

SI Table 1. A consolidated list of dynamically stable^a k=3 clique/communities^x in five different systems A, B, C, D, and E^y for Imin=3%.

MetRS	MetRS+ Met(L1)	MetRS+ ATP(L2)	MetRS+ MetAMP(L3)	tRNA +MetAMP EI (0.5-5.5ns)	tRNA +MetAMP EII (5.5-10.0ns)
:118F 197F 311G	:118F 197F 311G	:118F 197F 311G	:118F 197F 311G	:118F 197F 311G	:118F 197F 311G
:120K 193D 228Q	:120K 193D 228Q	:120K 193D 228Q	:120K193D228Q	:122R 191F 228Q	:122R 191F 228Q
:122R 191F 228Q	:122R 191F 228Q	:122R191F 228Q	:454Y 458Q 476I	:417L 454Y 479M	:417L 454Y 479M
:417L 454Y 479M	:417L454Y 479M	:417L 454Y 479M	:417L454Y479M	414D	
483L					
	:101E 266N 95H	:101E 266N 95H	:101E 266N 95H	:101E 266N 95H	
:266N 270K 93N	:266N 270K 93N	:266N 270K 93N	:266N 270K 93N	:266N 270K 93N	:266N 270K 93N
:412L418Y 482N	:412L418Y482N	:412L 418Y 482N	:412L 418Y 482N	:412L 418Y 482N	:412L 418Y 482N
	517Q		517Q	517Q	517Q
:428I 444I 490Y	:428I 444I 490Y	:428I 444I 490Y	:428I 444I 490Y	:418Y 422T 486V	:418Y 422T 486V
:486V 490Y 515I	:486V 490Y 515I	:486V 490Y 515I	:486V 490Y 515I	515I	:486V 490Y 515I
					:428I 444I 490Y
:292F 321F 435R	:290Y 292F 321F	:290Y 292F 321F	:292F 321F 34W	:428I 432W 444I	
	34W	34W 435R	290Y	490Y	
:33V 360T 437F					
	:295K325Y369D	:33V 360T 437F	:295K325Y369D	:295K 324G 325Y	
:295K 325Y 369D	324G		324G	369D	
324G					
	:205T 218M 222F		:205T 218M 222F		:357Y 384D 445M
:205T 218M 222F	210L 302S				
			:357Y 380R 384D		
:357Y 380R 384D	:357Y 384D 445M	:357Y 384D 388K			
:358Y 376D 380R	380R	445M			
:129D 136L 175S	:129D 136L 175S	:129D 132K 136L	:129D 132K 136L	:129D 136L 175S	:129D 132K 136L
178S	178S	175S 178S	175S 178S	178S	175S 178S
:136L 140F 56T		:136L 140F 56T	:136L 140F 60L		
		60L			
:22L 346W 355L	:22L 346W 355L				
:346W 50F 542L					
	:358Y362K376D				
:189H 234D 248K	:189H 230D 233R	:189H 234D 248K	:189H234D248K		
187S					
	:128Y 135F 185R	:128Y 135F 185R	:128Y 135F185R	:128Y 135F 185R	:128Y 135F 185R
	:187S 234D 248K	:126Q 135F 230D			:126Q 135F 187S
	135F	233R			

SI Table 1 (continued)

MetRS	MetRS+ Met(<i>L1</i>)	MetRS+ ATP(<i>L1</i>)	MetRS+ MetAMP(<i>L3</i>)	tRNA +MetAMP EI (0.5-5.5ns)	tRNA+MetAMP EII (5.5-10ns)
:110Y 242I 250F 119I 190F 232S	:110Y 242I 250F 119I 190F 232S	:110Y 244N 250F 114K 119I 190F 232S 242I	:110Y 242I 250F 119I 190F 232S :102N 106S 240F 250F 255D 258I 54H	:110Y 114K 119I :110Y 242I 250F	:110Y 242I 250F
:253W 300F 304F 229W	:264F 280Y 8L 277F 281W 289L 46N	:253W 300F 304F 229W	:221W 299Y 303L :229W 253W 299Y		
:264F 46N 280Y 277F 281W 289L 8L	:214V 293I 298V 322V :293I (#297I 301H 253W <i>L1</i>) 13L (:#260Y 291H 305W 301H) 10T :256A 52D <i>L1</i> :204W 305W 316K :200M 310E 316K	:264F 277F 280Y 281W 289 L46N 8L :105L 265K 277F	:264F 280Y 281W 289L 46N 8L :261M 281W 305W	:264F 280Y 281W 289L 46N 8L	:264F 280Y 281W 46N 8L
:293I 297I 301H :293I 298V 322V		:293I 297I 301H :291H 301H 305W :10T 260Y 291H :204W 305W 316K :200M 310E 316K	:293I 297I 301H <i>L3</i> 13L 10T (#260Y 291H 301H 305W) :27E 323H 294G <i>L3</i>	#253W 293I 297I 301H <i>L3</i> :293I 298V 322V :52D 256A <i>L3</i> :13L 260Y <i>L3</i> :10T 260Y 291H	#253W 293I 297I 301H <i>L3</i> :293I 298V 322V :52D 256A <i>L3</i> :13L 260Y <i>L3</i> :10T 260Y 291H
:354S 377F 381V 534I	:145C 148C 153Q 158C 165Y 169E	:27E 323H 294G <i>L2</i> : 21H 333M <i>L2</i> : 23D 326V <i>L2</i> : 15Y 139R <i>L2</i> : 325Y 332K <i>L2</i>	:21H 333M <i>L3</i> :52D 256A <i>L3</i> :204W 305 W316K :200M 310E316K	:350F 534I 538Q :346W 350F 377F 542L :346W 355L 87F	
:397A 505F 527F	:23G 326V 333M :26L 326V 359Y		:351D 354S 531Y 381V		:346W 355L 87F
:353D 495L 498L	:102N 240F 255D	:346W 350F 377F 355L 542L	:346W 350F 377F 381V 534I 538Q 542L	:200M 310E 316K	:200M 310E 316K
:508T 519L 522H	:30Q 363L 437F 323H :27E 294G 323H :341I 542L 546S :37Y 432W 512W	:354S 381V 385I 531Y 534I	:341I 542L 546S :346W 355L 87F	:205T 218M 222F :508T 519L 522H	
		:397A 505F 527F :356R 36R 495L :102N 106S 240F :194L 226L 303L :27E 294G 323H :347L 352A 87F :391N 395R 452N :492K 499T 503E	:356R 36R 495L :37Y 432W 512W :145C 148C 165Y 153Q :214V 322V 367I 105L 265K 277F :492K 499T 503E :396N 455V 459A :30Q 323H 435R	:134M 140F 177V :328V 333M 339T :378V 536M 539V :26L 326V 359Y :30Q 363L 435R :399F 473L 477C	:353D 495L 498L :508T 519L 522H :378V 536M 539V :30Q 363L 435R 399F 473L 477C

L1, ***L2*** and ***L3*** are the ligands Met, ATP and MetAMP respectively.

^a : 50% of snapshots in which the listed residues appear as cliques.

^x : The list of residues in a clique/community begins with the symbol “:” and each clique /community is separated by a blank space.

^y : The analysis of system E (presented in this Table and in Table 2) is carried out in two parts

(EI and EII), which exhibited different RMSD values in Figure 1b.

The list beginning with the symbol “#” are the cliques/communities with k=4 (clique of residues 260Y, 301H, 305W, 291H is present in systems B and D and of residues Met/MetAMP, 253W, 301H and 297I is present in system B and E). More than 3 residues representing communities, which share 2 residues in common are highlighted. The cliques/communities connected by a single residue are also highlighted and have been written one below the other without a blank space. The three largest communities in system D and their variants in other systems are highlighted in blue, magenta and red color boxes.

SI Table 2. A list^{*} of dynamically stable hubs^x ($I_{\min}=3\%$) in systems^y A, B, C, D, and E (EI and EII).

RES	A	B	C	D	EI	EII
8L	√	√	√	√	√	√
13L		√		√		√
20I		√		√	√	
24H			√	√		
28H	√		√	√		
30Q		√	√	√	√	√
32D	√	√	√	√	√	√
34W		√	√	√		
35V	√	√	√	√	√	√
36R	√		√	√	√	
37Y	√	√	√	√	√	√
38Q						√
39R	√	√	√	√		
47F	√					
49C				√		
54H	√	√	√	√	√	√
60L			√	√	√	
68T						√
84F	√	√	√	√	√	√
87F	√	√	√	√	√	√
91Y	√	√	√	√	√	√
93N	√	√	√	√	√	√
94Y	√	√		√	√	
95H		√		√	√	
106S			√	√		
110Y	√	√	√	√	√	√
126Q			√			√
129D	√	√	√	√	√	√
135F		√	√	√	√	√
136L	√	√	√	√	√	√
140F	√	√	√	√	√	
145C		√		√		
148C		√		√		
153Q		√		√		
158C		√				
175S	√	√	√	√	√	√
189H	√	√	√	√	√	
190F	√	√	√	√		
191F	√	√	√		√	√
197F	√	√	√	√	√	√
204W	√	√	√	√		
218M	√	√		√	√	√
221W				√		√
229W	√	√	√	√		
233R	√	√	√	√		
234D	√	√	√	√		
237Y		√	√	√	√	√
240F	√	√	√	√		
242I	√	√	√	√	√	√
250F	√	√	√	√	√	√
253W	√	√	√	√	√	√
255D		√		√		

RES	A	B	C	D	EI	EII
258I				√	√	
260Y	√	√	√	√	√	√
264F	√	√	√	√	√	√
265K		√	√	√		
266N	√	√	√	√	√	√
277F	√	√	√	√		
280Y	√	√	√	√	√	√
281W	√	√	√	√	√	√
289L	√	√	√	√	√	
291H	√	√	√	√	√	√
292F	√	√	√	√	√	√
293I	√	√	√	√	√	√
299Y		√		√		
300F	√	√		√		
301H	√	√	√	√	√	√
304F	√	√	√	√		
305W	√	√	√	√		
316K	√	√	√	√	√	√
321F	√	√	√	√		
322V	√	√	√	√	√	√
323H		√	√	√	√	√
326V		√	√		√	
346W	√	√	√	√	√	√
350F		√	√	√	√	√
356R		√	√	√		
357Y	√	√	√	√		√
358Y	√	√	√	√		
359Y		√	√		√	
377F	√	√	√	√	√	√
381V	√	√	√	√		
382N						√
384D	√	√	√	√		√
395R			√	√		
412L	√	√	√	√	√	√
417L	√	√	√	√	√	√
418Y	√	√	√	√	√	√
421F	√	√	√	√	√	√
432W	√	√	√	√	√	√
435R	√	√	√	√	√	√
437F	√	√	√	√	√	√
454Y	√	√	√	√	√	√
479M	√	√	√	√	√	√
484F		√	√			
486V	√	√	√	√	√	√
490Y	√	√	√	√	√	√
495L	√	√	√	√	√	√
503E		√	√	√		
512W		√	√	√		
534I	√	√	√	√	√	
542L		√	√	√		

^x : 50% of snapshots in which the listed residues appear as hubs.

^{*y} : All those residues which appear as hubs in at least one of the simulations are listed. A

(√) in the 1st column of a given system (e.g. A or B) represents that the residue is a hub in that simulation. A (√) in the 2nd column indicates that the residue is part of a clique.

^{*} : A: MetRS; B: MetRS+Met; C: MetRS+ATP; D: MetRS+MetAMP;

E: MetRS+MetAMP+ tRNA_f^{Met}

SI Table 3. Composition of residues in top three communities in systems D and E.

Community	Res	D [*]	E [*]	CP ^a	Conserved ^b
I	8L	√			
	10T	X	X		√
	13L	√	X		√
	21H	X			√
	27E	X			
	46N	X			
	52D	X	X		√
	200M	X			
	204W	√			
	256A	X	X		√
	260Y	√	X		√
	261M	X			√
	264F	√			
	280Y	√			√
	281W	√ ^o			√
	289L	X			
	291H	√	√ ^o		√
	293I	√	√ ^o		√
	294G	X			√
	297I	X	X		
	301H	√	√		√
	305W	√ ^o	√		√
	310E	X			
	316K	√ ^o			
	323H	√			
	333M	X			
II	87F	√	√	√	
	341I	X			√
	346W	√ ^o	√ ^o	√	
	350F	√	√ ^o	√	
	351D	X			
	354S	X			
	355L	X	X	√	
	377F	√	√	√	√
	381V	√ ^o		√	
	531Y	X		√	√
	534I	√	X	√	
	538Q	X	X	√	
	546S	X			
	542L	√ ^o	X		
III	54H	√			√
	102N	X			√
	106S	X			
	110Y	√	√ ^o		
	119I	X	X		√
	190F	X			
	232S	X			√
	240F	√			√
	242I	X	√		
	250F	√ ^o	X		
	255D	X			√
	258I	√			√

^{*} : The presence of residue in the community is shown by one of the symbols (X), ($\sqrt{}$) or ($\sqrt{\circ}$) where (X) represents a member of the clique, ($\sqrt{}$) represents that the clique member is a hub residue and ($\sqrt{\circ}$) indicates that the clique member is a hub and also connects two cliques.

^a : A ($\sqrt{}$) represents the conservation of the residue along different species of MetRS.

^b : A ($\sqrt{}$) represents the participation of the residue in communication paths (CP).

SI Figure 4. Sequence alignment of MetRSs. Abbreviation are as follows: T.ther, T. thermophilus; B.su, Bacillus subtilis; M.ge, Mycoplasma genitalium; M.p, Mycoplasma pneumoniae; A.aeol, A. aeolicus; H.i, Haemophilus influenzae; M.t, Methanobacterium thermoautotrophicum; B.b, Borrelia burgdorferi; T.p, Treponema pallidum; B. st, Bacillus stearothermophilus; S. ce, S. cerevisiae nuclear; HUMAN, Homo Sapiens. The symbols '*' , ':' and '.' below the alignment correspond respectively to completely conserved, partially conserved and mutationally conserved residues. Residues conserved along different families of MetRS and participating in communication paths and the three largest communities are highlighted in different colors. The markings α , ε , π on top of the alignment indicate the residues involved in top three communities, communication path and in both, respectively.

[illegible]