

Table S1. Amino acid usage in multispanning membrane proteins (mem), cytoplasmic proteins (cyto), and multispanning/cytoplasmic (mem/cyto)

Organism-location	W	F	L	I	S	Y	M	V	T	C	A	G	P	N	H	Q	R	K	D	E
ECOLI cyto	1.13	3.53	10.16	5.86	5.09	2.56	2.77	7.13	5.15	1.17	9.48	7.25	4.30	3.69	2.61	4.49	5.82	4.79	5.87	7.16
ECOLI mem	2.24	5.67	13.76	7.88	6.12	2.65	3.72	8.24	5.27	0.93	10.18	8.17	4.10	3.00	1.63	3.13	4.24	3.03	2.88	3.16
ECOLI mem/cyto	1.98	1.61	1.35	1.34	1.20	1.04	1.35	1.16	1.02	0.80	1.07	1.13	0.96	0.81	0.62	0.70	0.73	0.63	0.49	0.44
STRCO cyto	0.97	2.61	9.48	3.84	4.56	2.05	1.94	8.99	5.92	0.72	12.54	9.46	5.23	2.06	2.27	2.74	7.38	3.32	6.75	7.19
STRCO mem	1.92	4.60	11.75	5.02	5.25	2.20	2.50	9.49	5.88	0.57	13.20	10.40	4.89	1.99	1.69	2.41	5.82	2.51	3.96	3.91
STRCO mem/cyto	1.98	1.76	1.24	1.31	1.15	1.07	1.29	1.05	0.99	0.78	1.05	1.10	0.94	0.97	0.74	0.88	0.79	0.75	0.59	0.54
MYCLE cyto	0.99	2.72	9.81	4.72	5.42	2.12	2.08	9.58	5.90	0.93	11.68	8.76	4.64	2.45	2.30	3.08	7.20	2.99	6.69	5.93
MYCLE mem	1.90	4.53	11.75	6.14	5.82	2.30	2.60	9.82	6.55	0.89	11.68	8.67	4.88	2.62	1.93	2.80	5.93	2.23	3.71	3.27
MYCLE mem/cyto	1.92	1.66	1.20	1.30	1.07	1.08	1.25	1.03	1.11	0.96	1.00	0.99	1.05	1.07	0.84	0.91	0.82	0.75	0.55	0.55
BACSU cyto	0.71	3.63	8.96	6.97	5.41	3.16	2.80	7.17	5.28	0.84	7.71	7.33	3.65	3.78	2.49	3.75	4.50	7.30	5.89	8.67
BACSU mem	1.40	6.74	12.47	9.89	6.68	3.17	3.46	7.81	5.40	0.66	8.56	7.87	3.39	3.03	1.62	2.83	3.06	5.07	2.95	3.93
BACSU mem/cyto	1.98	1.86	1.39	1.42	1.23	1.00	1.24	1.09	1.02	0.79	1.11	1.07	0.93	0.80	0.65	0.76	0.68	0.69	0.50	0.45
ARCFU cyto	0.85	3.72	8.30	7.10	4.91	3.23	2.70	9.27	4.06	1.02	8.05	7.55	3.87	2.87	1.52	2.08	6.07	7.64	5.38	9.82
ARCFU mem	1.44	7.10	13.42	9.18	6.64	4.10	2.33	9.30	4.52	0.56	9.78	7.62	3.78	2.54	1.10	1.63	3.74	3.84	2.85	4.53
ARCFU mem/cyto	1.70	1.91	1.62	1.29	1.35	1.27	0.87	1.00	1.11	0.54	1.22	1.01	0.98	0.88	0.72	0.78	0.62	0.50	0.53	0.46
METJA cyto	0.57	3.54	8.58	9.82	3.91	3.53	2.54	7.26	4.22	1.23	6.69	6.86	3.62	4.57	1.54	1.67	3.89	10.53	5.72	9.73
METJA mem	1.00	6.61	13.08	13.83	5.99	4.61	2.76	7.39	4.41	0.89	6.74	7.44	3.23	3.74	1.03	1.05	2.32	6.56	3.07	4.25
METJA mem/cyto	1.76	1.87	1.52	1.41	1.53	1.30	1.09	1.02	1.05	0.72	1.01	1.09	0.89	0.82	0.66	0.63	0.60	0.62	0.54	0.44
YEAST cyto	0.90	3.97	8.63	6.09	7.77	3.29	1.99	6.23	5.64	1.17	6.61	5.66	4.59	5.53	2.33	3.95	5.04	8.32	5.68	6.59
YEAST mem	1.73	7.17	11.07	7.90	9.38	4.06	2.56	6.60	5.59	2.06	6.05	5.54	4.05	4.53	1.91	2.87	3.93	5.13	3.71	4.15
YEAST mem/cyto	1.93	1.81	1.28	1.30	1.21	1.24	1.28	1.06	0.99	1.76	0.92	0.98	0.88	0.82	0.82	0.73	0.78	0.62	0.65	0.63
ARATH cyto	1.04	4.17	8.64	5.57	7.25	2.89	2.67	7.45	5.26	1.61	7.12	7.33	4.64	3.96	2.25	3.49	5.02	6.85	5.78	7.03
ARATH mem	1.64	6.02	11.08	6.97	8.08	3.20	2.79	7.83	5.53	1.62	7.84	7.21	4.03	3.48	1.78	2.91	4.53	4.90	3.89	4.69
ARATH mem/cyto	1.58	1.44	1.28	1.25	1.11	1.11	1.04	1.05	1.05	1.01	1.10	0.98	0.87	0.88	0.79	0.83	0.90	0.72	0.67	0.67
CAEEL cyto	0.93	3.84	8.59	5.77	6.93	2.89	2.61	6.80	5.41	1.49	7.54	6.02	3.99	4.56	2.37	4.25	5.42	7.02	6.05	7.53
CAEEL mem	1.66	7.07	10.82	8.52	7.91	4.39	3.04	7.19	6.06	2.25	6.20	4.76	4.05	4.21	2.13	3.13	4.32	4.56	3.56	4.15
CAEEL mem/cyto	1.79	1.84	1.26	1.48	1.14	1.52	1.17	1.06	1.12	1.51	0.82	0.79	1.01	0.92	0.90	0.74	0.80	0.65	0.59	0.55
MOUSE cyto	1.13	3.66	9.51	4.62	7.31	2.75	2.45	6.31	5.02	2.09	6.83	6.37	5.87	3.61	2.41	4.75	5.43	6.62	5.41	7.84
MOUSE mem	1.78	5.93	12.70	6.12	8.05	3.53	2.75	7.51	5.60	2.71	7.44	6.28	4.77	3.35	2.25	3.27	4.68	3.81	3.26	4.22
MOUSE mem/cyto	1.58	1.62	1.33	1.33	1.10	1.28	1.12	1.19	1.12	1.30	1.09	0.99	0.81	0.93	0.93	0.69	0.86	0.58	0.60	0.54
HUMAN cyto	1.13	3.64	9.56	4.67	7.20	2.76	2.39	6.20	5.02	2.04	6.87	6.47	5.87	3.64	2.39	4.74	5.43	6.67	5.33	7.96
HUMAN mem	1.63	6.04	12.91	6.37	7.93	3.53	2.89	7.50	5.62	2.79	7.54	6.22	4.86	3.30	2.33	3.15	4.49	3.76	3.16	3.99
HUMAN mem/cyto	1.44	1.66	1.35	1.36	1.10	1.28	1.21	1.21	1.12	1.37	1.10	0.96	0.83	0.91	0.98	0.67	0.83	0.56	0.59	0.50

Table S2. Summary of Table S1 and average \pm SD

Organism mem/cyto	W	F	L	I	S	Y	M	V	T	C	A	G	P	N	H	Q	R	K	D	E
ECOLI	1.98	1.61	1.35	1.34	1.20	1.04	1.35	1.16	1.02	0.80	1.07	1.13	0.96	0.81	0.62	0.70	0.73	0.63	0.49	0.44
STRCO	1.98	1.76	1.24	1.31	1.15	1.07	1.29	1.05	0.99	0.78	1.05	1.10	0.94	0.97	0.74	0.88	0.79	0.75	0.59	0.54
MYCLE	1.92	1.66	1.20	1.30	1.07	1.08	1.25	1.03	1.11	0.96	1.00	0.99	1.05	1.07	0.84	0.91	0.82	0.75	0.55	0.55
BACSU	1.98	1.86	1.39	1.42	1.23	1.00	1.24	1.09	1.02	0.79	1.11	1.07	0.93	0.80	0.65	0.76	0.68	0.69	0.50	0.45
ARCFU	1.70	1.91	1.62	1.29	1.35	1.27	0.87	1.00	1.11	0.54	1.22	1.01	0.98	0.88	0.72	0.78	0.62	0.50	0.53	0.46
METJA	1.76	1.87	1.52	1.41	1.53	1.30	1.09	1.02	1.05	0.72	1.01	1.09	0.89	0.82	0.66	0.63	0.60	0.62	0.54	0.44
YEAST	1.93	1.81	1.28	1.30	1.21	1.24	1.28	1.06	0.99	1.76	0.92	0.98	0.88	0.82	0.82	0.73	0.78	0.62	0.65	0.63
ARATH	1.58	1.44	1.28	1.25	1.11	1.11	1.04	1.05	1.05	1.01	1.10	0.98	0.87	0.88	0.79	0.83	0.90	0.72	0.67	0.67
CAEEL	1.79	1.84	1.26	1.48	1.14	1.52	1.17	1.06	1.12	1.51	0.82	0.79	1.01	0.92	0.90	0.74	0.80	0.65	0.59	0.55
MOUSE	1.58	1.62	1.33	1.33	1.10	1.28	1.12	1.19	1.12	1.30	1.09	0.99	0.81	0.93	0.93	0.69	0.86	0.58	0.60	0.54
HUMAN	1.44	1.66	1.35	1.36	1.10	1.28	1.21	1.21	1.12	1.37	1.10	0.96	0.83	0.91	0.98	0.67	0.83	0.56	0.59	0.50
Total	19.64	19.04	14.82	14.79	13.19	13.19	12.91	11.92	11.70	11.54	11.49	11.09	10.15	9.81	8.65	8.32	8.41	7.07	6.30	5.77
Average	1.79	1.73	1.35	1.34	1.20	1.20	1.17	1.08	1.06	1.05	1.04	1.01	0.92	0.89	0.79	0.76	0.76	0.64	0.57	0.52
SD	0.19	0.14	0.12	0.07	0.14	0.15	0.14	0.07	0.05	0.38	0.11	0.09	0.07	0.08	0.12	0.09	0.10	0.08	0.06	0.08

Table S3. Phe, Ile, and Leu codon usage in multispanning membrane proteins (mem), cytoplasmic proteins (cyto), and multispanning/cytoplasmic (mem/cyto)

Amino acid name	Codon	mem % usage	Total mem codons	cyto % usage	Total cyto codons	Usage mem/cyto
<i>E. coli</i>						
Phe	TTC	43.66	6,079	48.87	2,662	0.893390628
Phe	TTT	56.34	7,846	51.13	2,785	1.101897125
Ile	ATA	5.85	1,146	3.66	323	1.598360656
Ile	ATC	42.16	8,254	46.9	4,135	0.898933902
Ile	ATT	51.98	10,176	49.43	4,358	1.051588104
Leu	CTA	3.56	1,231	2.68	418	1.328358209
Leu	CTC	10.25	3,544	10.31	1,607	0.994180407
Leu	CTG	50.36	17,418	55.9	8,714	0.900894454
Leu	CTT	9.14	3,160	9.65	1,504	0.947150259
Leu	TTA	12.46	4,311	10.52	1,640	1.184410646
Leu	TTG	14.24	4,926	10.94	1,705	1.301645338
<i>M. Jannaschii</i>						
Phe	TTC	19.85	461	25.55	382	0.776908023
Phe	TTT	80.15	1,862	74.45	1,113	1.076561451
Ile	ATA	44.56	2,192	43.25	1,676	1.030289017
Ile	ATC	10.49	516	10.25	397	1.023414634
Ile	ATT	44.95	2,211	46.5	1,802	0.966666667
Leu	CTA	9.26	433	6.89	240	1.343976778
Leu	CTC	3.72	174	2.73	95	1.362637363
Leu	CTG	3.29	154	1.92	67	1.713541667
Leu	CTT	10.83	506	7.49	261	1.445927904
Leu	TTA	52.63	2,460	60.75	2,116	0.866337449
Leu	TTG	20.26	947	20.21	704	1.002474023
<i>A. thaliana</i>						
Phe	TTC	53.77	11,838	52.37	2,513	1.026732862
Phe	TTT	46.23	10,177	47.63	2,286	0.97060676
Ile	ATA	24.62	6,506	18.04	1,151	1.364745011
Ile	ATC	37.46	9,900	39.35	2,511	0.951969504
Ile	ATT	37.91	10,019	42.61	2,719	0.889697254
Leu	CTA	10.96	4,536	9.75	974	1.124102564
Leu	CTC	18.68	7,730	18.35	1,833	1.017983651
Leu	CTG	9.49	3,927	10.84	1,083	0.875461255
Leu	CTT	26.3	10,886	29.84	2,981	0.881367292
Leu	TTA	13.63	5,640	10.42	1,041	1.30806142
Leu	TTG	20.95	8,672	20.79	2,077	1.007696008
<i>M. musculus</i>						
Phe	TTC	60.84	26,035	53.84	7,667	1.130014859
Phe	TTT	39.16	16,759	46.16	6,574	0.848353553
Ile	ATA	14.08	6,357	15.71	2,780	0.89624443
Ile	ATC	55.33	24,979	49.06	8,684	1.127802691
Ile	ATT	30.59	13,809	35.24	6,237	0.868047673
Leu	CTA	6.88	6,414	7.55	2,866	0.911258278
Leu	CTC	23.08	21,520	18.59	7,059	1.241527703
Leu	CTG	40.72	37,958	40.06	15,210	1.016475287
Leu	CTT	11.8	10,999	13.35	5,070	0.883895131
Leu	TTA	5.35	4,984	7.16	2,717	0.747206704
Leu	TTG	12.18	11,351	13.3	5,050	0.915789474