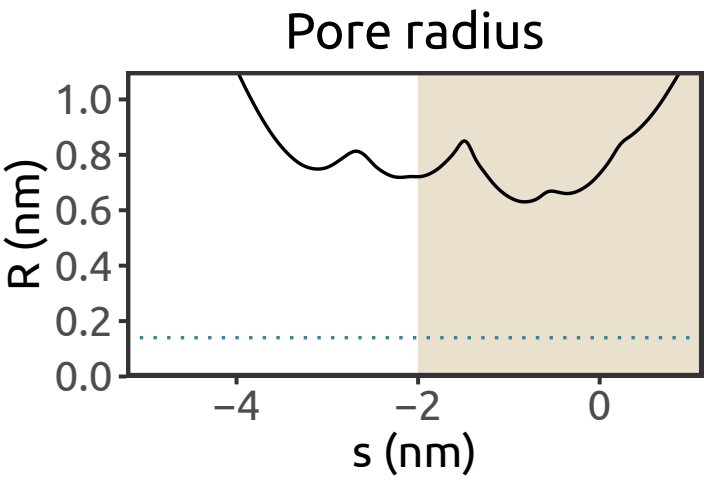
Simulation result:

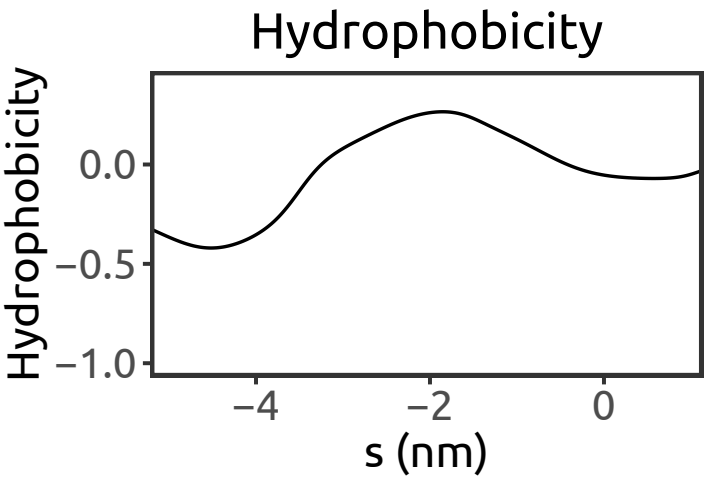
barrier to water

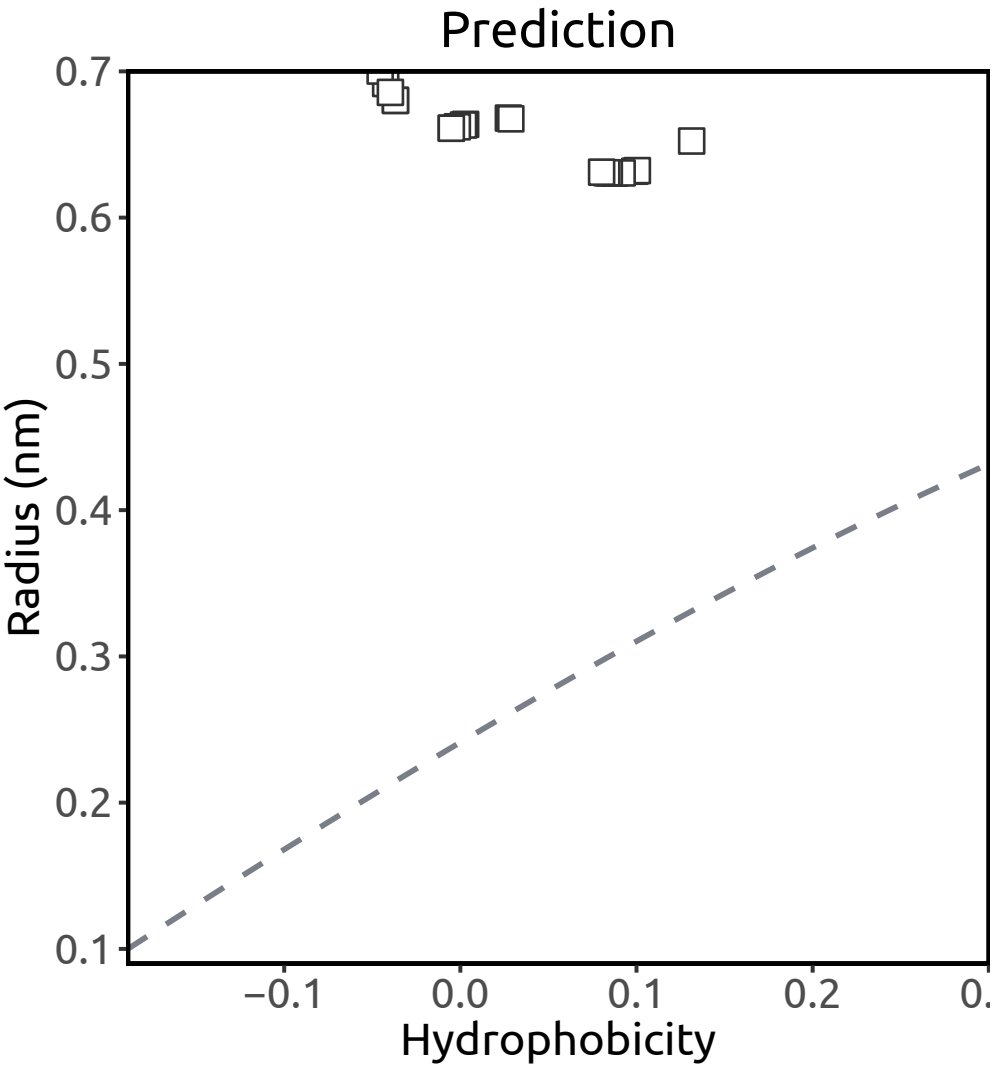
MscS (PDB ID: 2VV5)

Escherichia coli
X–ray (3.45 Å)

Wang et al., 2008







Heuristic score:
0 (n = 0)

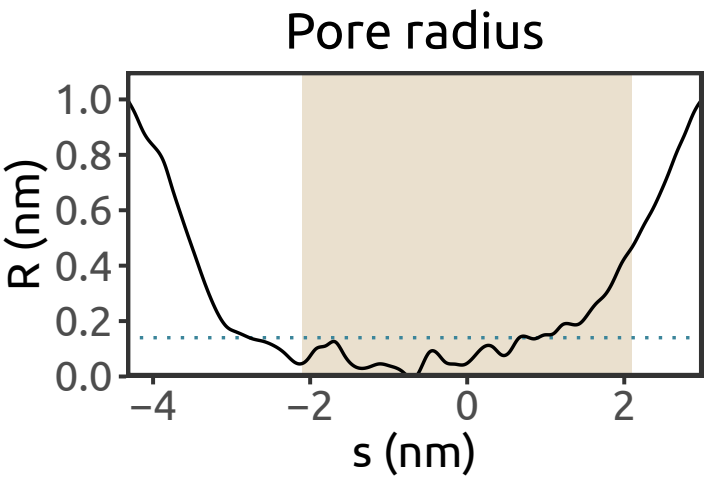
Simulation result:
hydrated channel

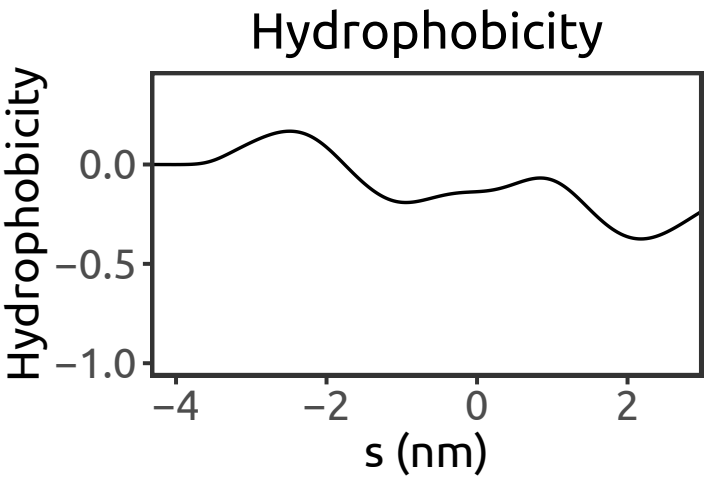
NNT (PDB ID: 5UNI)

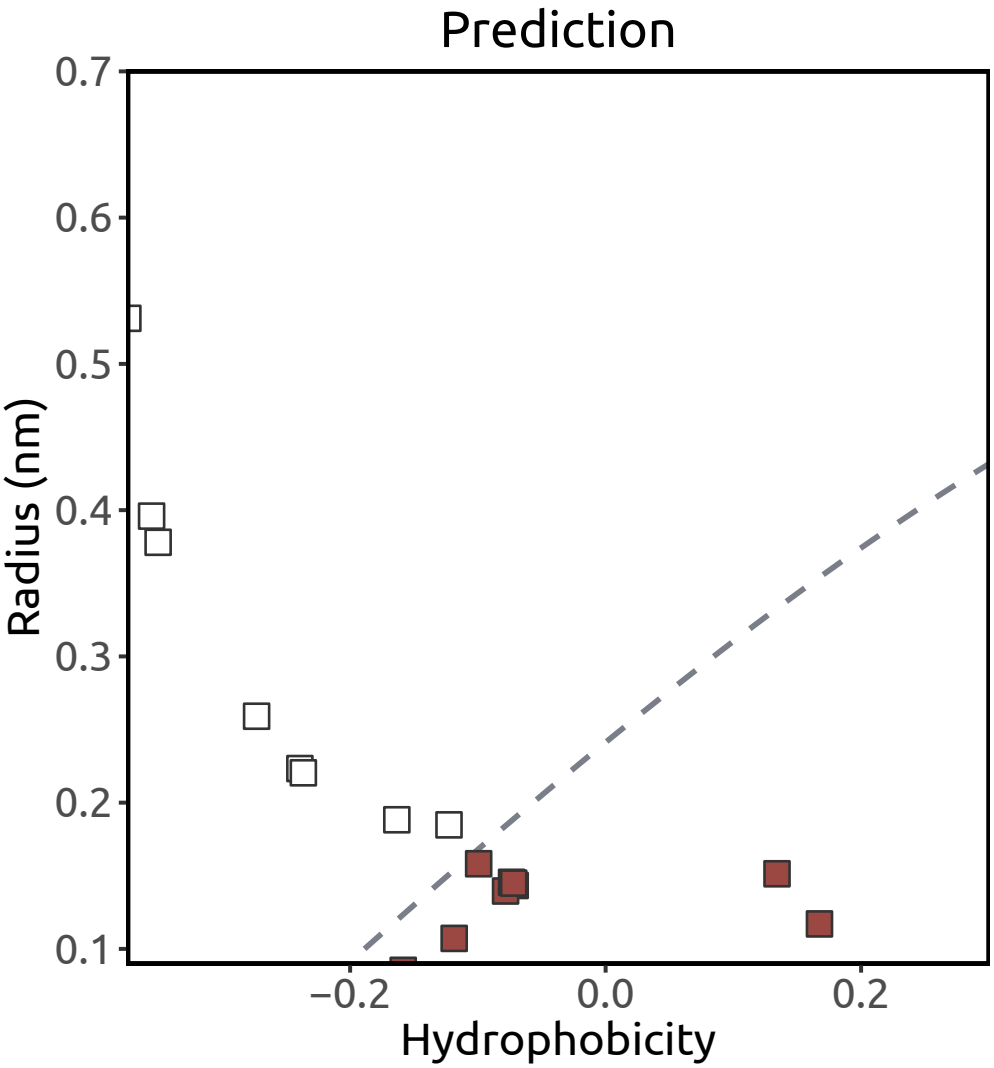
Thermus thermophilus

X–ray (2.2 Å)

Padayatti et al., 2017







Heuristic score:

1.72 (n = 20)

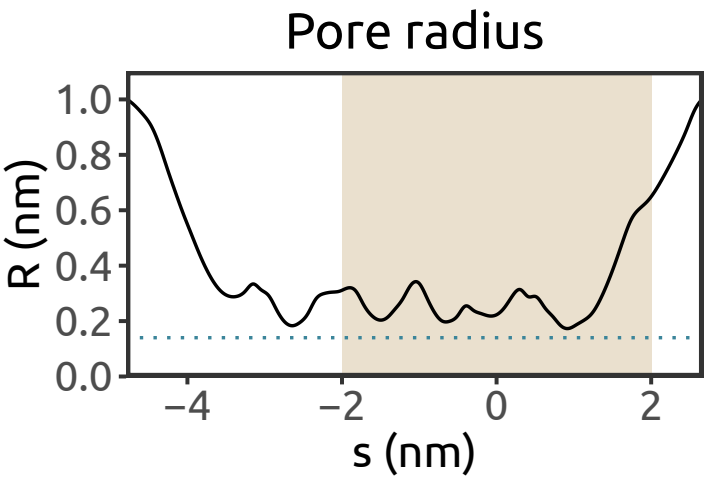
Simulation result:

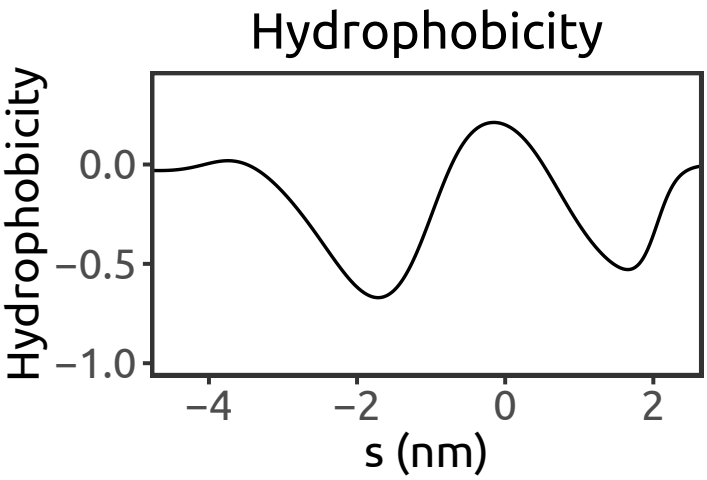
barrier to water

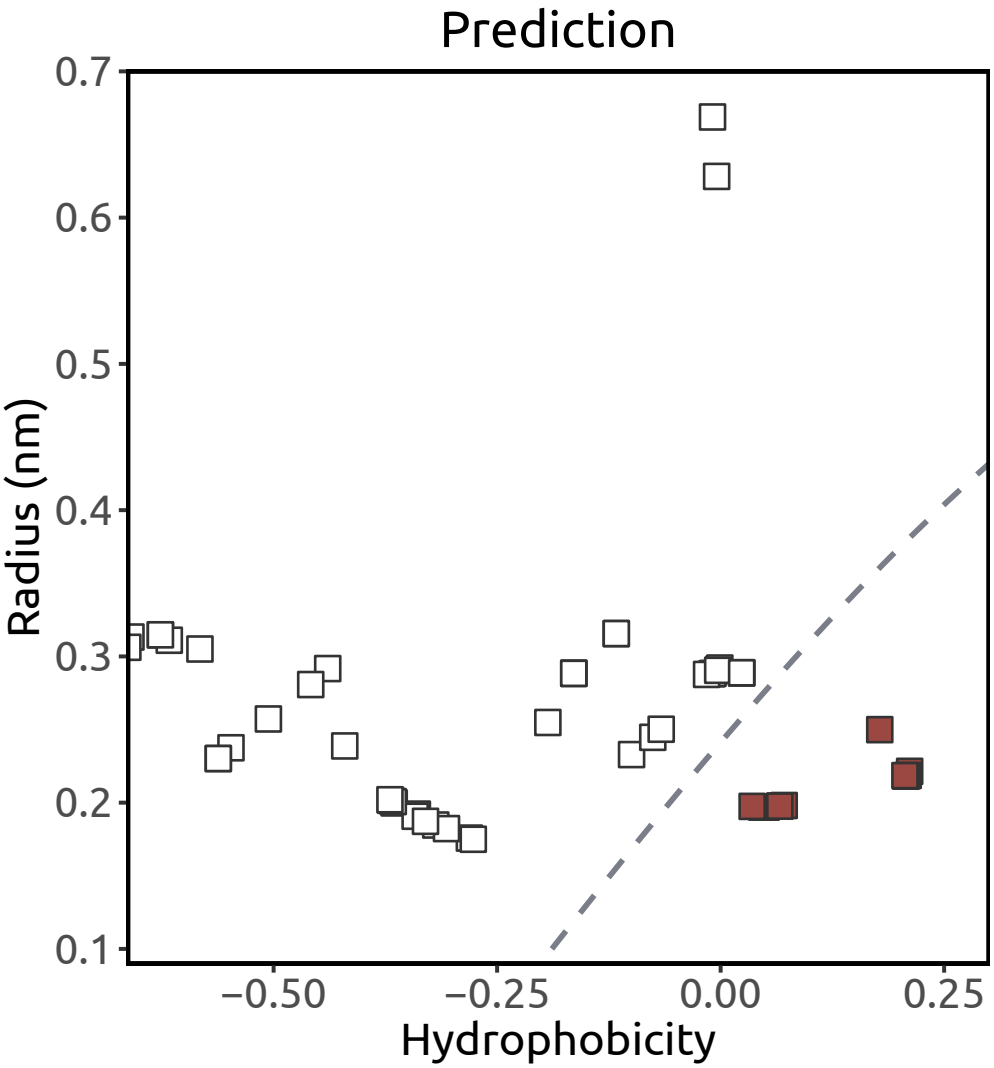
Orai (PDB ID: 4HKR)

Drosophila melanogaster
X–ray (3.35 Å)

Hou et al., 2012







Heuristic score:
1.18 (n = 12)

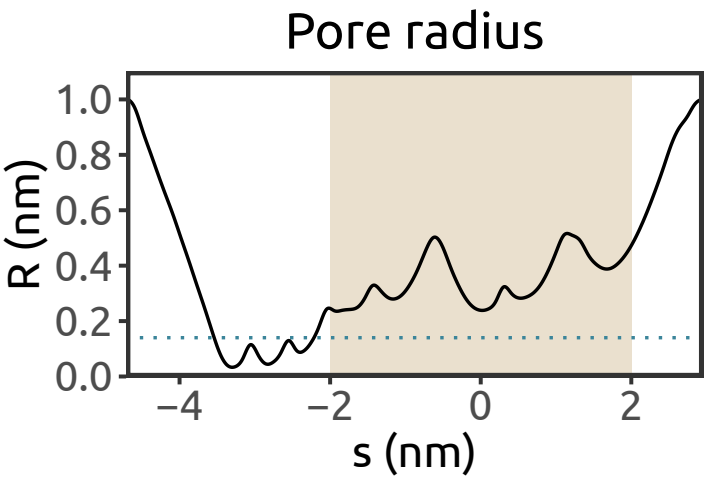
Simulation result:
barrier to water

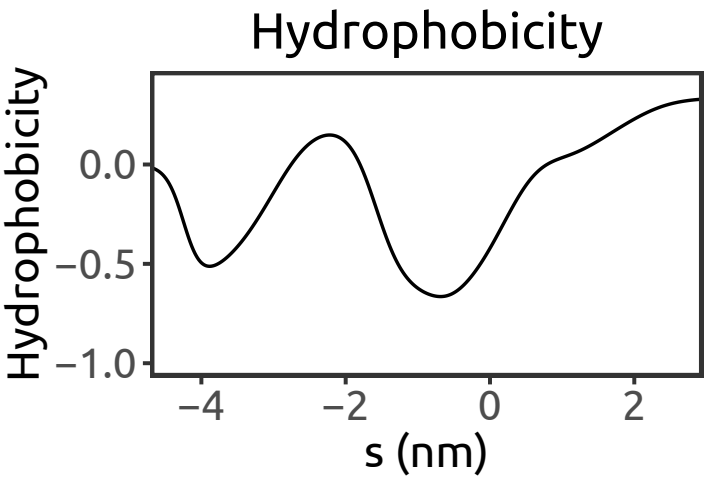
Piezo1 (PDB ID: 6BPZ)

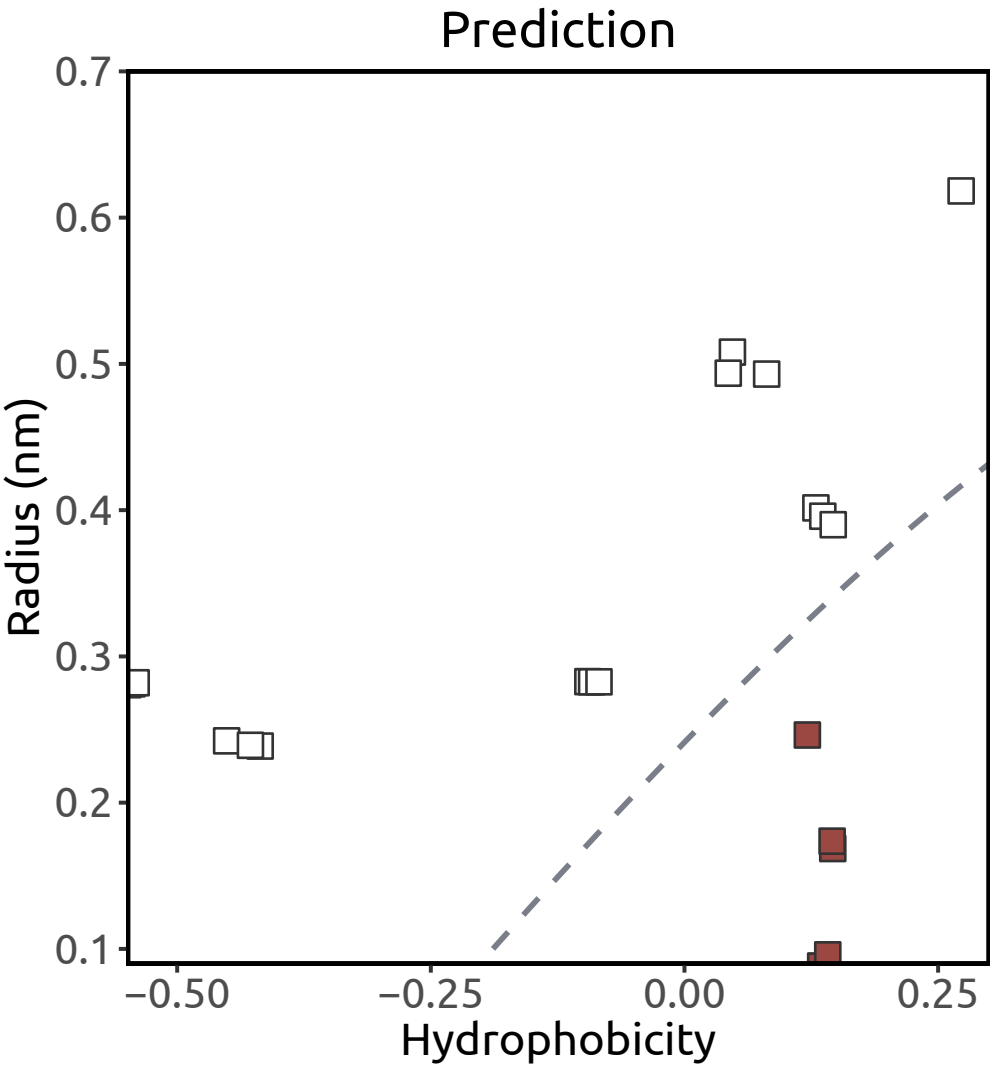
Mus musculus

cryo–EM (3.8 Å)

Saotome et al., 2017







Heuristic score:

1.33 (n = 9)

Simulation result:

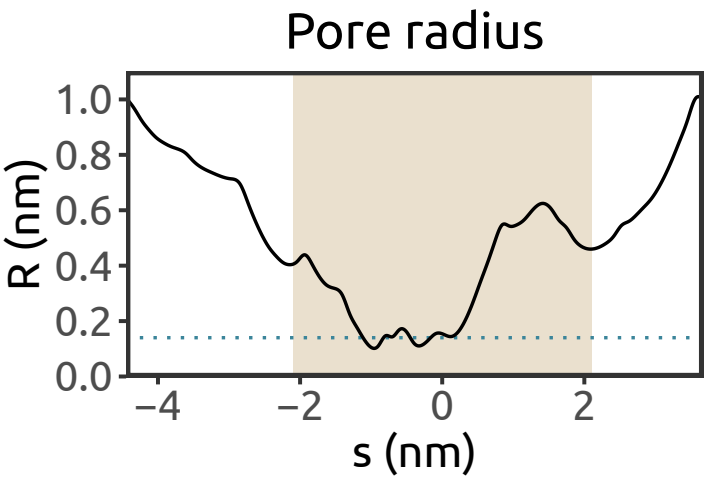
barrier to water

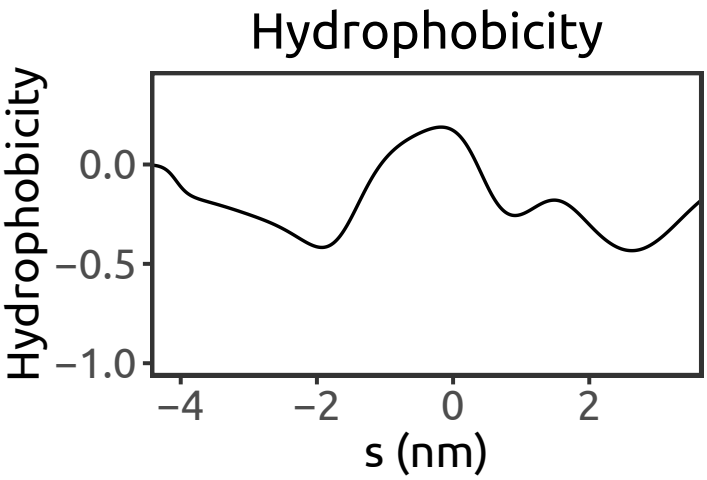
TMEM175 (PDB ID: 5VRE)

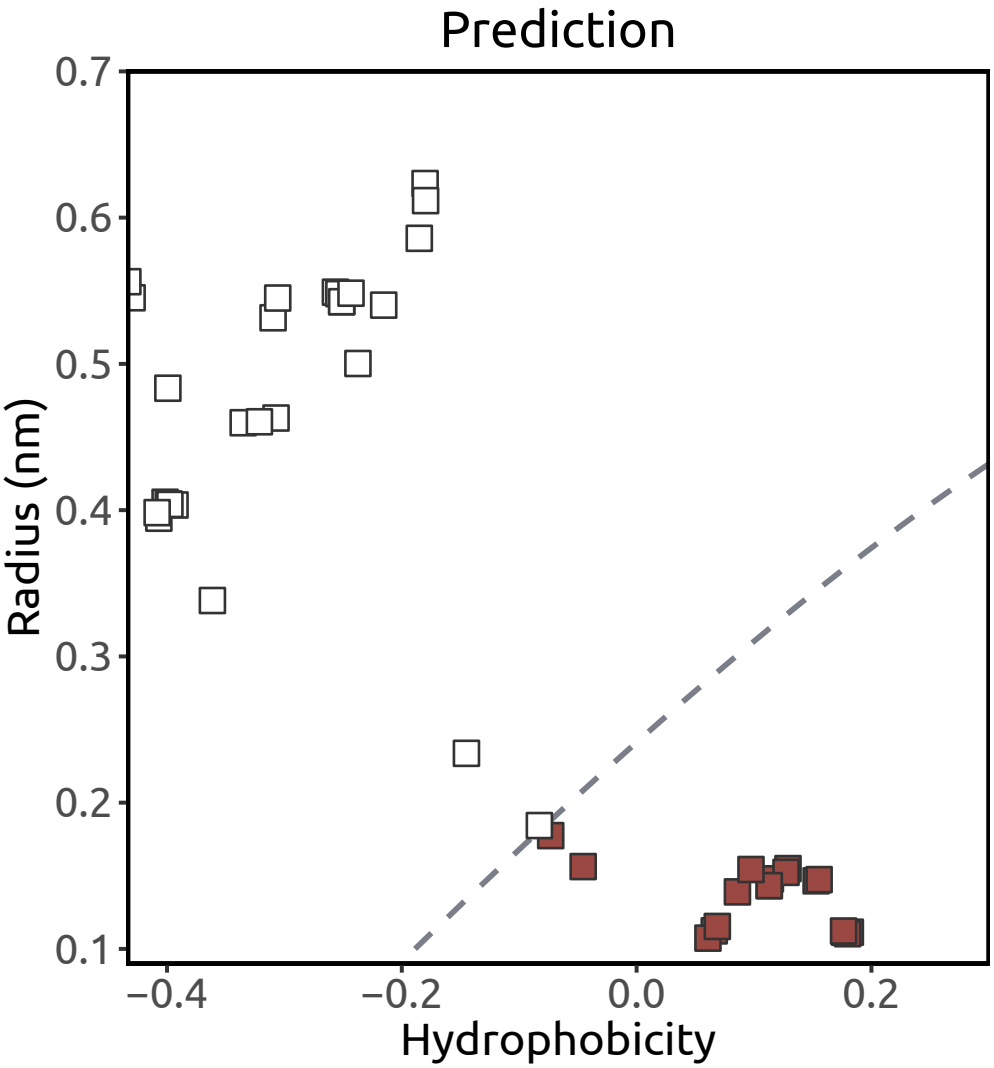
Chamaesiphon minutus

X–ray (3.30 Å)

Lee et al., 2017







Heuristic score:

2.63 (n = 18)

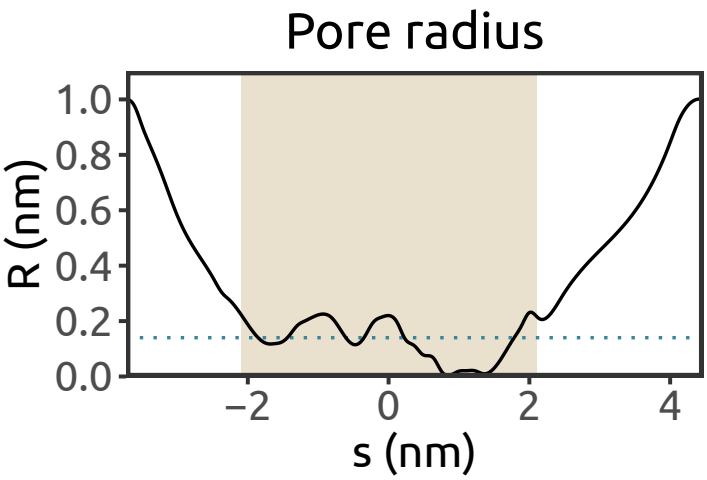
Simulation result:

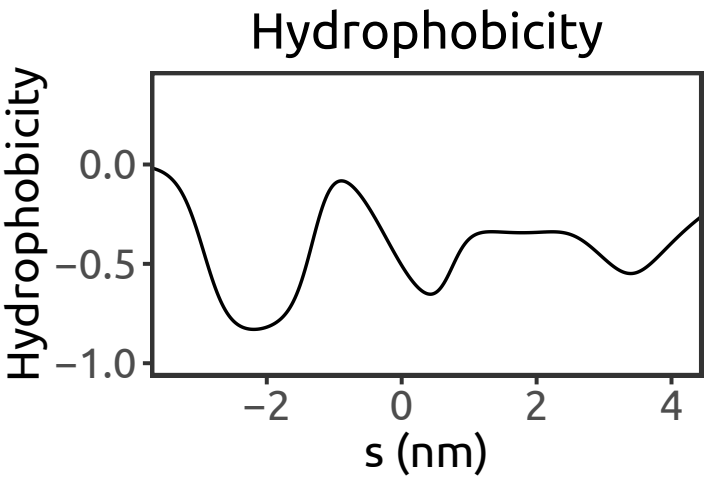
barrier to water

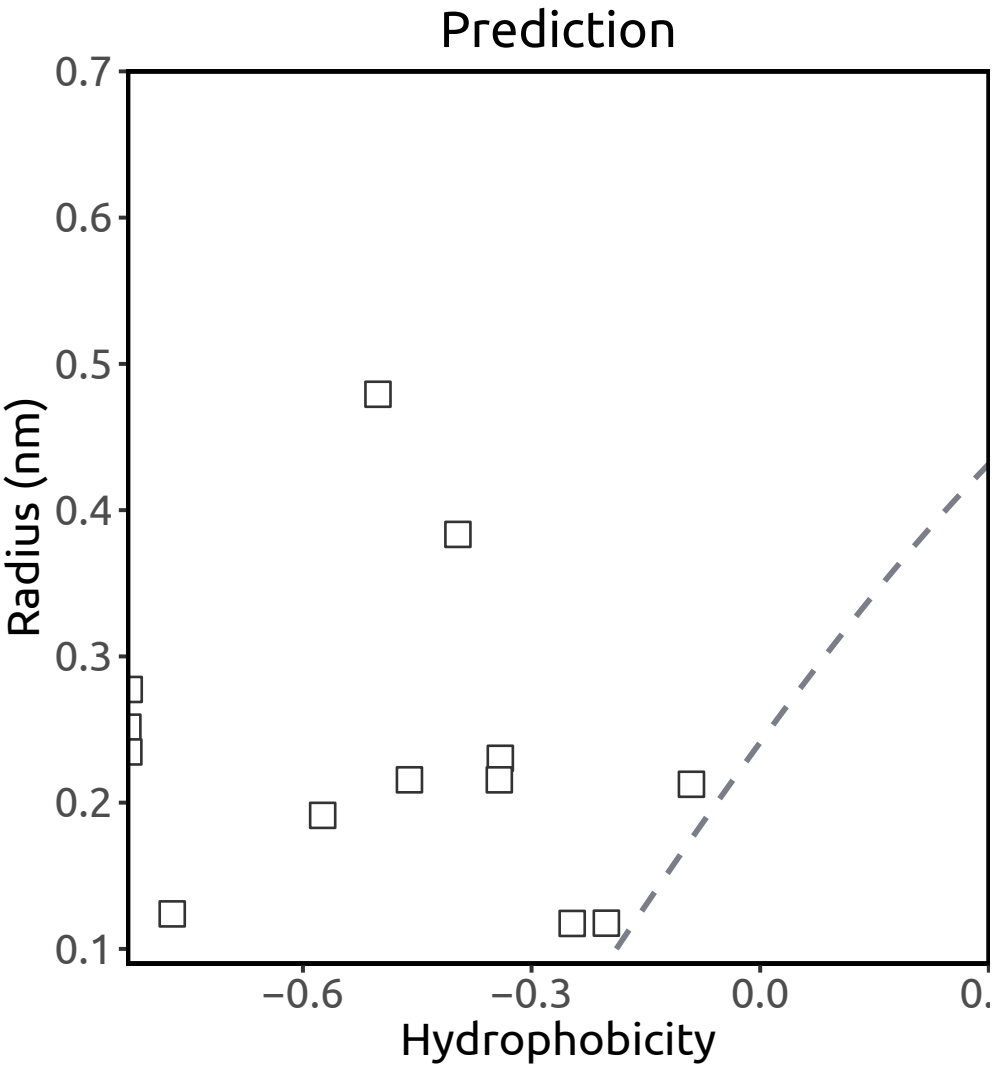
TRIC (PDB ID: 5EGI)

Caenorhabditis elegans
X–ray (3.3 Å)

Yang et al., 2016







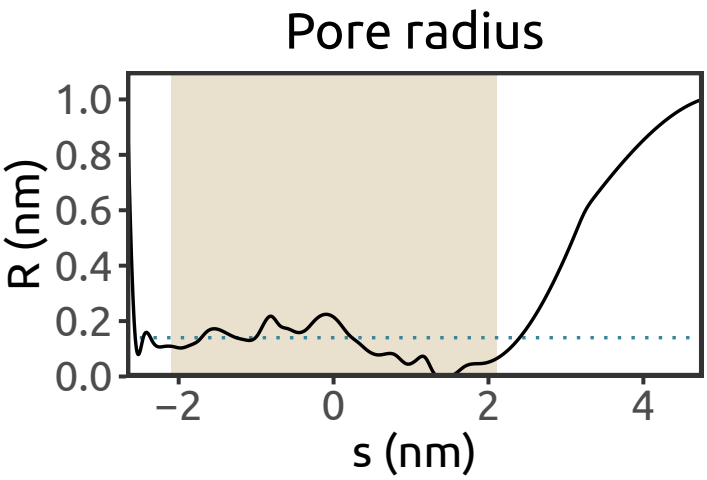
Heuristic score:
0 (n = 0)

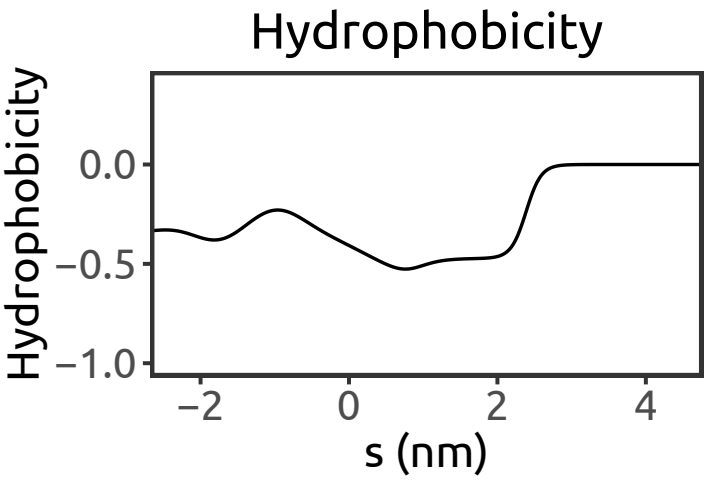
Simulation result:
barrier to water

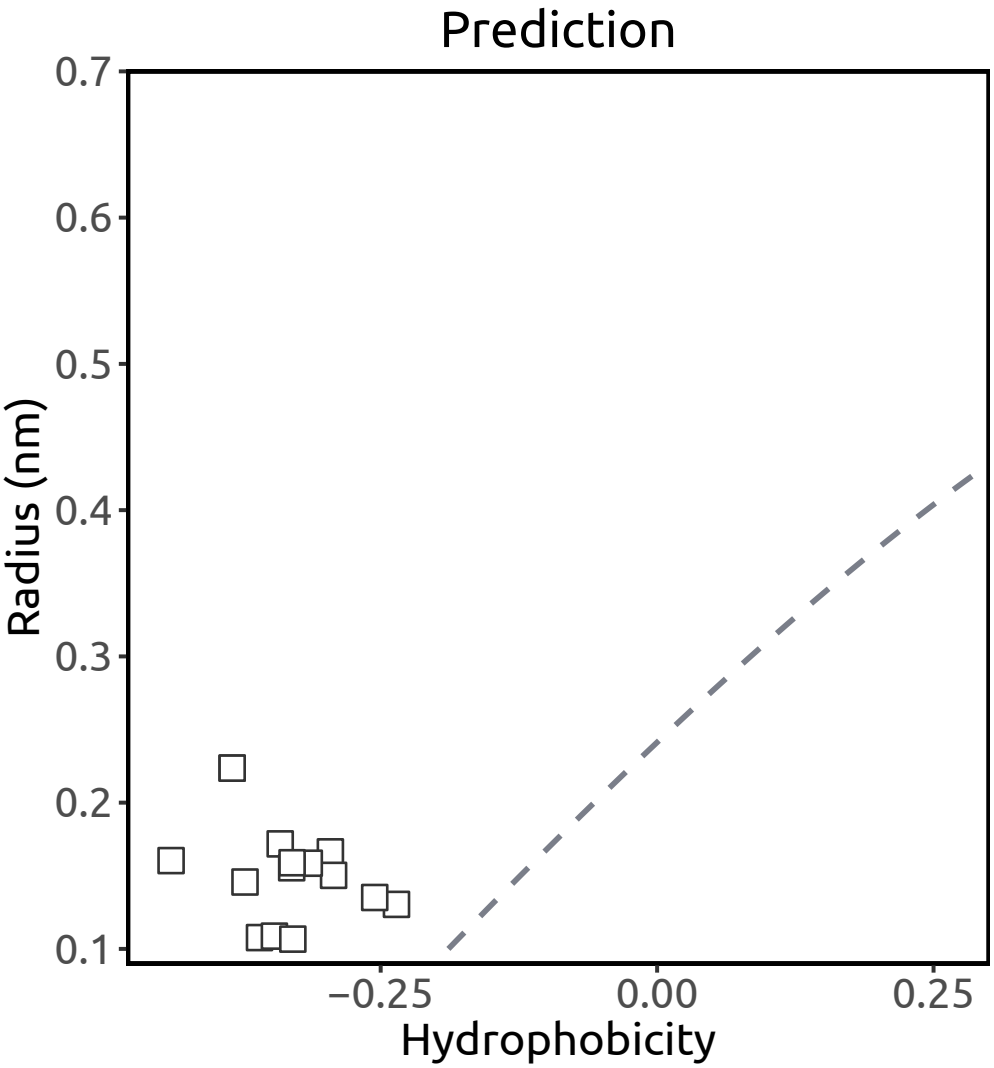
TRIC (PDB ID: 5EIK)

Caenorhabditis elegans
X–ray (2.3 Å)

Yang et al., 2016







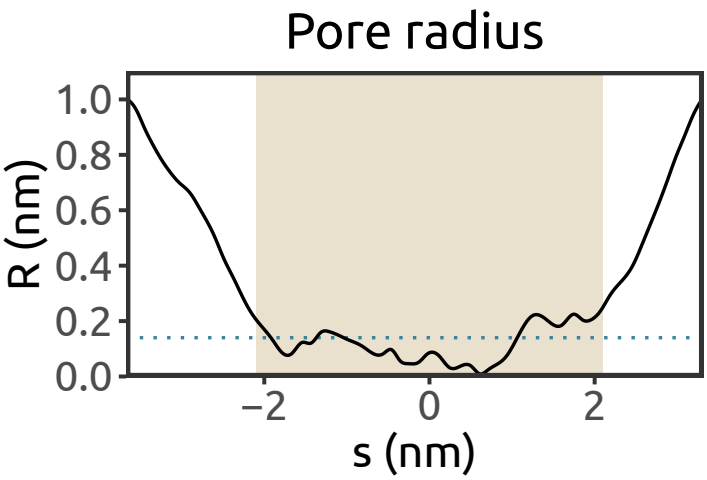
Heuristic score:
0 (n = 0)

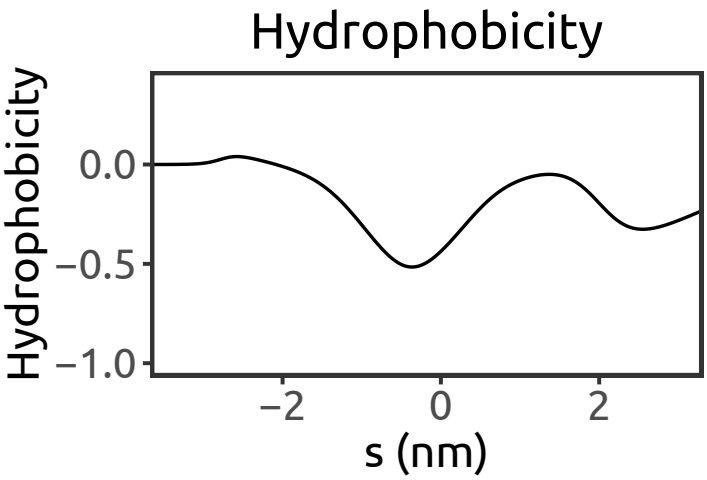
Simulation result:
barrier to water

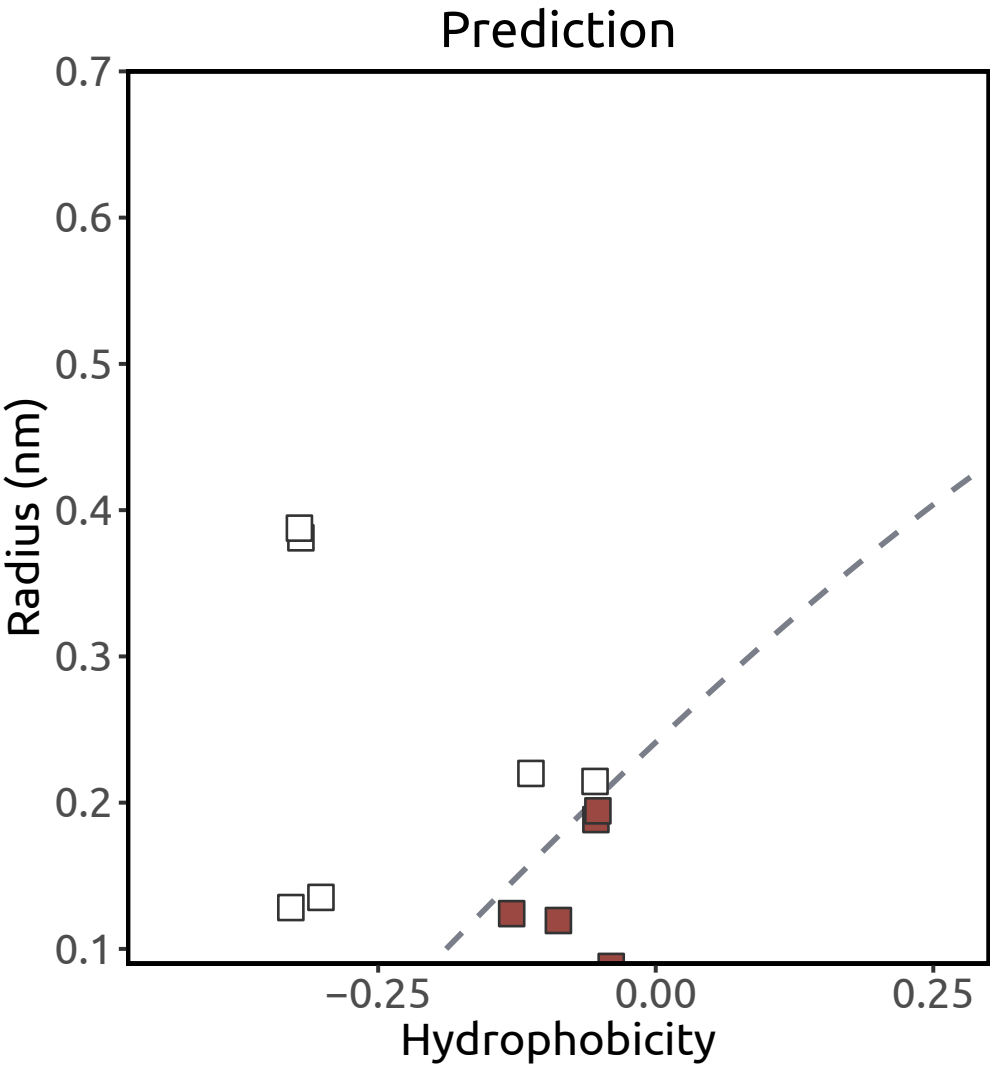
TRIC (PDB ID: 5WUC)

Sulfolobus acidocaldarius
X–ray (1.6 Å)

Su et al., 2017







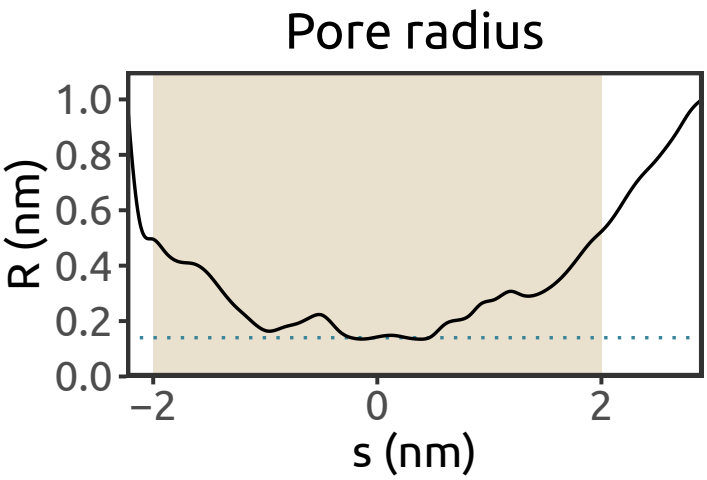
Heuristic score:
0.27 (n = 6)

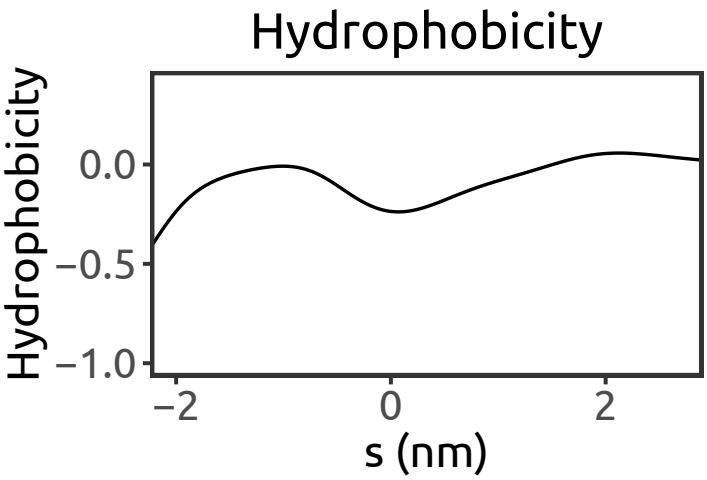
Simulation result:
barrier to water

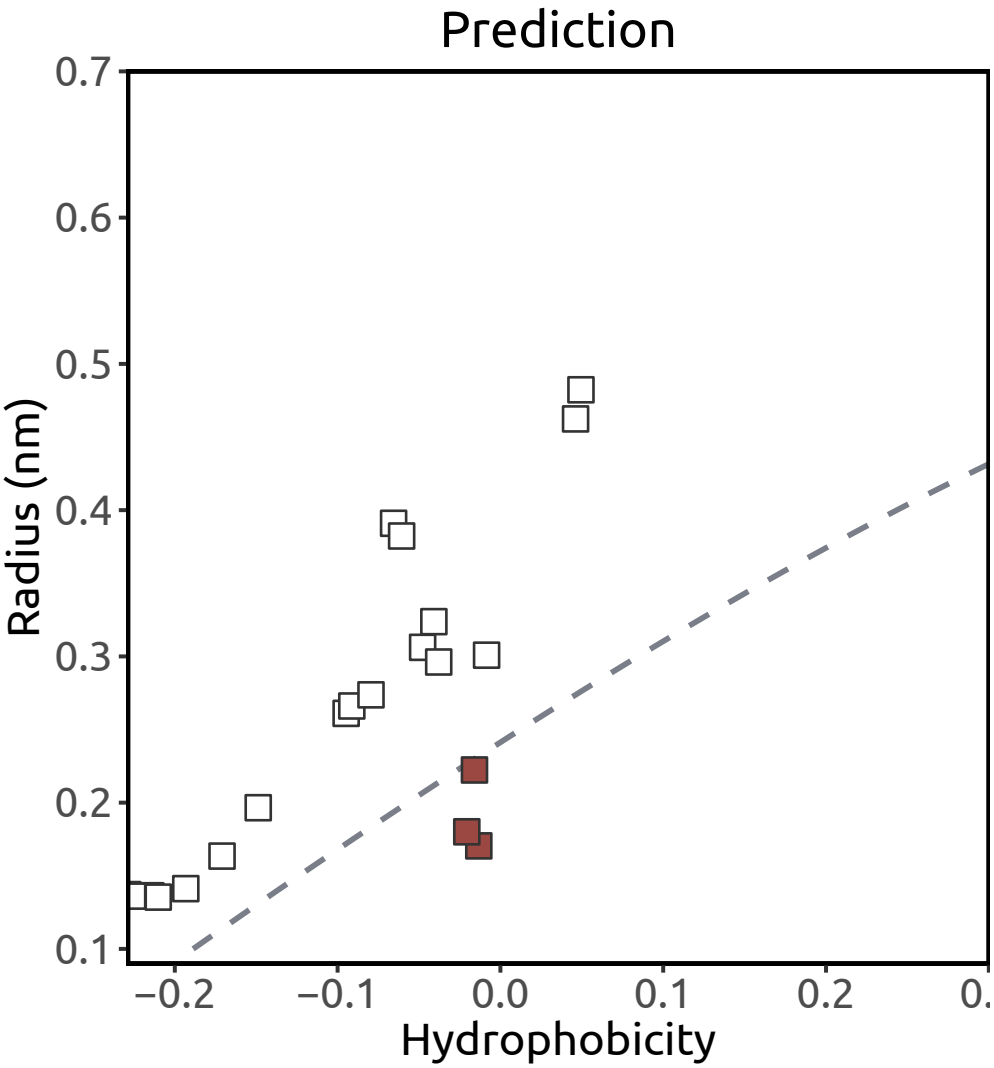
TRIC (PDB ID: 5WUE)

Sulfolobus acidocaldarius
X–ray (2.4 Å)

Su et al., 2017







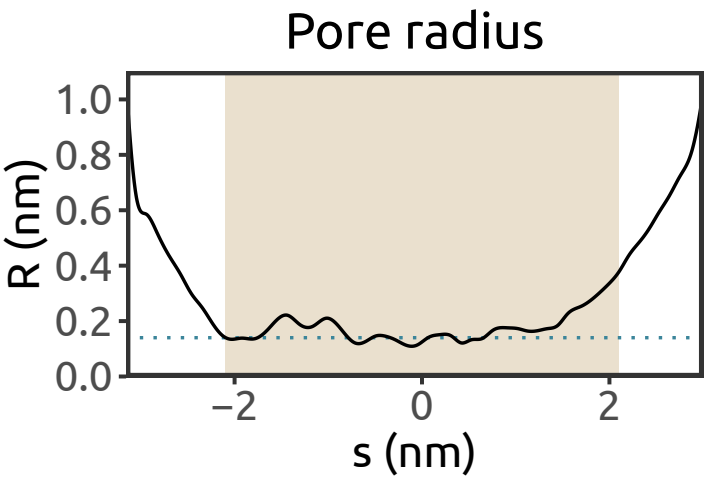
Heuristic score:
0.09 (n = 3)

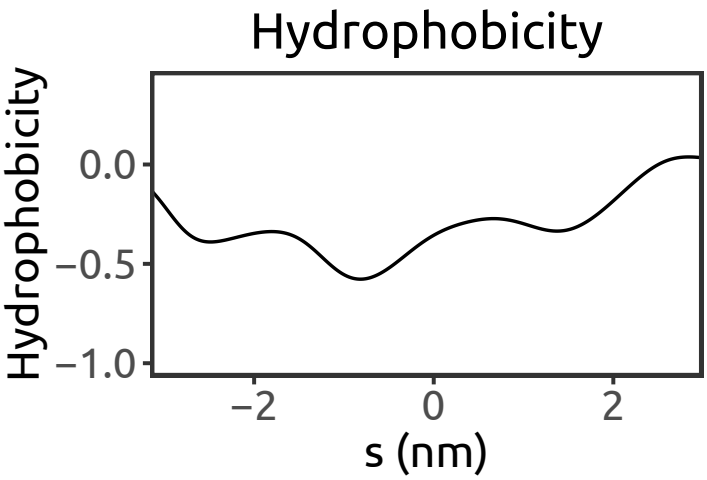
Simulation result:
hydrated channel

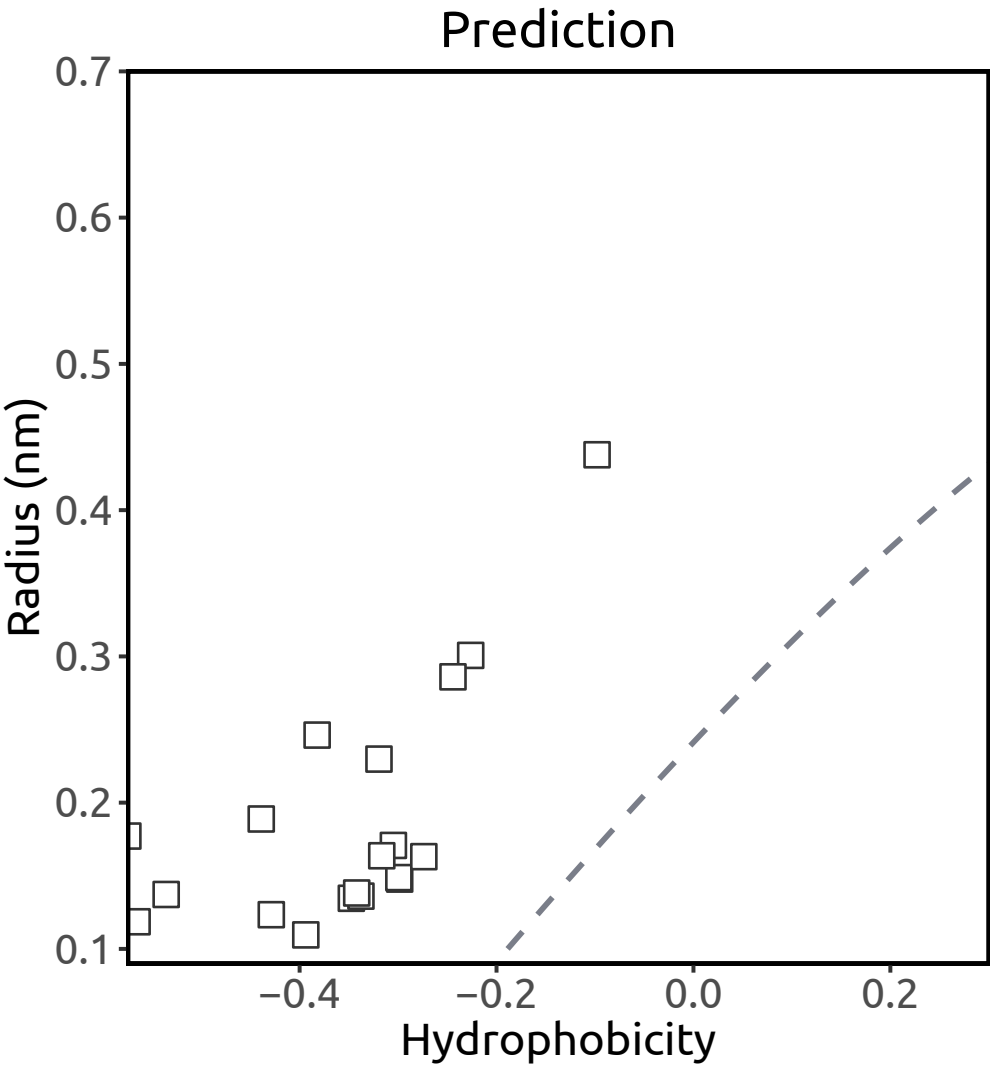
TRIC (PDB ID: 5WUF)

Colwellia psychrerythraea
X–ray (2.40 Å)

Su et al., 2017







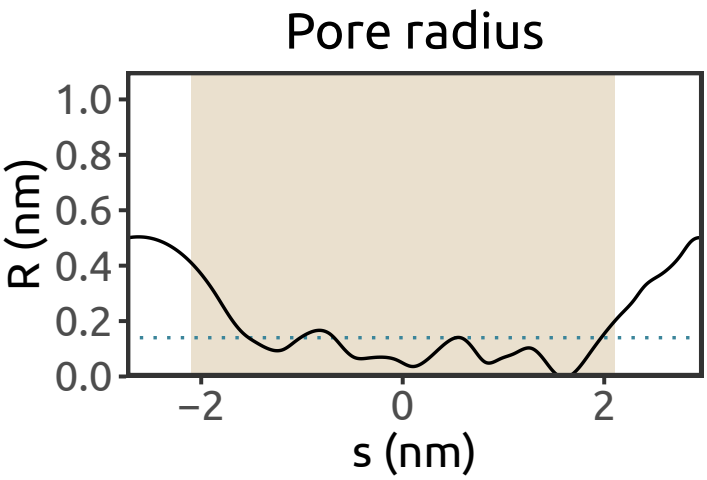
Heuristic score:
0 (n = 0)

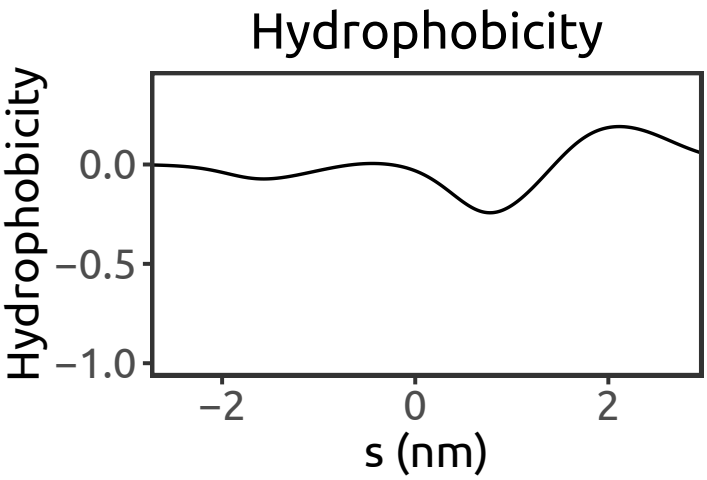
Simulation result:
hydrated channel

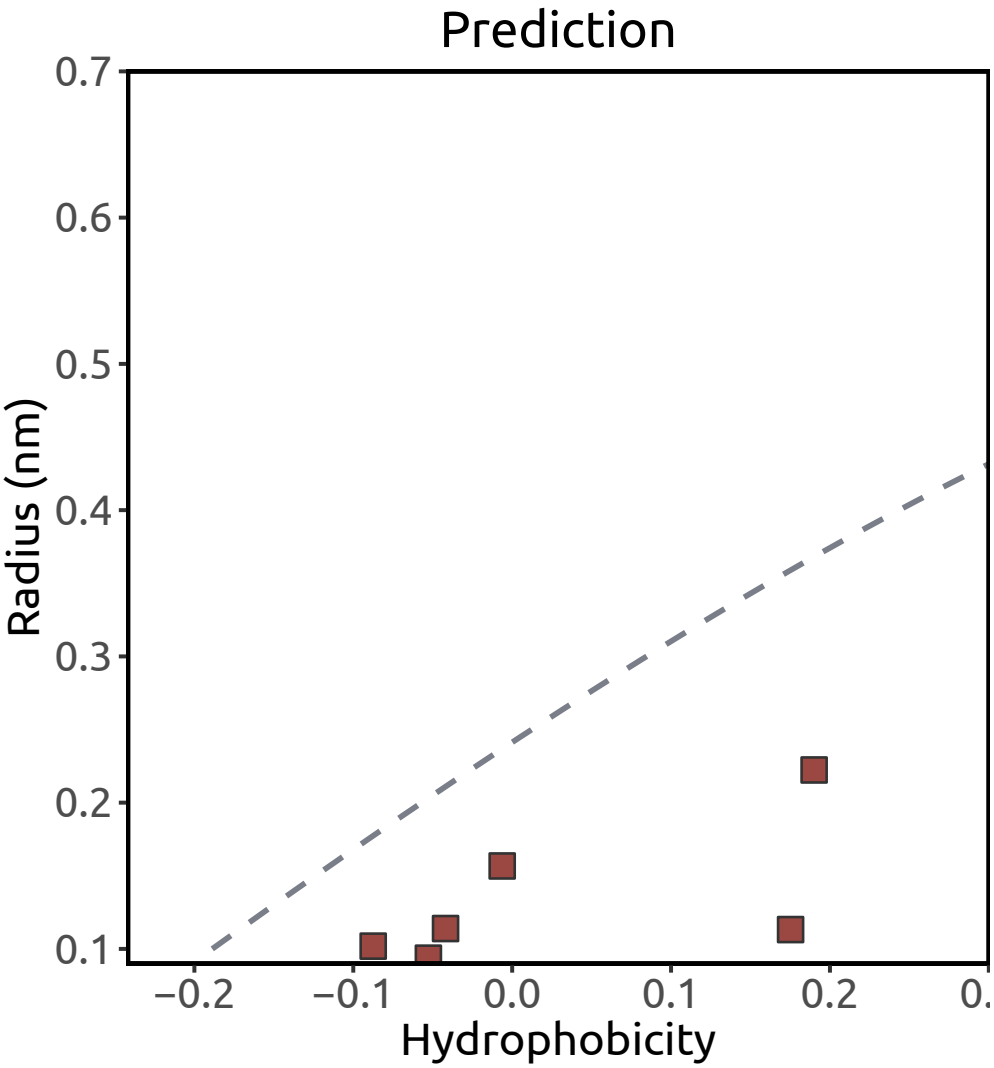
YetJ (PDB ID: 4PGR)

Bacillus subtilis
X–ray (1.95 Å)

Chang et al., 2014







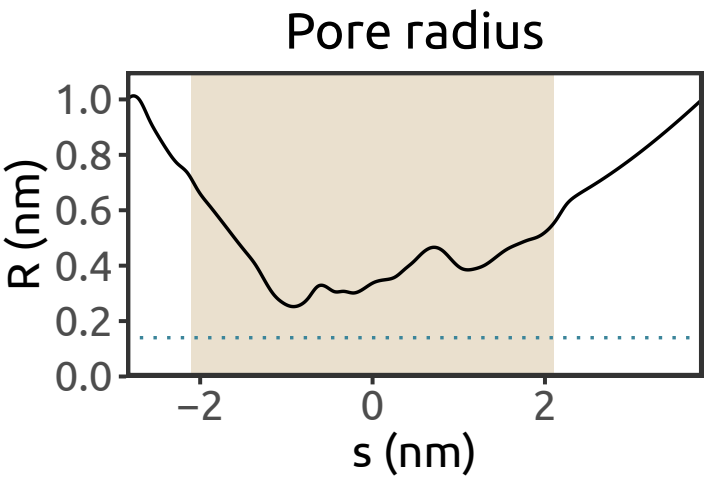
Heuristic score:
1.18 (n = 11)

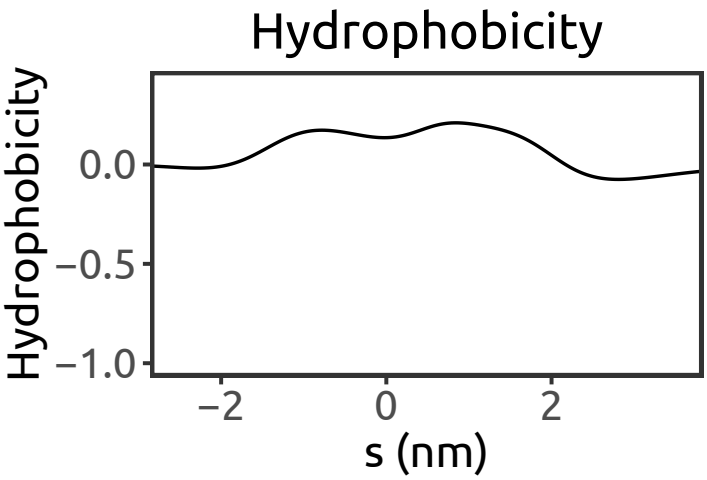
Simulation result:
barrier to water

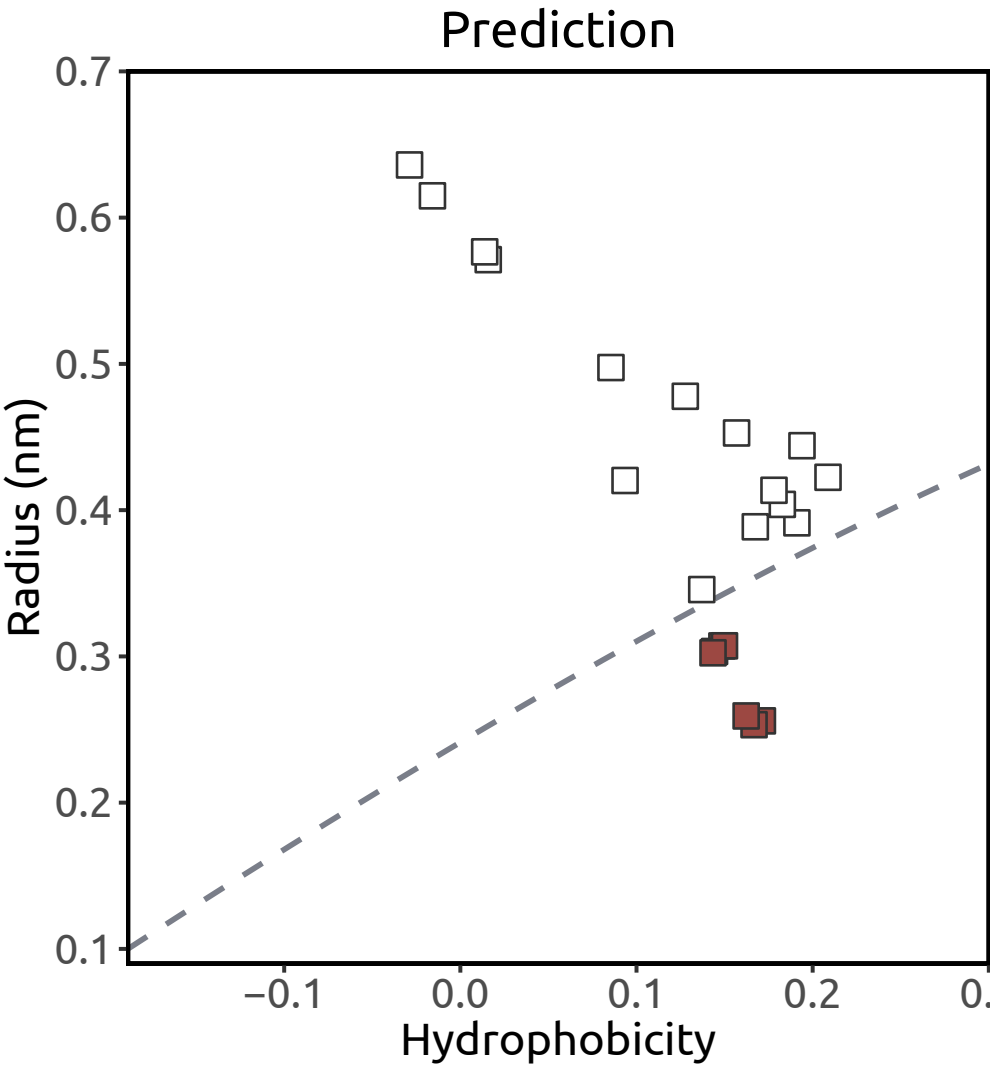
YetJ (PDB ID: 4PGS)

Bacillus subtilis
X–ray (2.5 Å)

Chang et al., 2014







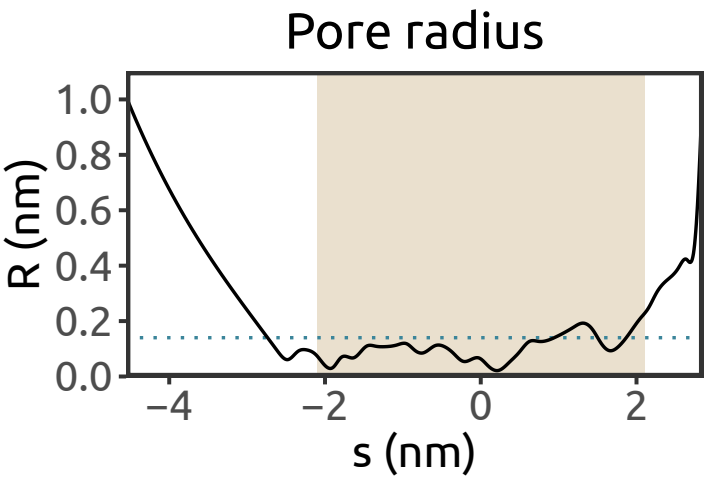
Heuristic score:
0.37 (n = 7)

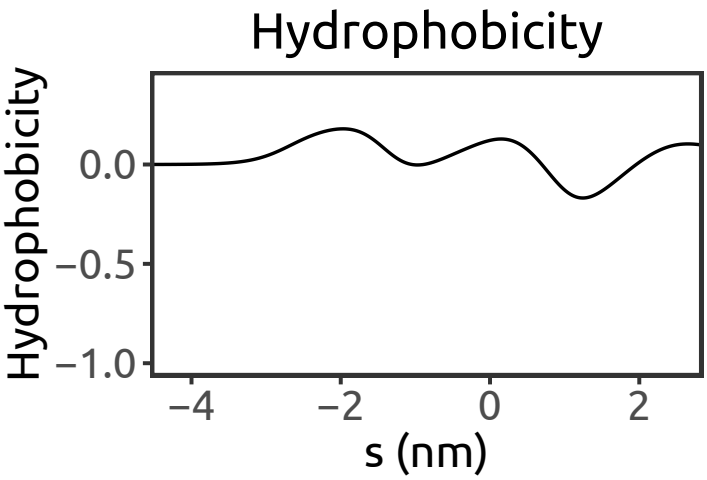
Simulation result:
barrier to water

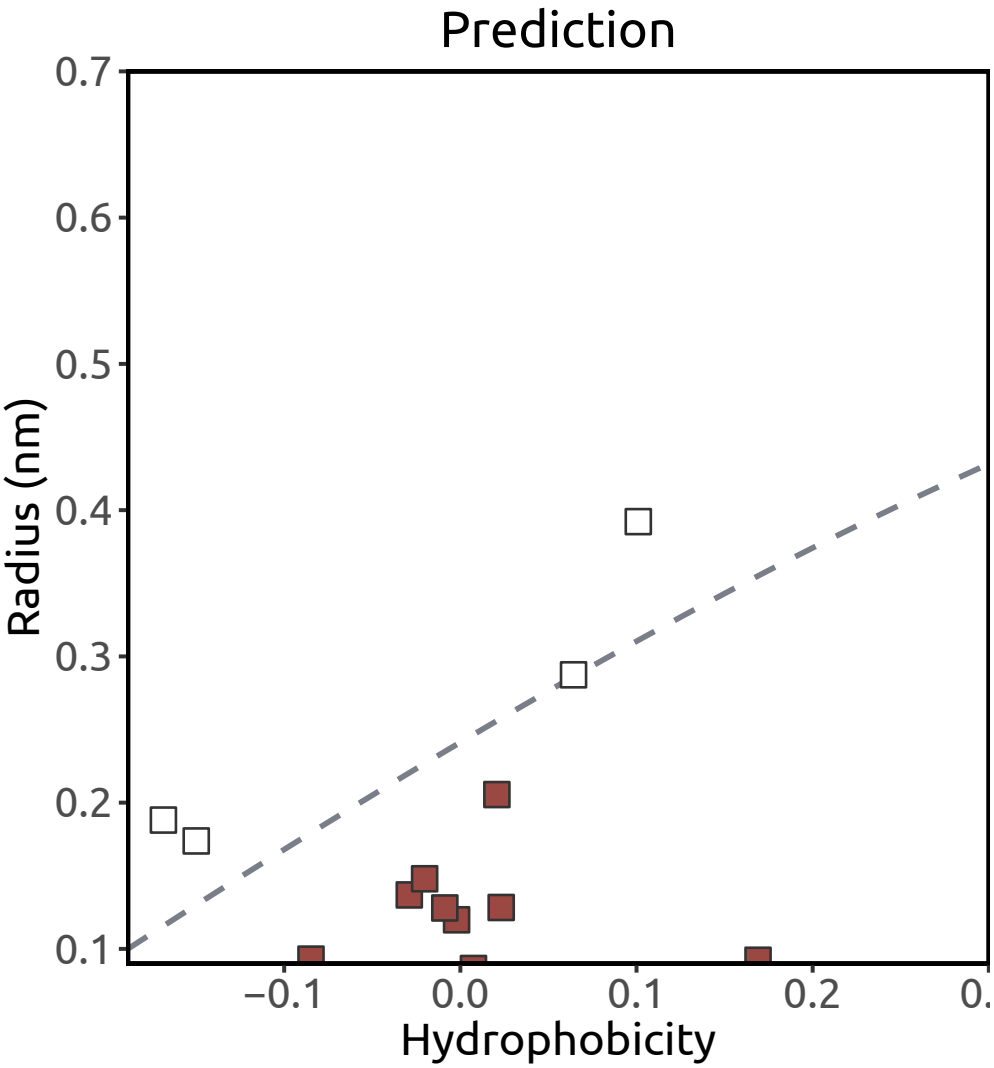
YetJ (PDB ID: 4PGU)

Bacillus subtilis
X–ray (3.40 Å)

Chang et al., 2014







Heuristic score:
2 (n = 14)

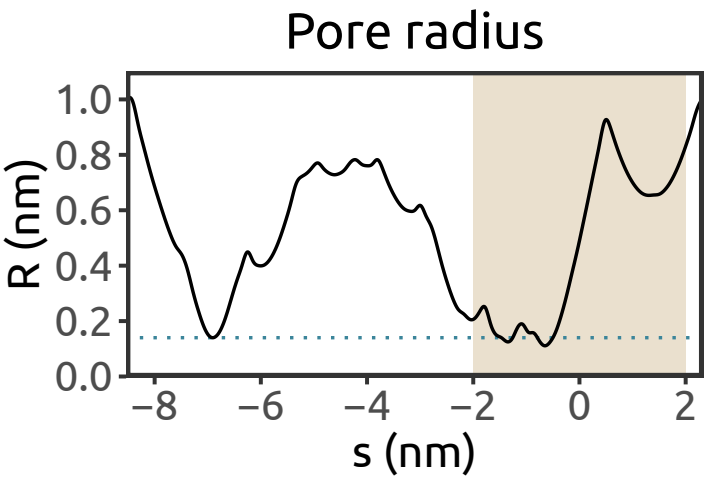
Simulation result:
barrier to water

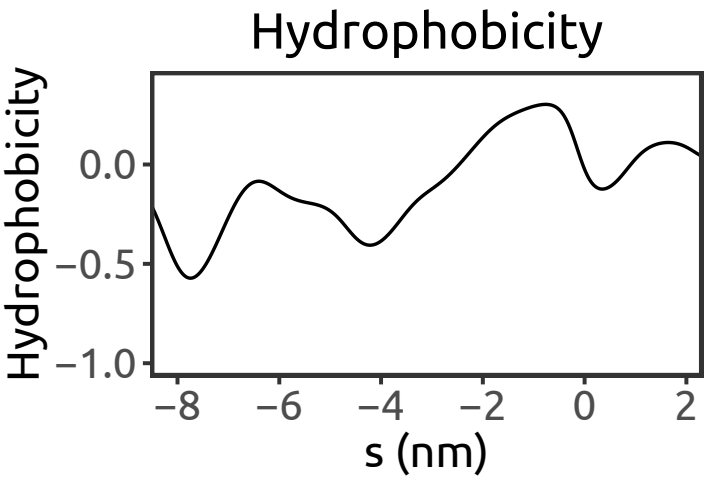
BEST1 (PDB ID: 4RDQ)

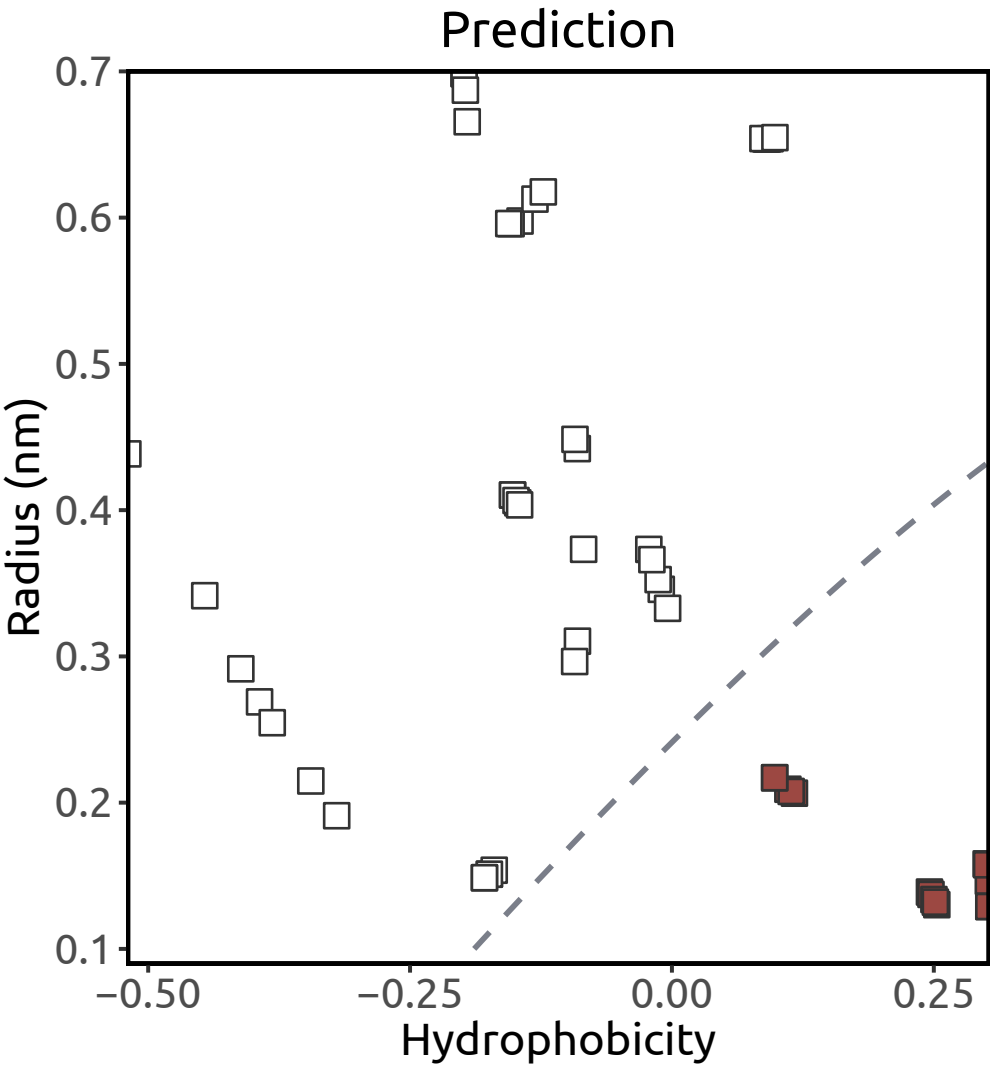
Gallus gallus

X–ray (2.85 Å)

Kane et al., 2014







Heuristic score:

2.82 (n = 15)

Simulation result:

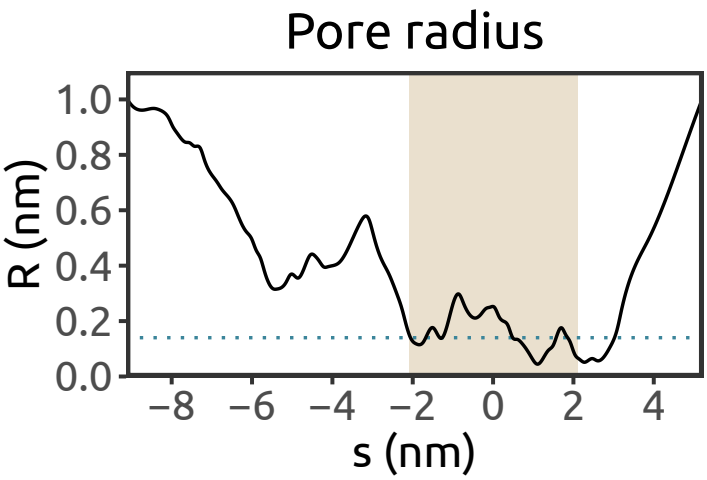
barrier to water

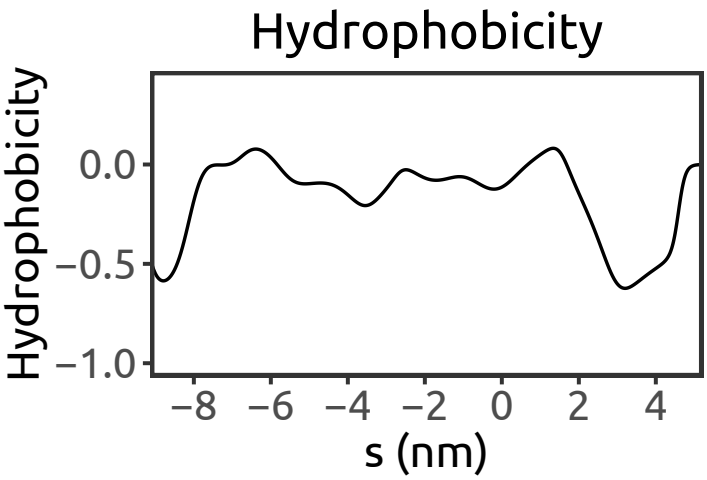
CFTR (PDB ID: 5UAK)

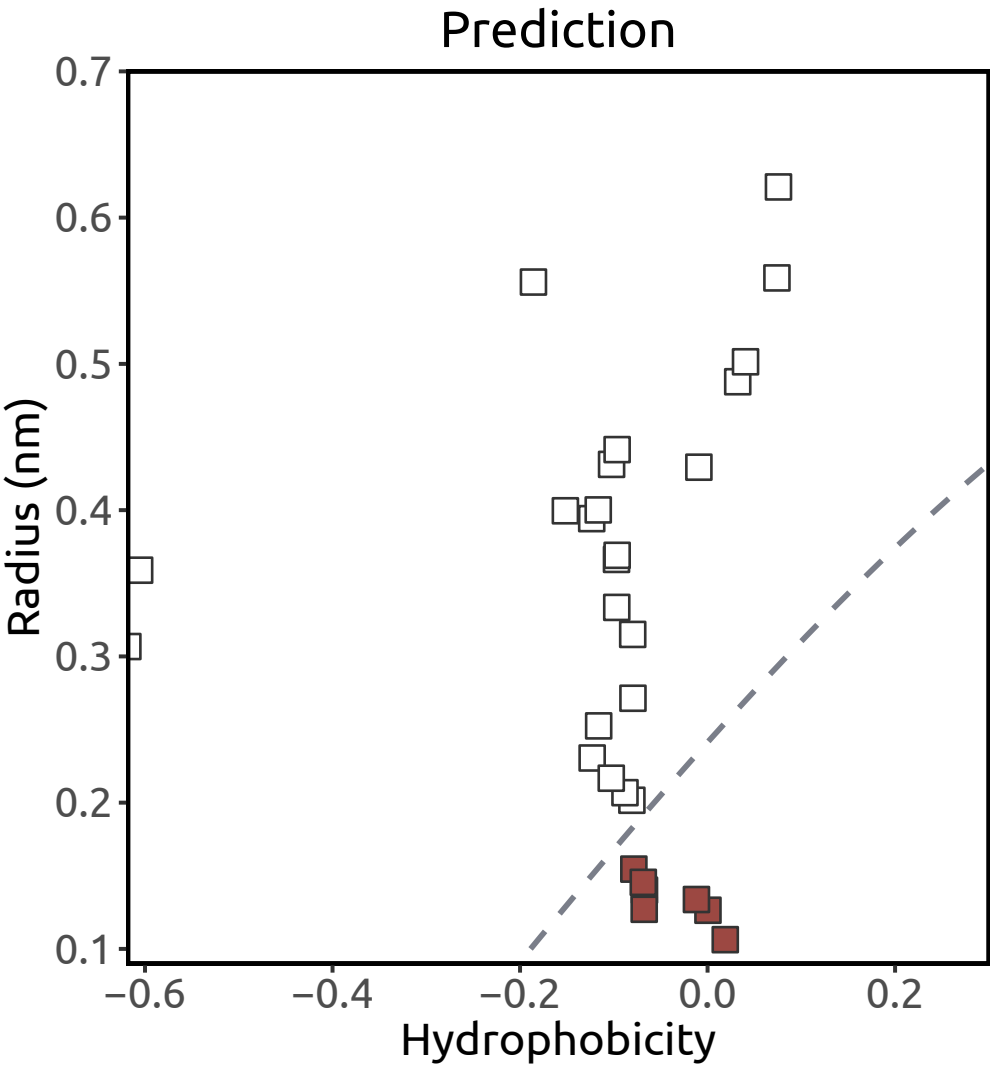
Homo sapiens

cryo–EM (3.87 Å)

Liu et al., 2017







Heuristic score:

0.64 (n = 8)

Simulation result:

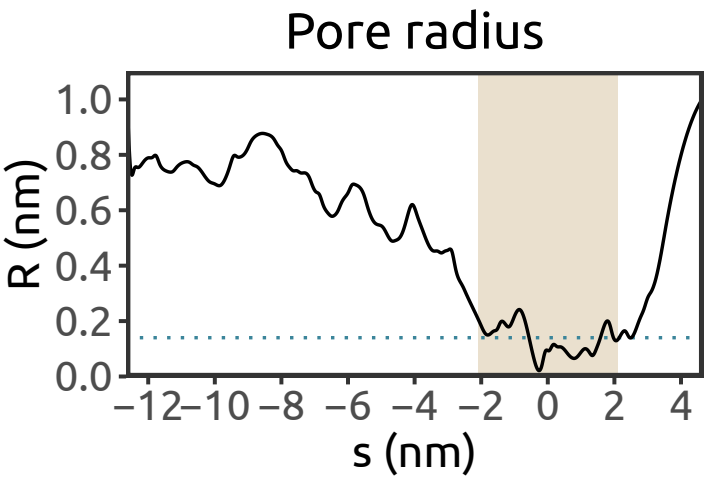
barrier to water

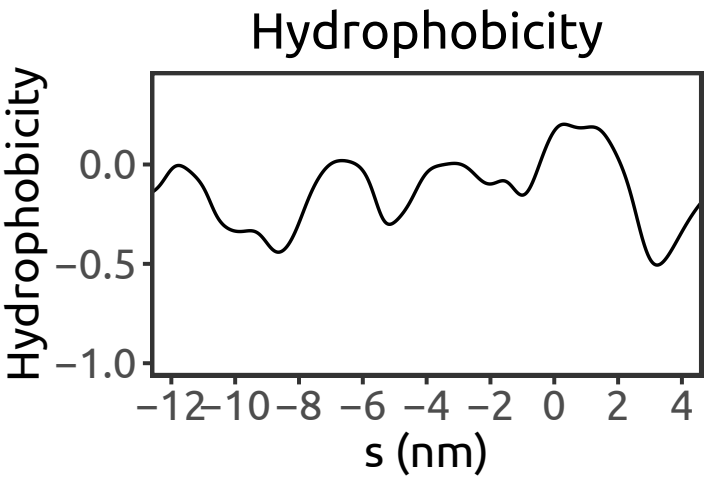
CFTR (PDB ID: 5UAR)

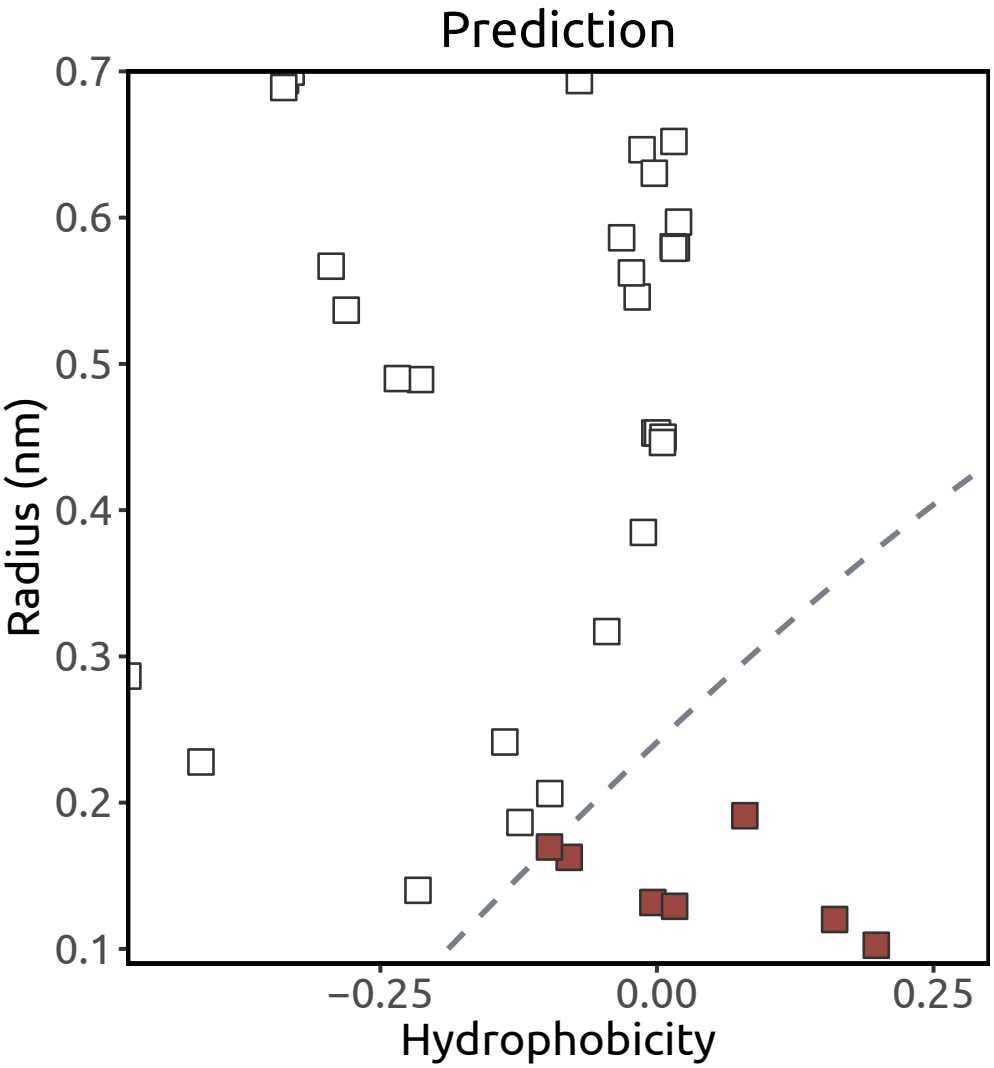
Danio rerio

cryo–EM (3.73 Å)

Zhang & Chen, 2016







Heuristic score:

1.83 (n = 12)

Simulation result:

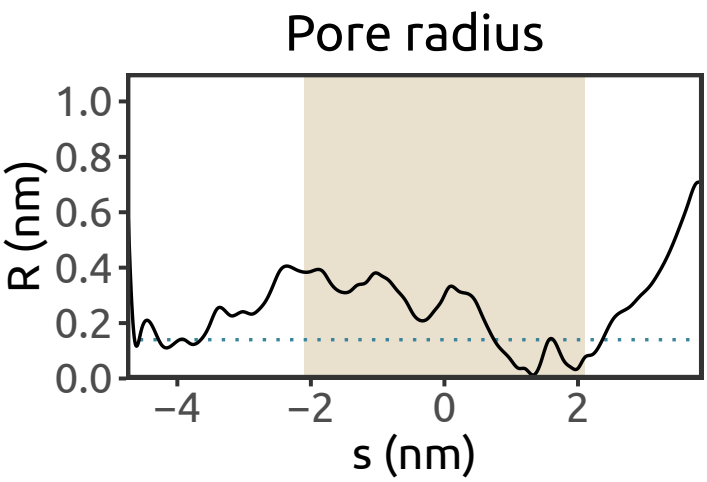
barrier to water

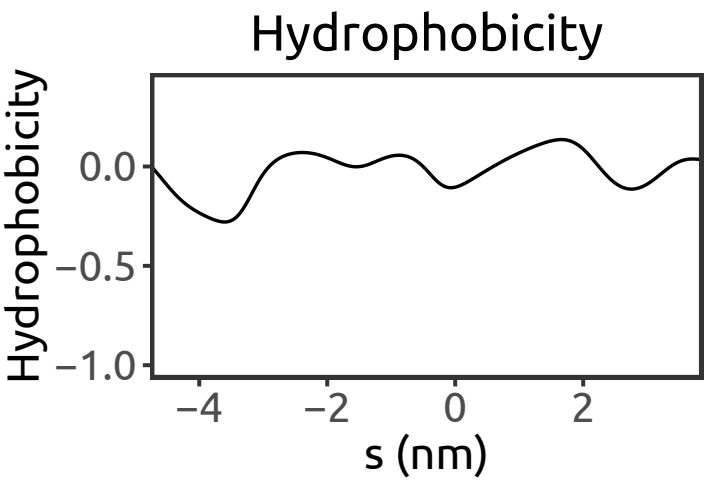
CFTR (PDB ID: 5W81)

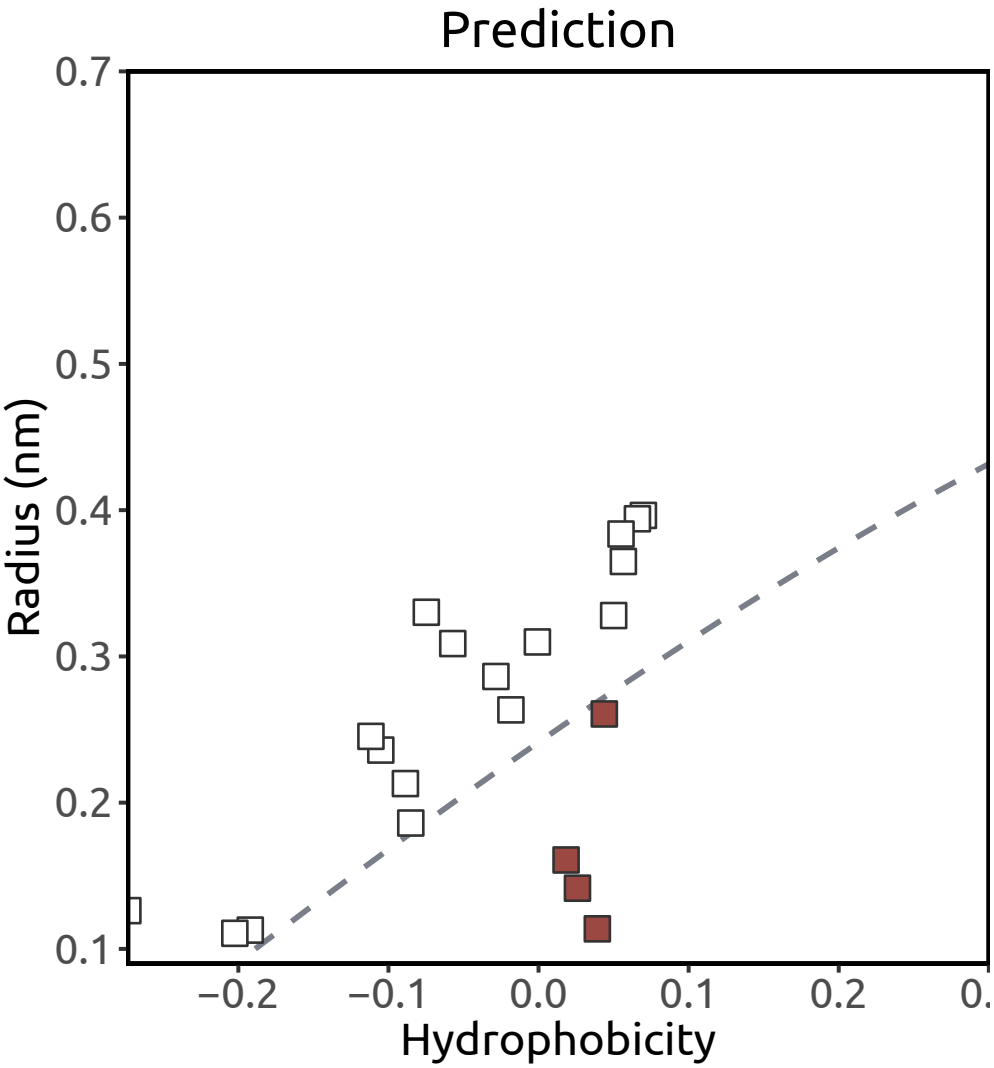
Danio rerio

cryo–EM (3.37 Å)

Zhang et al., 2017







Heuristic score:

1.37 (n = 9)

Simulation result:

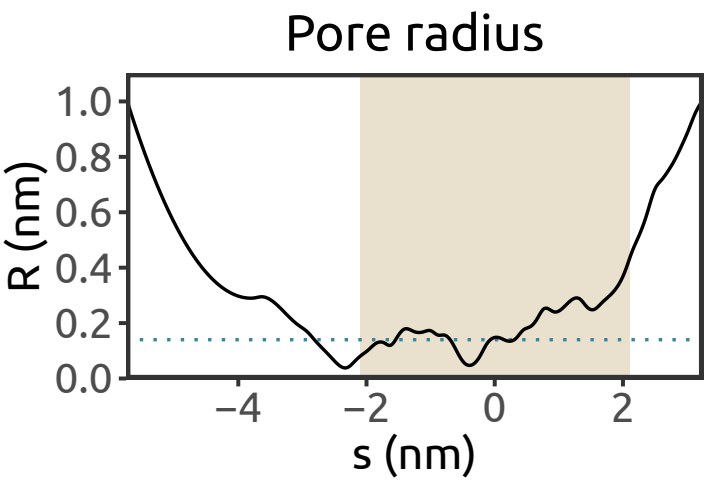
barrier to water

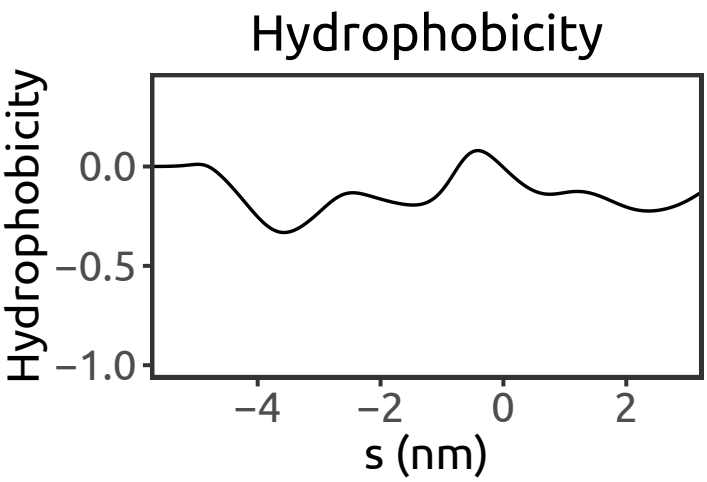
CLC (PDB ID: 5TQQ)

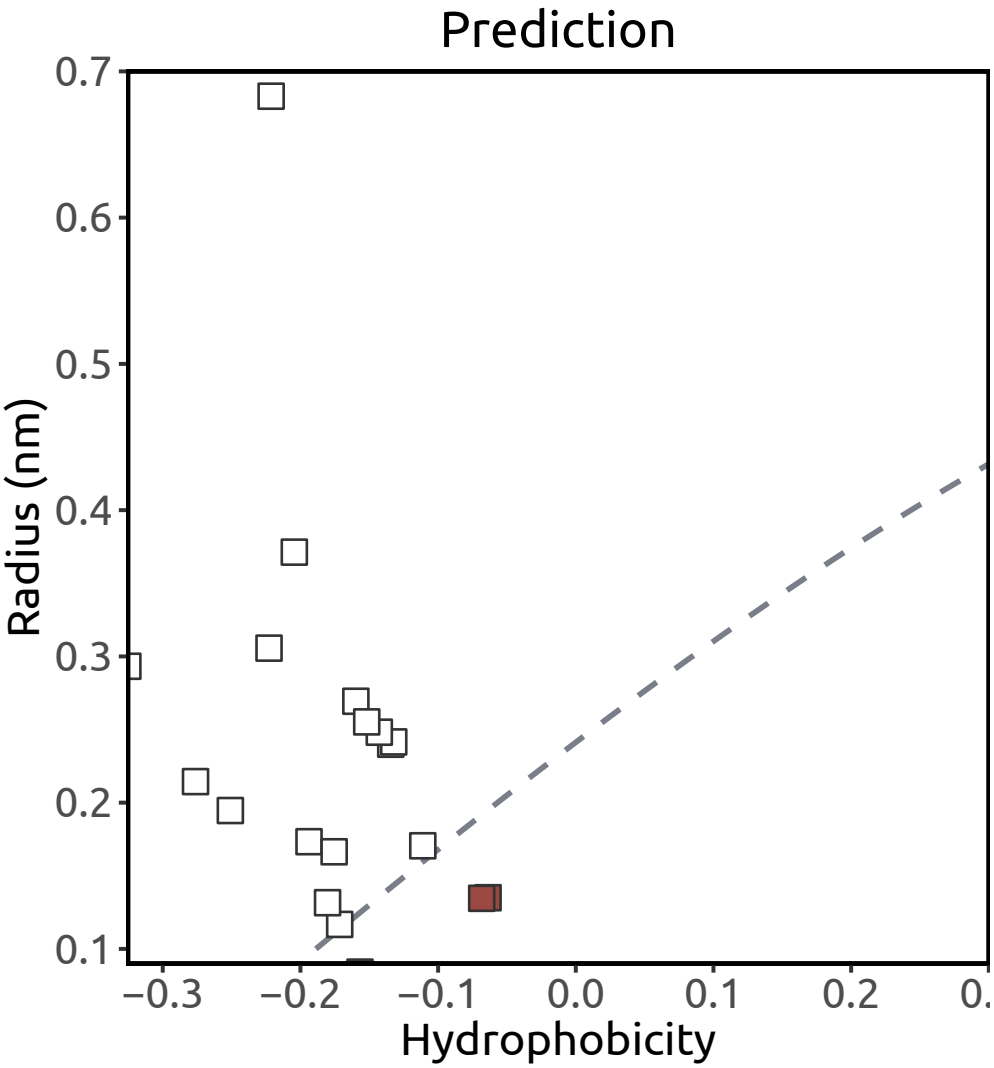
Bos taurus

cryo–EM (3.76 Å)

Park et al., 2017







Heuristic score:

0.41 (n = 5)

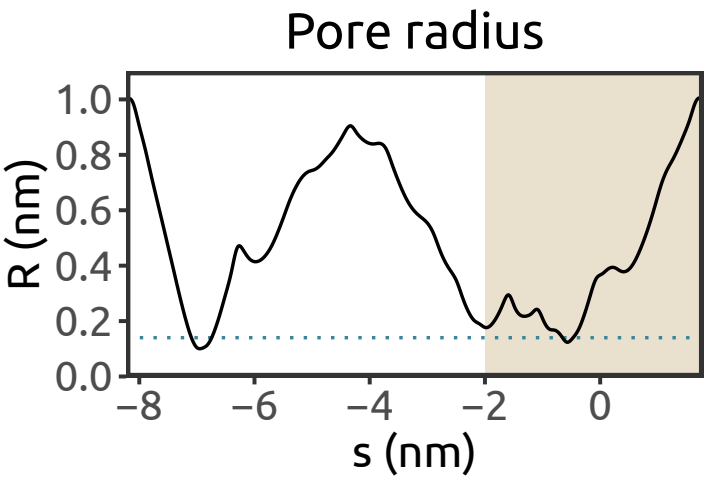
Simulation result:

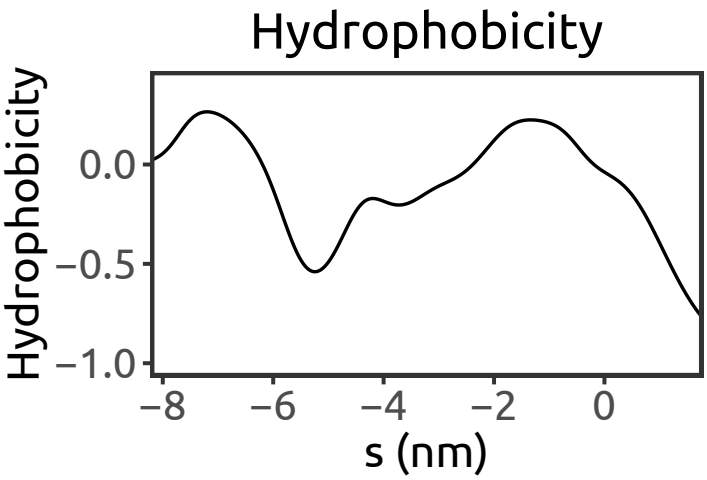
barrier to water

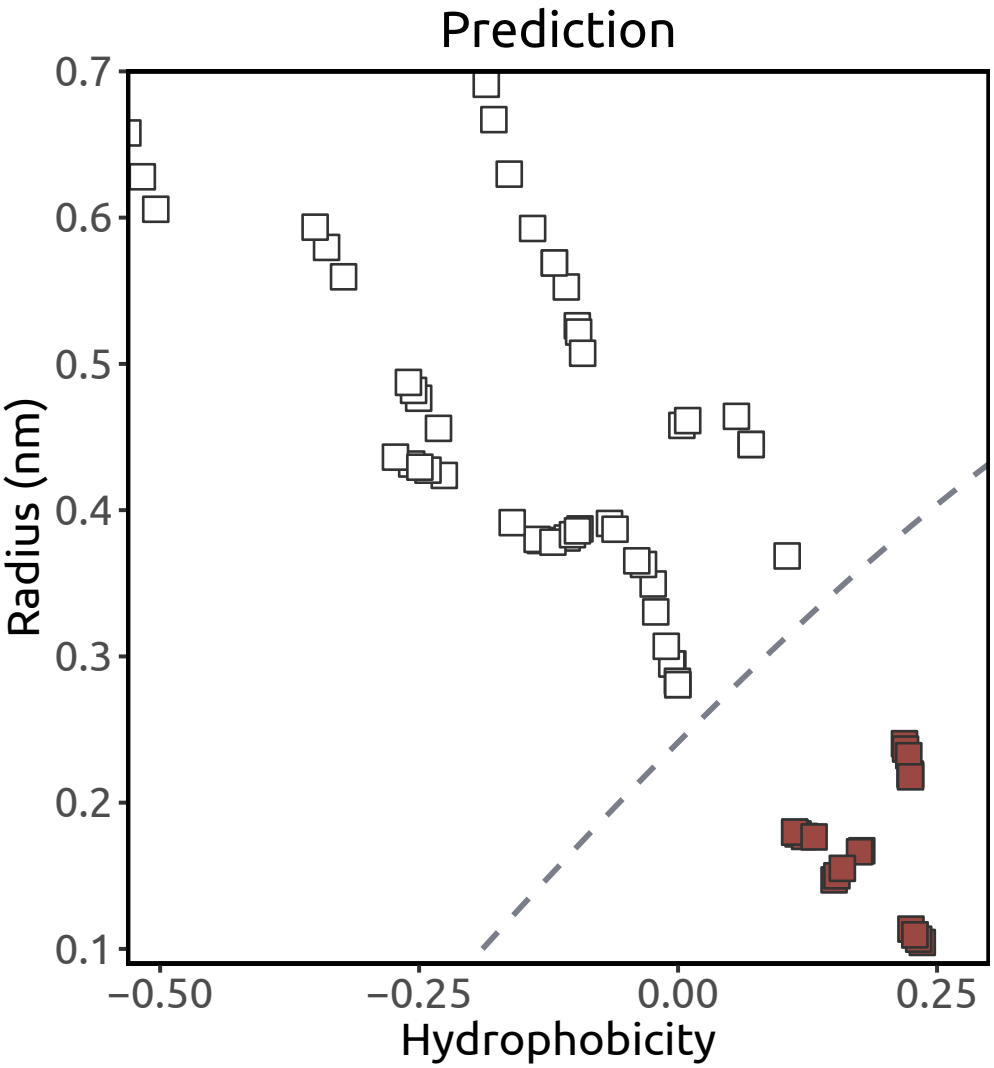
KpBest (PDB ID: 4WD8)

Klebsiella pneumoniae
X–ray (2.3 Å)

Yang et al., 2014







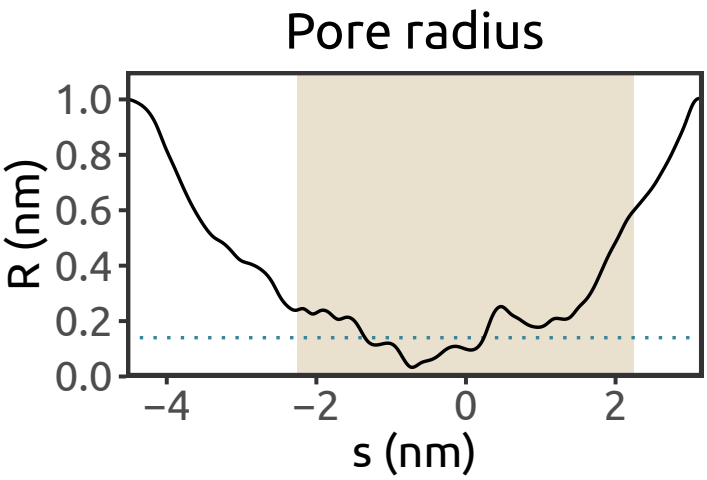
Heuristic score:
3.57 (n = 22)

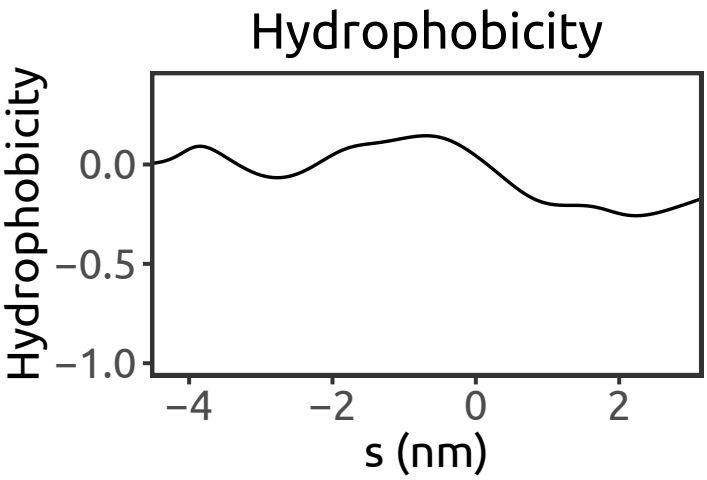
Simulation result:
barrier to water

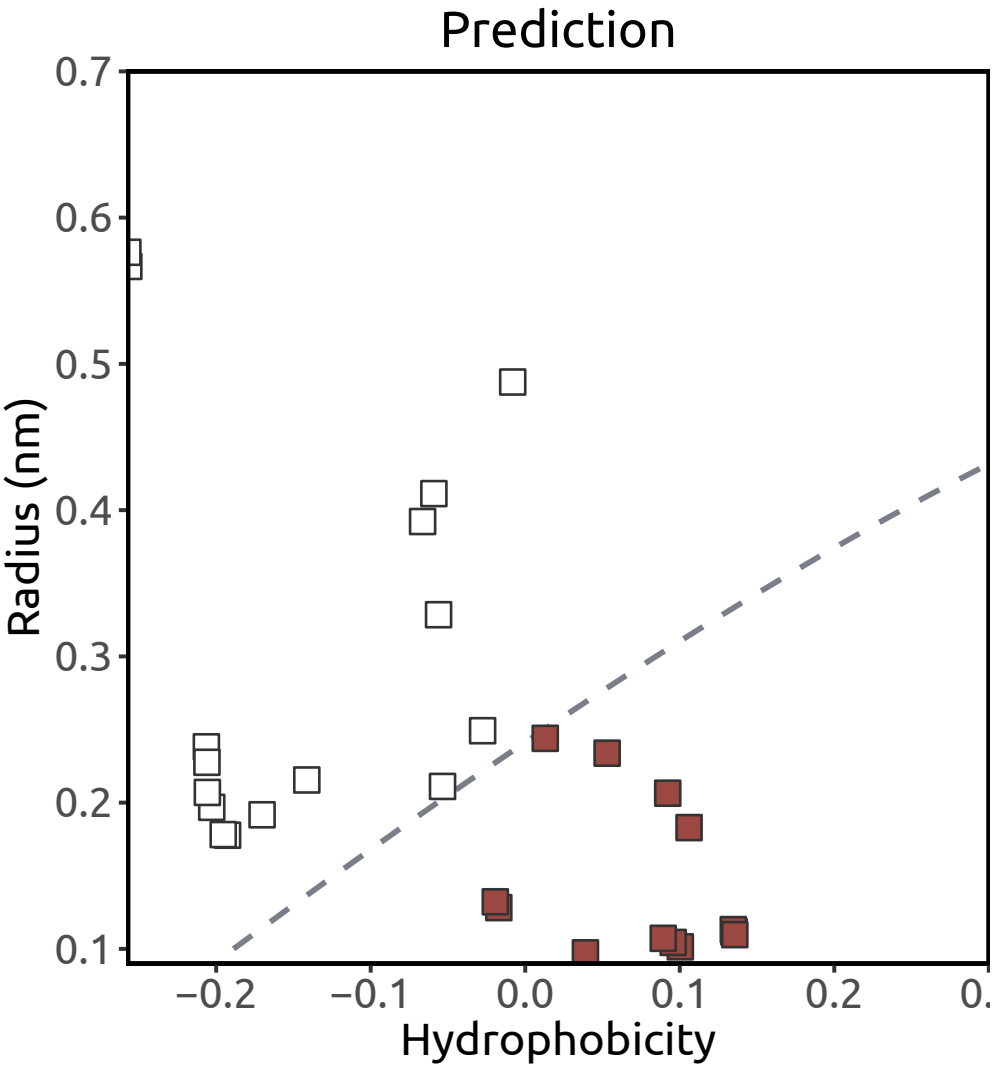
TehA (PDB ID: 3M71)

Haemophilus influenzae
X–ray (1.2 Å)

Chen et al., 2010







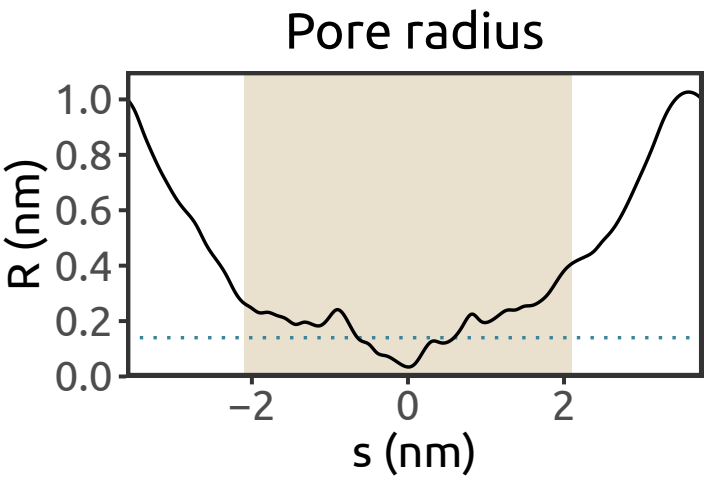
Heuristic score:
2.51 (n = 17)

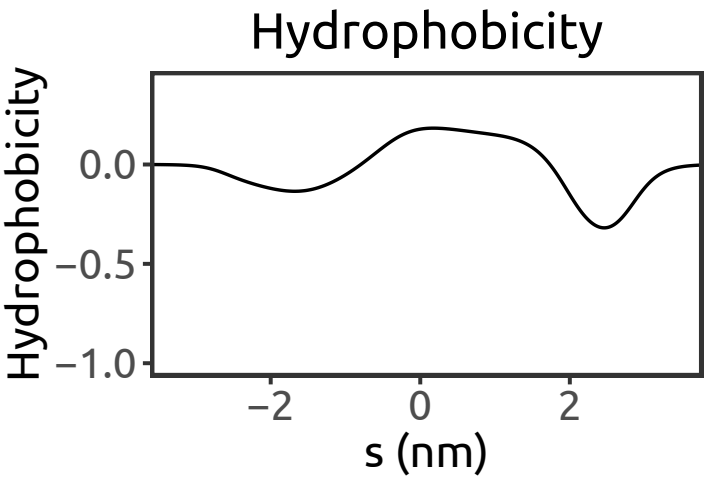
Simulation result:
barrier to water

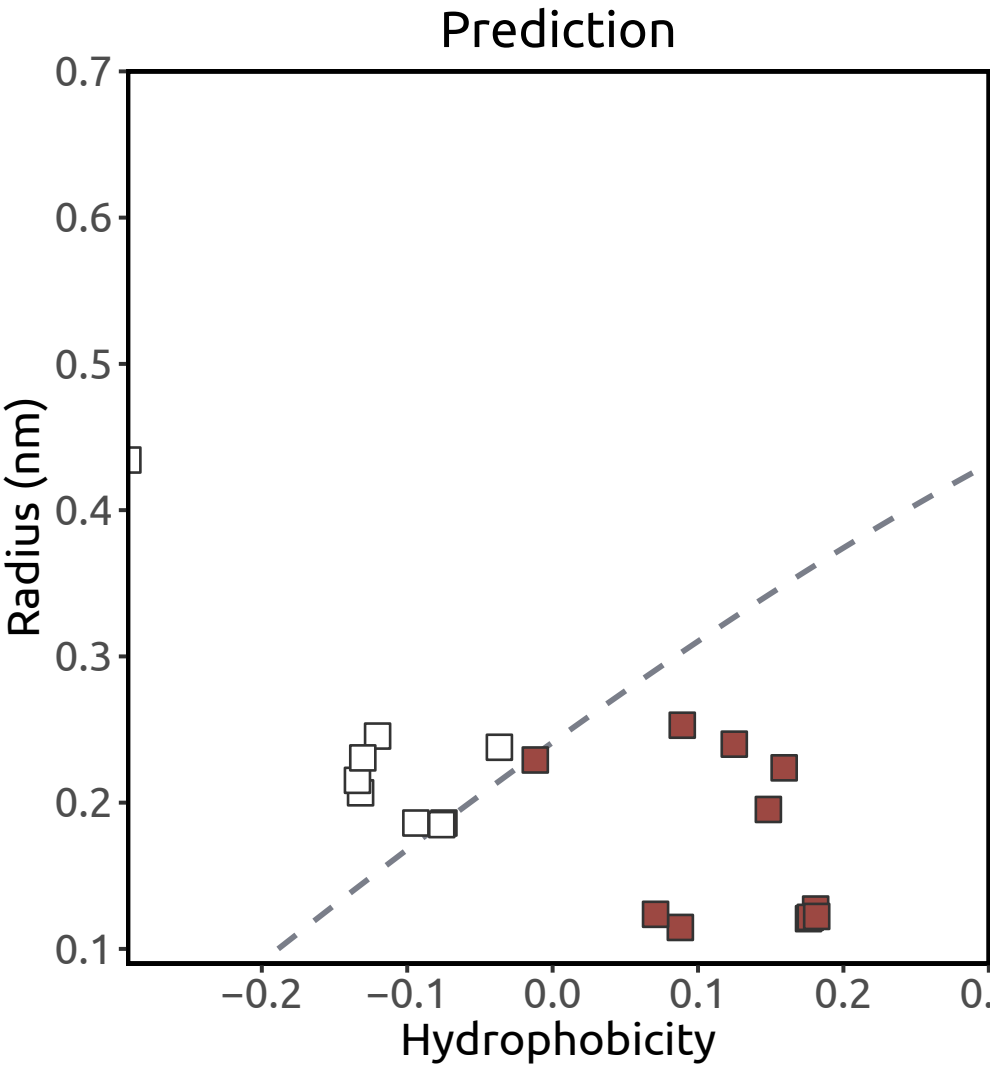
TehA (PDB ID: 4YCR)

Haemophilus influenzae
X–ray (2.3 Å)

Axford et al., 2015







Heuristic score:
1.96 (n = 14)

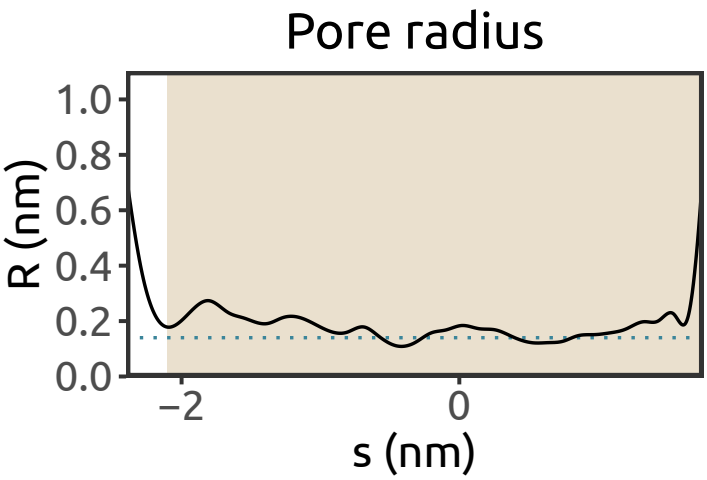
Simulation result:
barrier to water

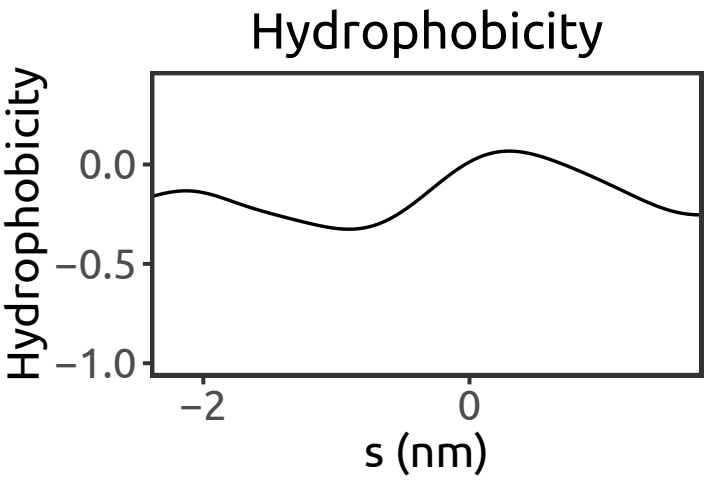
TMEM16A (PDB ID: 5OYB)

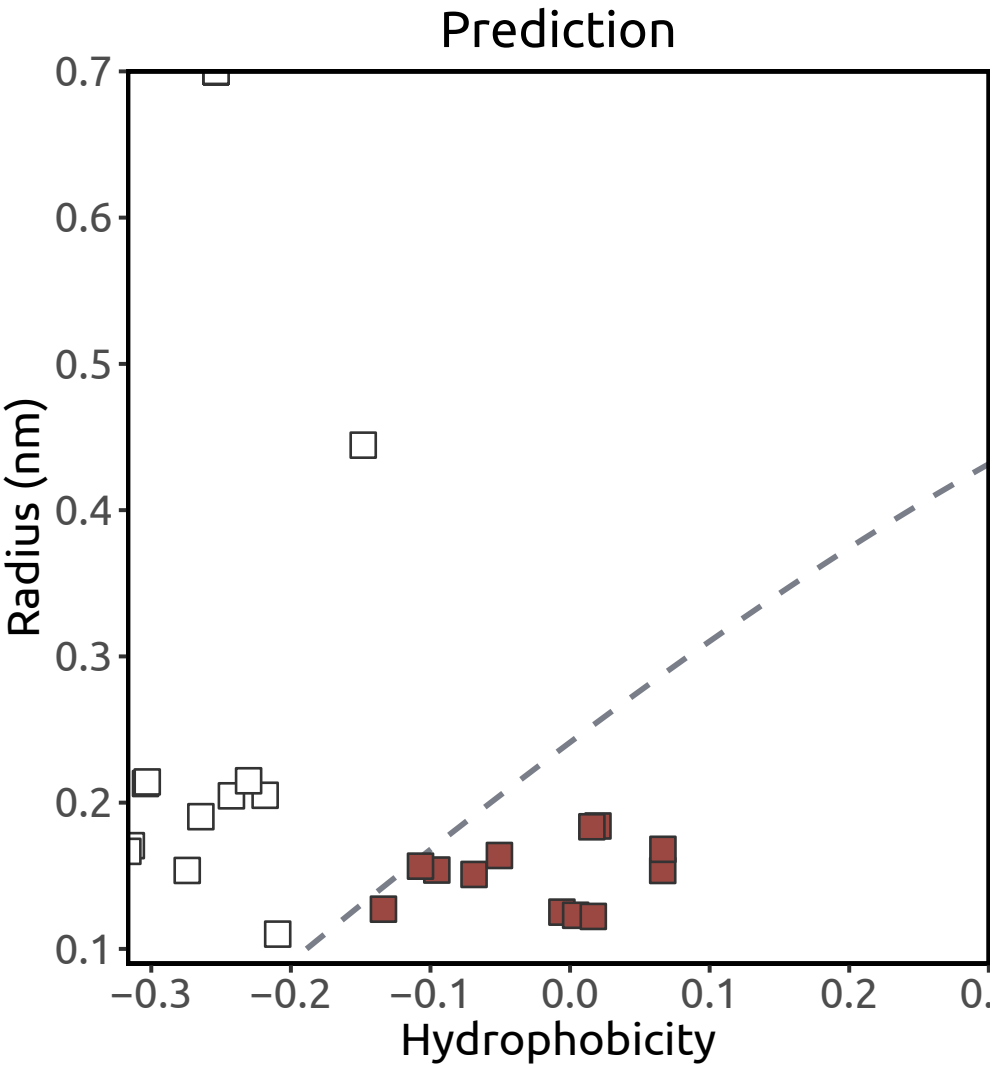
Mus musculus

cryo–EM (3.75 Å)

Paulino et al., 2017







Heuristic score:

0.71 (n = 12)

Simulation result:

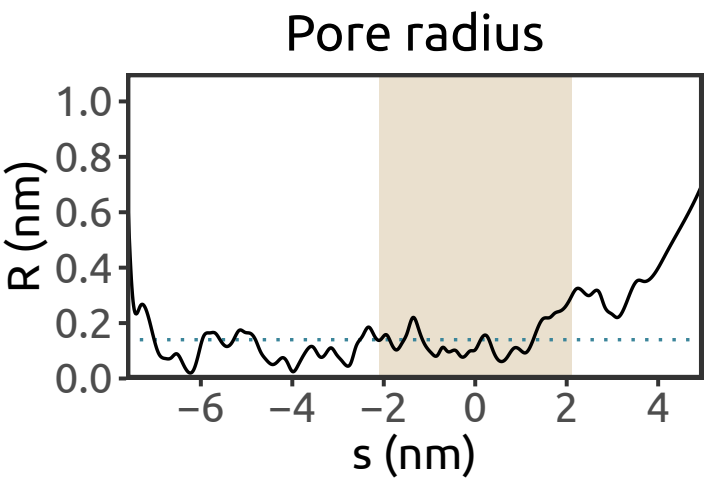
barrier to water

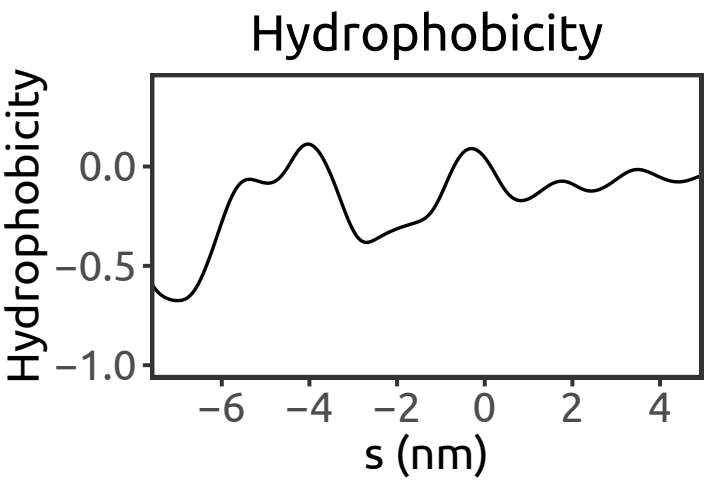
TMEM16A (PDB ID: 5OYG)

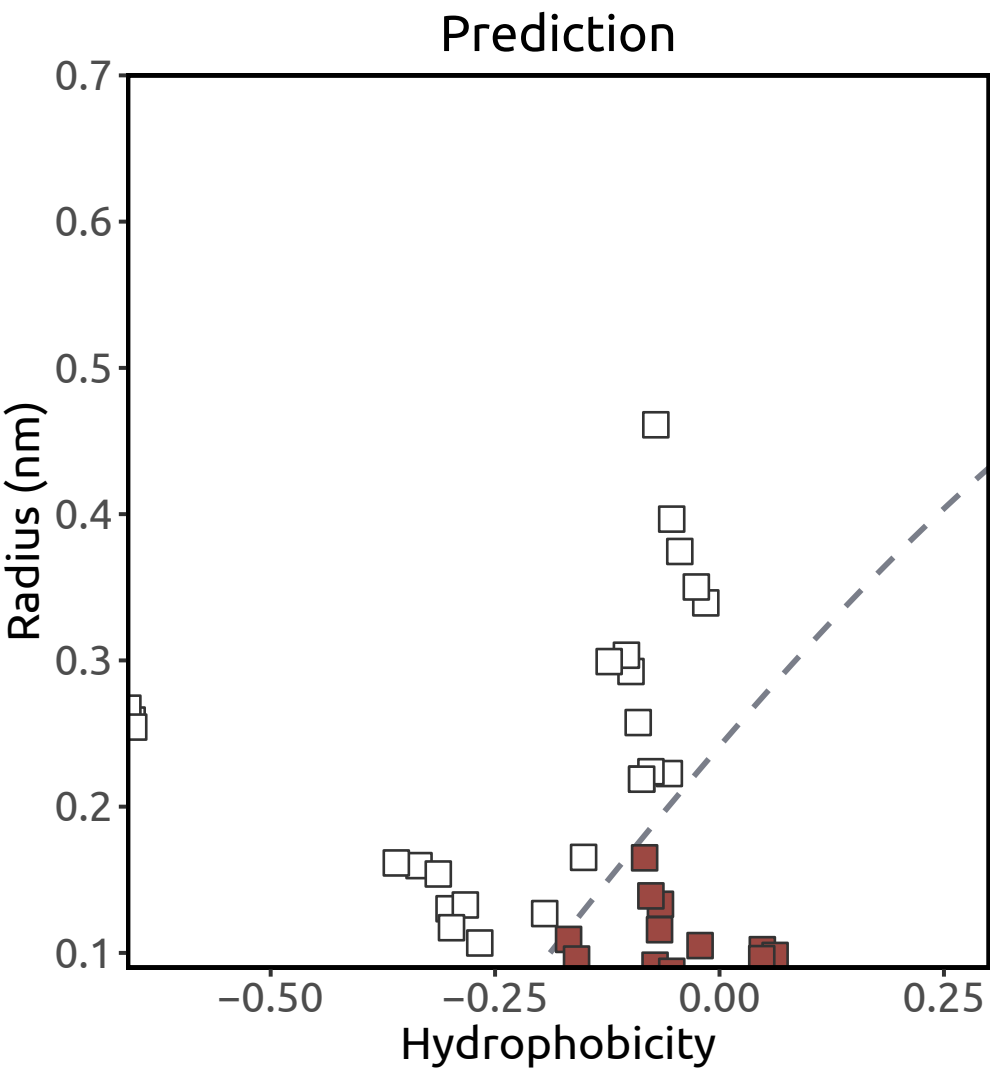
Mus musculus

cryo–EM (4.06 Å)

Paulino et al., 2017







Heuristic score:

1.36 (n = 15)

Simulation result:

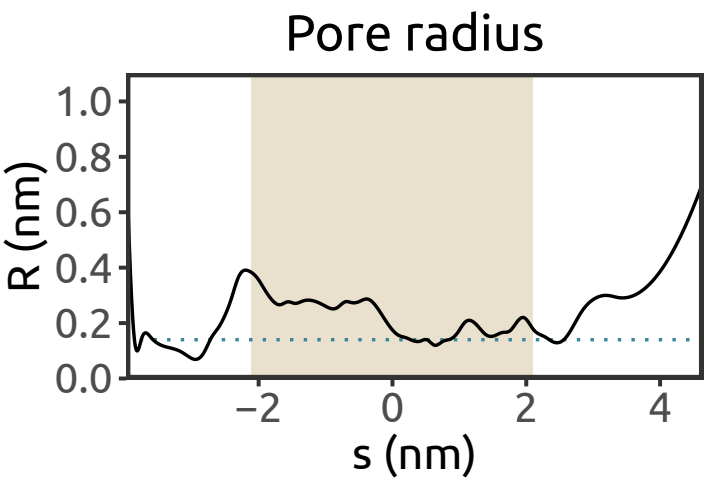
barrier to water

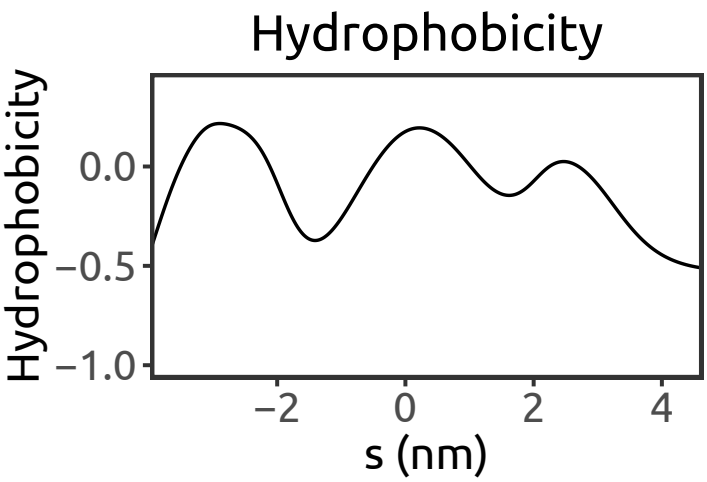
TMEM16A (PDB ID: 6BGI)

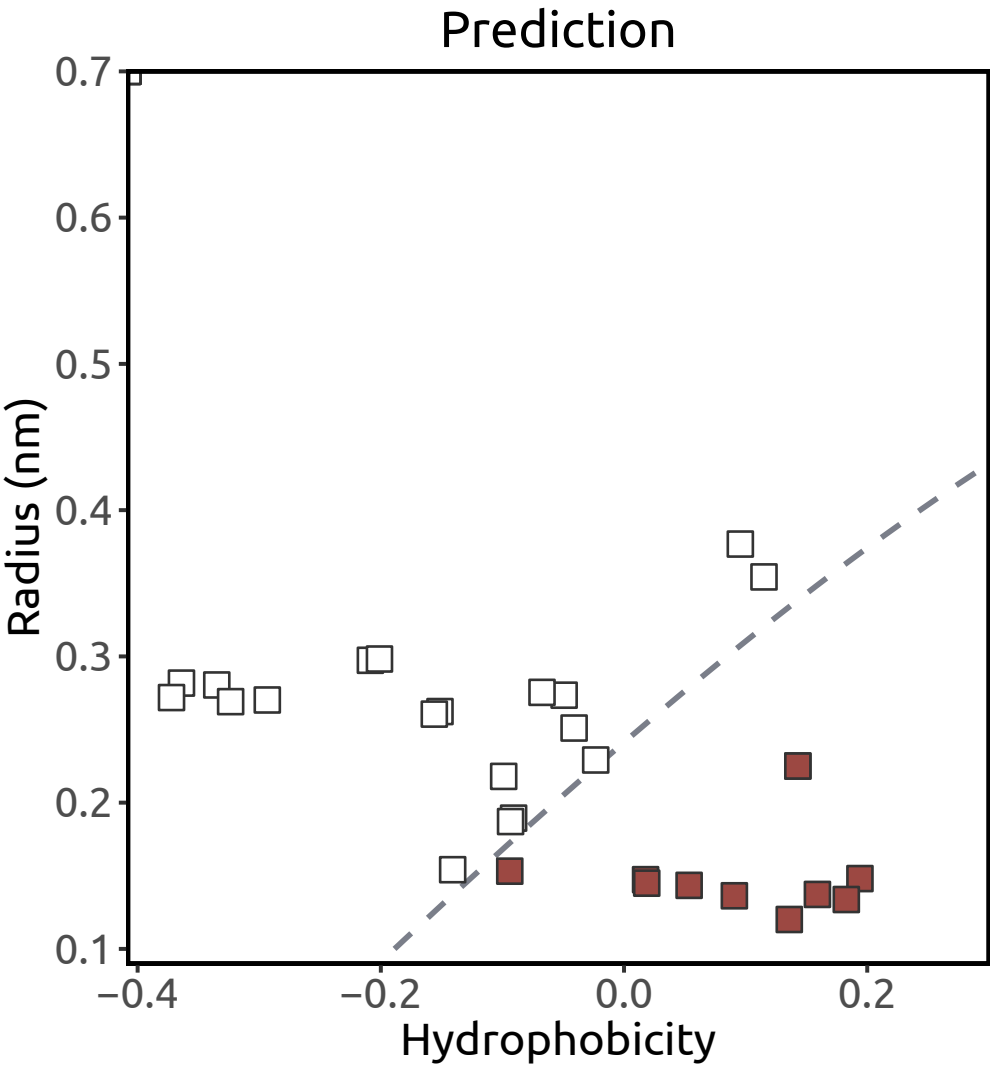
Mus musculus

cryo–EM (3.8 Å)

Dang et al., 2017







Heuristic score:

1.36 (n = 11)

Simulation result:

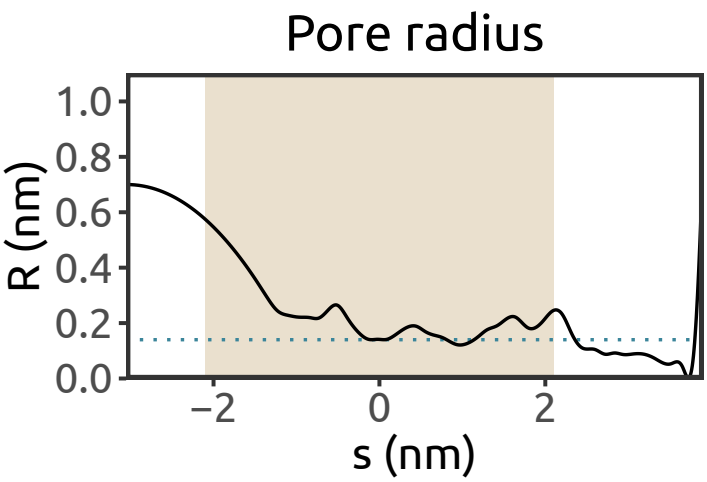
barrier to water

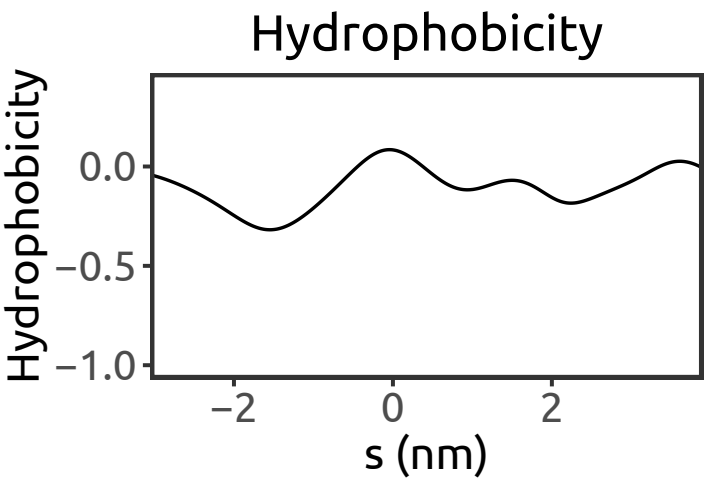
TMEM16A (PDB ID: 6BGJ)

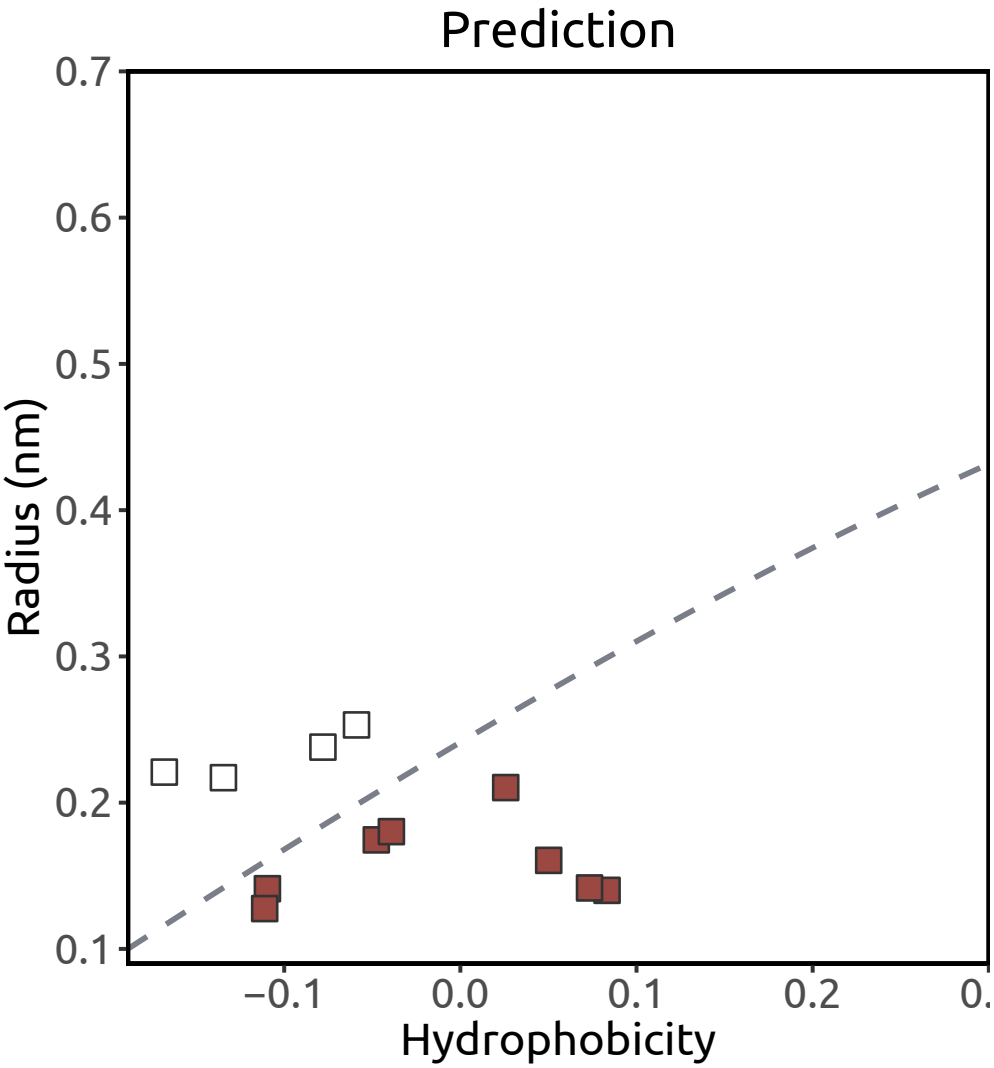
Mus musculus

cryo–EM (3.8 Å)

Dang et al., 2017







Heuristic score:

0.48 (n = 8)

Simulation result:

barrier to water