Supporting Information: Effect of pH on the supramolecular structure of Helicobacter pylori urease by molecular dynamics simulations.

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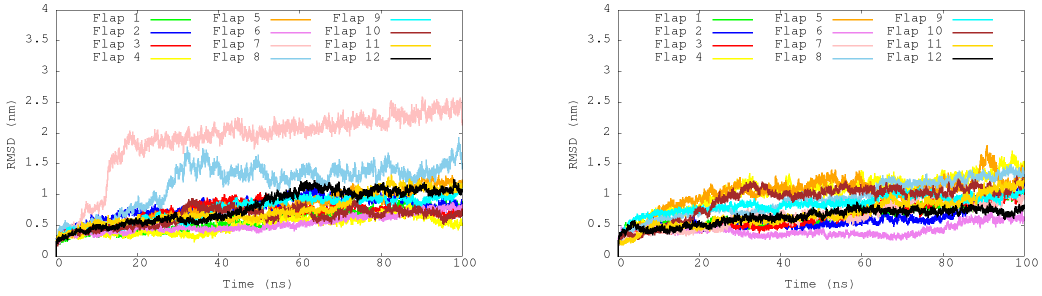
Table S1: Number of water molecules and ions used in the molecular dynamics simulations at different pHs

pH	**TIP4P Water**	**Ions**
2	148944	1373 Cl
3	149121	1208 Cl
4	149573	810 Cl
5	149987	438 Cl
6	150261	189 Cl
7	150465	3 Na
7.5	150391	83 Na

Table S2: Percentile scores of Sidechain and Ramachandran angles of residues of urease for crystal structure and for obtained structures after NVT and NPT simulations.

Structural model	**Poor rotamers**	**Favored rotamers**	**Ramachandran outliers**	**Ramachandran favored**
Crystal	9.90%	77.60%	7.10%	76.10%
After 10 ns NVT simulations				
pH2	6.6%	81.6%	3.0%	86.4%
pH3	6.9%	81.7%	2.8%	87.0%
pH4	6.5%	82.5%	2.6%	87.9%
pH5	6.6%	82.3%	2.7%	87.9%
pH6	6.4%	82.9%	2.6%	87.3%
pH7	6.3%	82.7%	2.5%	88.2%
pH7.5	6.5%	82.0%	2.6%	87.7%
After 100 ns NPT simulations				
pH2	4.2%	86.4%	1.9%	87.0%
pH3	3.9%	86.5%	2.3%	86.6%
pH4	4.2%	85.5%	2.1%	87.1%
pH5	4.1%	86.4%	2.1%	87.2%
pH6	4.8%	84.8%	2.0%	87.4%
pH7	4.9%	85.3%	2.1%	87.1%
pH7.5	4.6%	85.4%	1.8%	87.4%
After 200 ns NPT simulations				
pH2	3.7%	87.1%	2.0%	87.1%
pH7.5	4.4%	85.9%	2.0%	87.4%



(a) pH 2

(b) pH 3

(c) pH 4

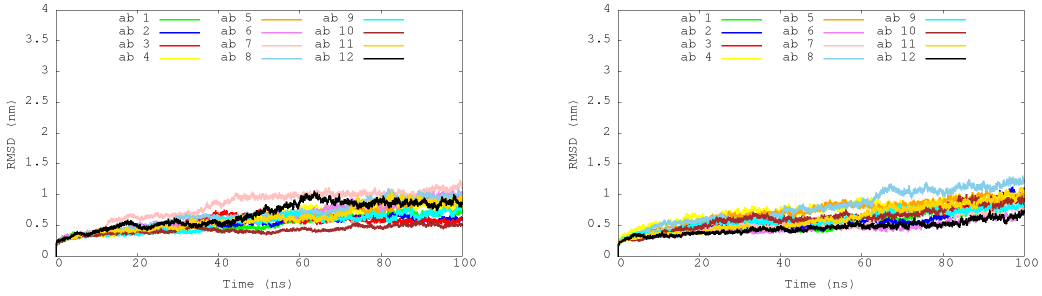
(d) pH 5

(e) pH 6

(f) pH 7

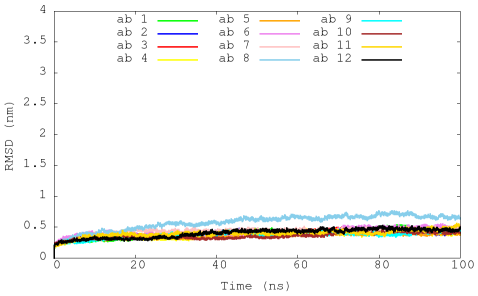
(g) pH 7.5

Figure S1: MD analysis of flap mobility at different pHs. Representation of the temporal evolution of the RMSD of the 12 flaps of urease enzyme at pH 2, 3, 4, 5, 6, 7 and 7.5.

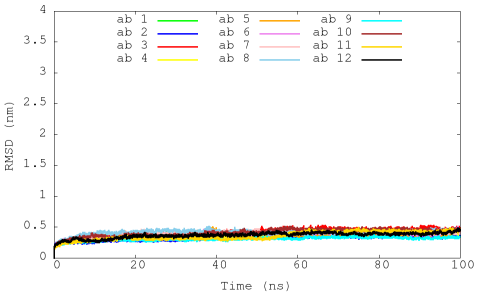


(a) pH2

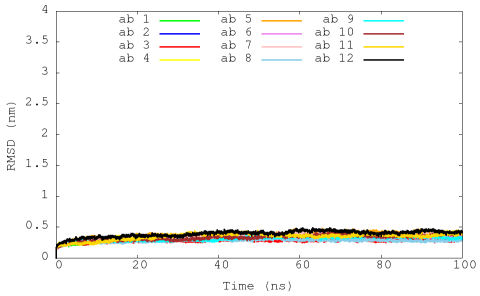
(b) pH3



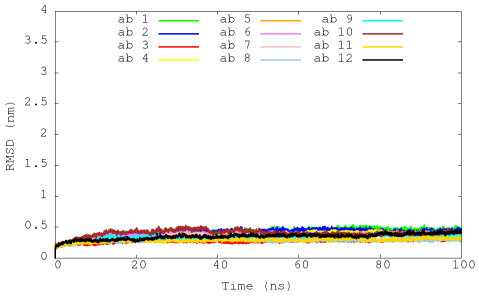
(c) pH4



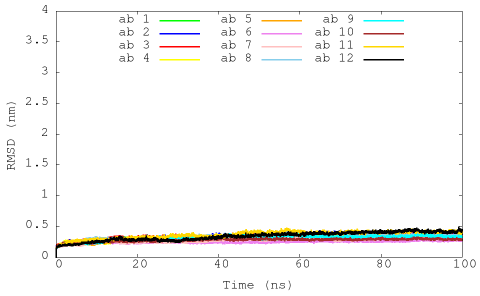
(d) pH5



(e) pH6



(f) pH7



(g) pH7.5

Figure S2: Representation of the temporal evolution of the RMSD values of each of the 12 urease dimers at different pHs.

Forde field parameters

Force field parameters of the modified carbamylated lysine amino acid used in the Gromacs molecular dynamics simulations.

```
;OPLS-AA force field for KCX


[  KCX ]


[ atoms ]
  N      opls_238   -0.500     1
  H      opls_241    0.300     1
  CA  opls_224B   0.140     1
  HA  opls_140    0.060     1
  CB  opls_136   -0.120     2
  HB1  opls_140    0.060     2
  HB2  opls_140    0.060     2
  CG  opls_136   -0.120     3
  HG1  opls_140    0.060     3
  HG2  opls_140    0.060     3
  CD  opls_136   -0.120     4
  HD1  opls_140    0.060     4
  HD2  opls_140    0.060     4
  CE  opls_906    0.060     5
  HE1  opls_911    0.060     5
  HE2  opls_911    0.060     5
  NZ  opls_238   -0.500     6
  HZ1  opls_241    0.300     6
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```
  C      opls_235    0.500     7
  O      opls_236   -0.500     7
  CX  opls_271    0.700     8
  OQ1  opls_272   -0.840     8
  OQ2  opls_272   -0.840     8

[ bonds ]
 OQ2    CX
 OQ1    CX
 HE1    CE
 HD2    CD
 CE     HE2
 HD1    CD
 HB2    CB
 CG     HG2
 CG     HG1
 HB1    CB
 CA     HA
 CX     NZ
 CE     NZ
 CA     N
 CE     CD
 CD     CG
 CG     CB
 CB     CA
 NZ     HZ1
 H      N
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```
 CA     C
 O      C
 -C     N

[ angles ]
  NZ   CX  OQ2 dhTPP_NT_C_3_O2
  NZ   CX  OQ1 dhTPP_NT_C_3_O2

[ dihedrals ] ; override some with residue-specific ones
     N    CA    CB    CG    dih_LYS_chi1_N_C_C_C
    CG    CB    CA     C    dih_LYS_chi1_C_C_C_CO
    CD    CE    NZ   HZ1    dih_LYS_chi5_C_C_N_H
   OQ2    CX    NZ    CE    dhTPP_O2_C_3_NT_CT
   OQ1    CX    NZ    CE    dhTPP_O2_C_3_NT_CT
     N    CA     C     O    dhTPP_NT_CT_C_2_O_2

[ impropers ]
  NZ  OQ1   CX  OQ2 improper_O_C_X_Y
  -C   CA    N    H improper_Z_N_X_Y
  CA   +N    C    O improper_O_C_X_Y
```

```
;OPLS-AA force field for Niquel

[ NIK ]

 [ atoms ]
  NI1  opls_966   2.000     0
  NI2  opls_966   2.000     0

 [ bonds ]
    NI1  NI2

;OPLS-AA force field for OH

[ OH ]

 [ atoms ]
    OW   opls_116   -1.20      0
   HW1   opls_117    0.20      0

 [ bonds ]
    OW   HW1
```

pKa values of the *H. pylori* urease residues obtained from Propka3 software.

Group	pKa	model-pKa
ASP 9 A	4.41	3.80
ASP 68 A	3.96	3.80
ASP 69 A	3.21	3.80
ASP 72 A	3.99	3.80
ASP 89 A	3.52	3.80
ASP 117 A	3.98	3.80
ASP 136 A	4.49	3.80
ASP 155 A	4.14	3.80
ASP 157 A	3.50	3.80
ASP 167 A	3.63	3.80
ASP 188 A	2.82	3.80
ASP 203 A	5.05	3.80
ASP 207 A	4.09	3.80
ASP 229 A	3.10	3.80
ASP 230 A	3.43	3.80
GLU 7 A	4.59	4.50
GLU 18 A	4.35	4.50
GLU 25 A	4.00	4.50
GLU 34 A	2.96	4.50
GLU 45 A	2.51	4.50
GLU 46 A	5.22	4.50
GLU 56 A	4.09	4.50
GLU 60 A	3.62	4.50

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GLU  80 A    4.43      4.50
GLU  84 A    4.64      4.50
GLU 101 A    4.52      4.50
GLU 110 A    4.99      4.50
GLU 116 A    4.26      4.50
GLU 122 A    4.13      4.50
GLU 149 A    8.95      4.50
GLU 159 A    4.11      4.50
GLU 177 A    4.57      4.50
GLU 180 A    3.76      4.50
GLU 181 A    3.46      4.50
GLU 185 A    3.95      4.50
GLU 209 A    3.66      4.50
GLU 220 A    3.98      4.50
GLU 238 A    2.42      4.50
C-  238 A    2.10      3.20
HIS  14 A    3.02      6.50
HIS  42 A    5.76      6.50
HIS  79 A    6.43      6.50
HIS  97 A    6.73      6.50
HIS 144 A    3.41      6.50
HIS 146 A    2.74      6.50
HIS 216 A    7.40      6.50
HIS 224 A    6.37      6.50
CYS 153 A   10.69      9.00
TYR  15 A   16.40     10.00
TYR  32 A   12.58     10.00
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TYR 232 A   12.01     10.00
LYS   2 A    7.01     10.50
LYS   6 A   12.19     10.50
LYS  10 A   10.29     10.50
LYS  21 A   10.86     10.50
LYS  22 A    8.90     10.50
LYS  24 A    9.82     10.50
LYS  26 A   10.63     10.50
LYS  29 A   10.18     10.50
LYS  51 A   10.27     10.50
LYS  52 A   11.78     10.50
LYS  66 A   11.02     10.50
LYS  92 A    8.34     10.50
LYS 105 A   10.50     10.50
LYS 114 A   10.60     10.50
LYS 124 A    9.01     10.50
LYS 125 A    9.86     10.50
LYS 130 A   11.48     10.50
LYS 132 A   10.51     10.50
LYS 160 A   11.59     10.50
LYS 164 A   10.24     10.50
LYS 182 A   10.53     10.50
LYS 211 A   10.70     10.50
LYS 212 A   11.34     10.50
LYS 219 A   10.33     10.50
LYS 227 A   10.57     10.50
LYS 234 A   10.76     10.50
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LYS 237 A   10.21     10.50
ARG  23 A   14.03     12.50
ARG  48 A   12.32     12.50
ARG  62 A   12.37     12.50
ARG 137 A   15.83     12.50
ARG 152 A   13.27     12.50
ARG 158 A    8.81     12.50
ARG 165 A   12.20     12.50
ARG 175 A   11.59     12.50
ARG 193 A   11.64     12.50
ARG 194 A   12.46     12.50
ARG 204 A   11.96     12.50
ARG 217 A   12.72     12.50
ARG 221 A   11.96     12.50
N+    1 A    3.03      8.00
ASP 257 B    5.14      3.80
ASP 263 B    6.41      3.80
ASP 265 B    3.40      3.80
ASP 273 B    4.97      3.80
ASP 305 B    6.04      3.80
ASP 315 B    6.12      3.80
ASP 323 B    6.64      3.80
ASP 328 B    3.86      3.80
ASP 341 B    5.61      3.80
ASP 344 B    3.58      3.80
ASP 372 B    7.14      3.80
ASP 403 B    4.05      3.80
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ASP	442	B	4.10	3.80
ASP	447	B	4.30	3.80
ASP	461	B	7.98	3.80
ASP	474	B	3.58	3.80
ASP	477	B	4.44	3.80
ASP	480	B	3.92	3.80
ASP	488	B	8.54	3.80
ASP	498	B	5.29	3.80
ASP	523	B	3.16	3.80
ASP	554	B	4.90	3.80
ASP	563	B	4.02	3.80
ASP	569	B	5.91	3.80
ASP	574	B	4.24	3.80
ASP	586	B	7.98	3.80
ASP	590	B	4.67	3.80
ASP	600	B	10.36	3.80
ASP	619	B	2.78	3.80
ASP	634	B	3.38	3.80
ASP	636	B	4.51	3.80
ASP	671	B	4.64	3.80
ASP	700	B	6.52	3.80
ASP	726	B	3.67	3.80
ASP	738	B	3.94	3.80
ASP	764	B	4.06	3.80
ASP	786	B	4.05	3.80
GLU	246	B	4.52	4.50
GLU	269	B	5.57	4.50

GLU 271 B	3.42	4.50
GLU 279 B	2.68	4.50
GLU 280 B	7.15	4.50
GLU 291 B	6.50	4.50
GLU 302 B	4.70	4.50
GLU 303 B	6.46	4.50
GLU 357 B	6.82	4.50
GLU 362 B	1.59	4.50
GLU 425 B	4.47	4.50
GLU 426 B	2.74	4.50
GLU 450 B	4.03	4.50
GLU 460 B	8.53	4.50
GLU 492 B	5.92	4.50
GLU 497 B	3.74	4.50
GLU 514 B	6.61	4.50
GLU 530 B	4.84	4.50
GLU 549 B	5.22	4.50
GLU 551 B	4.19	4.50
GLU 568 B	5.23	4.50
GLU 585 B	10.99	4.50
GLU 609 B	2.54	4.50
GLU 624 B	3.72	4.50
GLU 630 B	3.15	4.50
GLU 631 B	7.26	4.50
GLU 659 B	4.26	4.50
GLU 665 B	3.47	4.50
GLU 715 B	3.79	4.50

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GLU 743 B    4.13      4.50
GLU 744 B    4.28      4.50
GLU 748 B    3.86      4.50
GLU 775 B    4.27      4.50
GLU 779 B    4.64      4.50
GLU 789 B    5.92      4.50
C-  807 B    3.17      3.20
HIS 272 B    6.27      6.50
HIS 374 B   -2.00      6.50
HIS 376 B    3.00      6.50
HIS 459 B   -0.21      6.50
HIS 471 B    6.75      6.50
HIS 486 B   -4.46      6.50
HIS 509 B    1.72      6.50
HIS 512 B    1.30      6.50
HIS 520 B    3.76      6.50
HIS 531 B    6.21      6.50
HIS 552 B    2.77      6.50
HIS 560 B    1.91      6.50
HIS 561 B    5.65      6.50
HIS 589 B    1.03      6.50
HIS 655 B    3.30      6.50
HIS 719 B    6.35      6.50
HIS 720 B    3.44      6.50
HIS 773 B    6.76      6.50
HIS 782 B    6.61      6.50
CYS 495 B   12.64      9.00
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CYS 559 B   13.26      9.00
CYS 757 B   12.64      9.00
TYR 247 B   19.13     10.00
TYR 251 B   16.45     10.00
TYR 274 B   10.29     10.00
TYR 277 B   11.88     10.00
TYR 316 B   13.35     10.00
TYR 320 B   12.91     10.00
TYR 427 B   15.98     10.00
TYR 479 B   12.32     10.00
TYR 643 B   16.38     10.00
TYR 647 B   13.31     10.00
TYR 660 B   12.67     10.00
TYR 712 B   13.90     10.00
TYR 713 B   14.77     10.00
TYR 725 B   15.83     10.00
TYR 737 B   10.36     10.00
TYR 781 B   10.72     10.00
LYS 240 B    9.69     10.50
LYS 241 B   10.51     10.50
LYS 245 B   10.48     10.50
LYS 258 B   10.50     10.50
LYS 282 B   10.96     10.50
LYS 287 B    8.08     10.50
LYS 301 B   10.45     10.50
LYS 321 B    9.00     10.50
LYS 327 B   10.56     10.50
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LYS 330 B    9.91     10.50
LYS 336 B    9.98     10.50
LYS 340 B   10.25     10.50
LYS 347 B    7.98     10.50
LYS 418 B    9.40     10.50
LYS 436 B    6.60     10.50
LYS 478 B   10.78     10.50
LYS 526 B   10.48     10.50
LYS 564 B    9.78     10.50
LYS 567 B   10.54     10.50
LYS 620 B    9.18     10.50
LYS 622 B   10.22     10.50
LYS 623 B   10.77     10.50
LYS 629 B   11.38     10.50
LYS 632 B   10.43     10.50
LYS 641 B   10.24     10.50
LYS 646 B    5.42     10.50
LYS 668 B    9.14     10.50
LYS 683 B    8.92     10.50
LYS 689 B    7.92     10.50
LYS 722 B   11.31     10.50
LYS 724 B    9.60     10.50
LYS 739 B   10.02     10.50
LYS 742 B    9.87     10.50
LYS 755 B   10.79     10.50
LYS 762 B    7.28     10.50
LYS 763 B   10.36     10.50
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LYS 788 B   10.24     10.50
LYS 793 B   11.38     10.50
LYS 797 B    9.81     10.50
ARG 244 B   12.75     12.50
ARG 260 B   12.41     12.50
ARG 290 B   12.92     12.50
ARG 414 B   12.51     12.50
ARG 415 B   11.60     12.50
ARG 422 B   13.12     12.50
ARG 506 B   11.54     12.50
ARG 576 B   11.24     12.50
ARG 578 B   10.49     12.50
ARG 606 B   16.57     12.50
ARG 613 B   11.68     12.50
ARG 627 B   12.65     12.50
ARG 639 B   13.61     12.50
ARG 642 B   11.13     12.50
ARG 714 B   13.98     12.50
ARG 749 B    9.71     12.50
ARG 758 B   11.10     12.50
N+  239 B    8.37      8.00
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