The Function Wars and How to Survive Them (part 1, work-in-progress)

Biological Information Discussion Group
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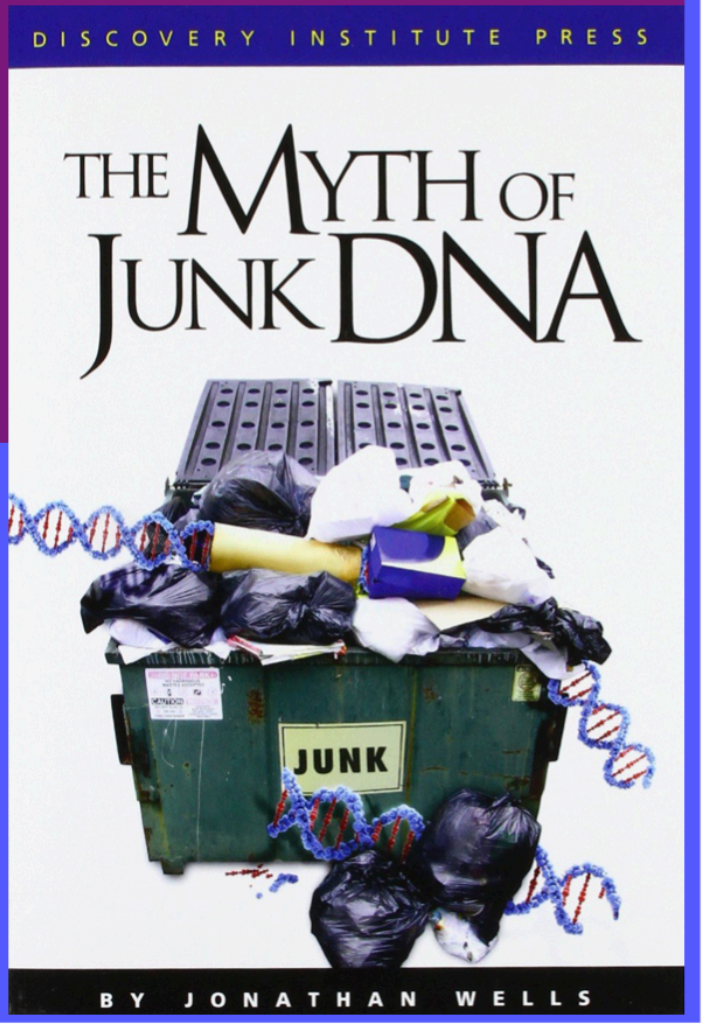
So what are the "Function Wars," and do they involve us?

Most definitely: fear of intelligent design
has, to a remarkable extent, been the
main motive behind much of what has been published
in this area over the past decade.

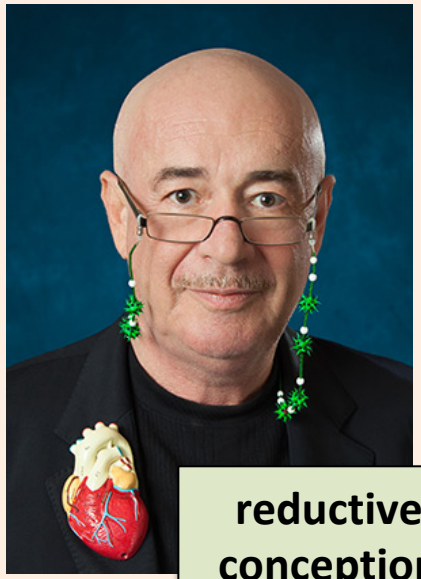
Example: from Dan Graur's 2016 Sinauer textbook,
Molecular and Genome Evolution: **"Because genomes are the products of evolution rather than 'intelligent design,' all genomes contain functional and nonfunctional parts."** (p. 492)

Three problems: (1) If the human genome is indeed devoid of junk DNA as implied by the ENCODE project, then a long, undirected **evolutionary process**, cannot explain the human genome.

If, on the other hand, organisms are **designed**, then all DNA, or as much as possible, is expected to exhibit function. If **ENCODE** is **right**, then **Evolution** is **wrong**.



Dramatis personae



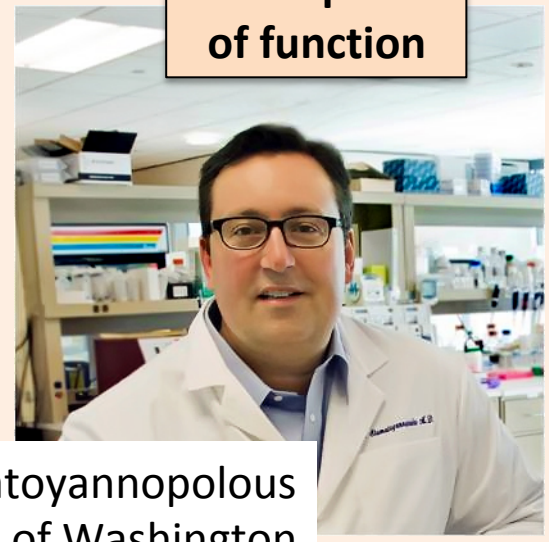
Dan Graur
University of Houston

reductive conception of function

W. Ford Doolittle
Dalhousie University

John Mattick
Garvan Institute of Medical Research

expansive conception of function



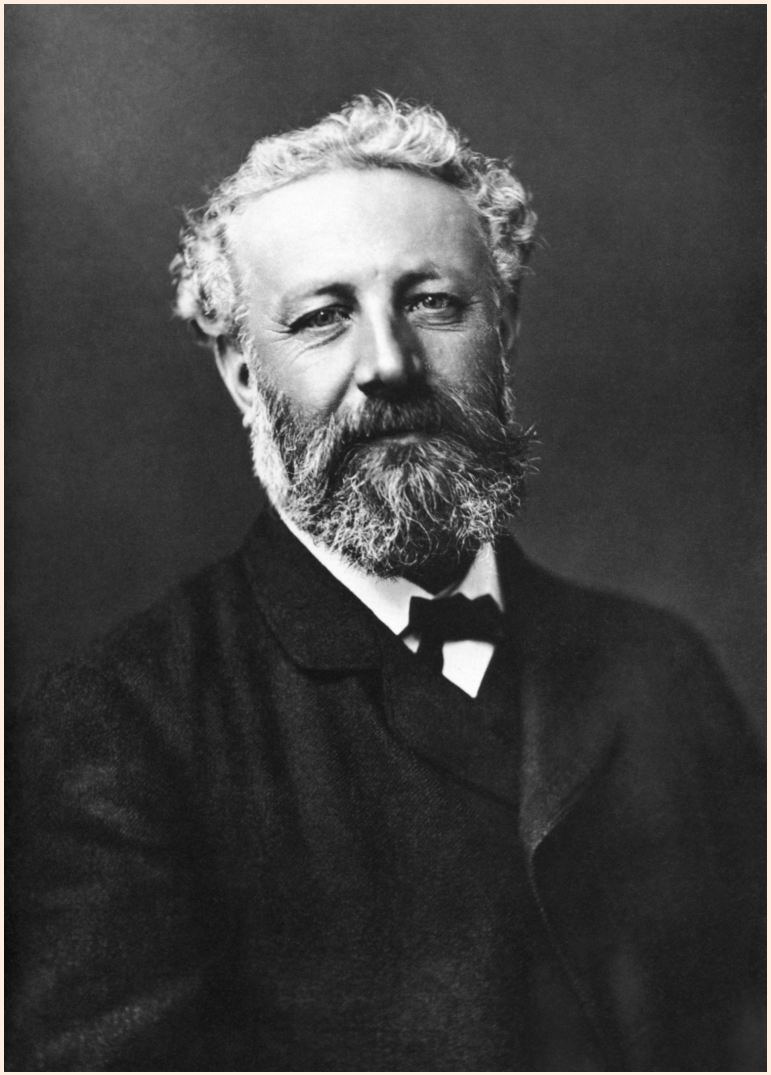
John Stamatoyannopolous
University of Washington

Thesis for discussion: the unreasonable, albeit entirely understandable, **fear of intelligent design** − along with the insistence that "nothing in biology makes sense except in the light of evolution" (Saint Theodosius, 1972) − is hindering biological discovery along several important fronts.

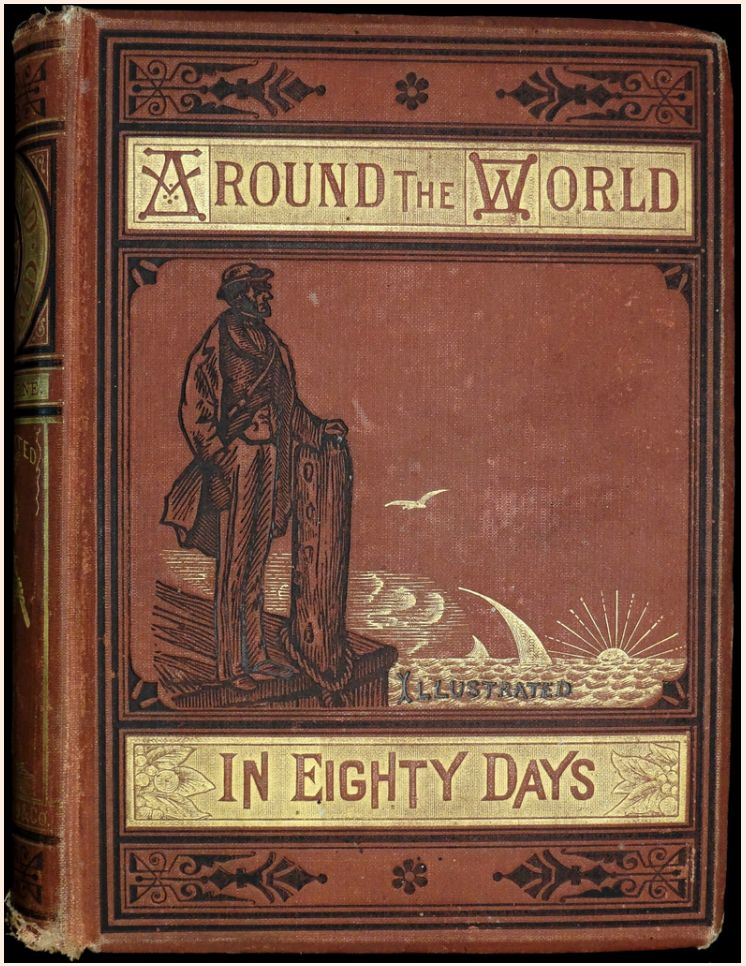
Challenge to be met: how can we help diminish this fear of ID, which is not going away any time soon, while not surrendering any potentially fruitful design insights of our own?

Let’s start with what Daniel Dennett calls an “**intuition pump**”...

...in this case, a memorable episode from a late Victorian novel, later rendered in a classic 1956 movie.

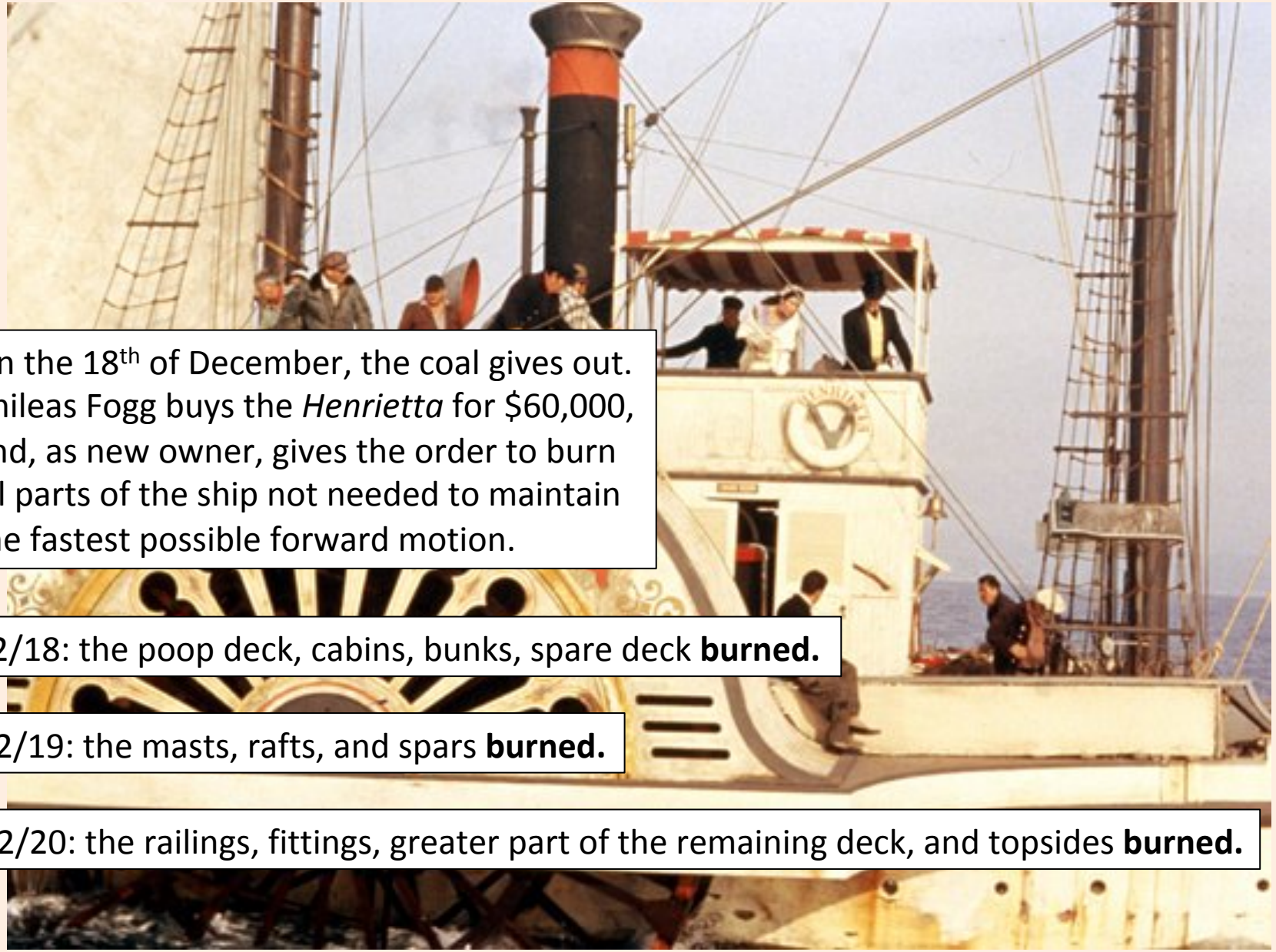


Jules Verne (1828-1905)



Around the World in 80 Days
(1873, French;
1874, first English edition)

"The next day was the 12th of December. From seven in the morning of the 12th to a quarter before nine in the evening of the 21st there were nine days, thirteen hours, and forty-five minutes."

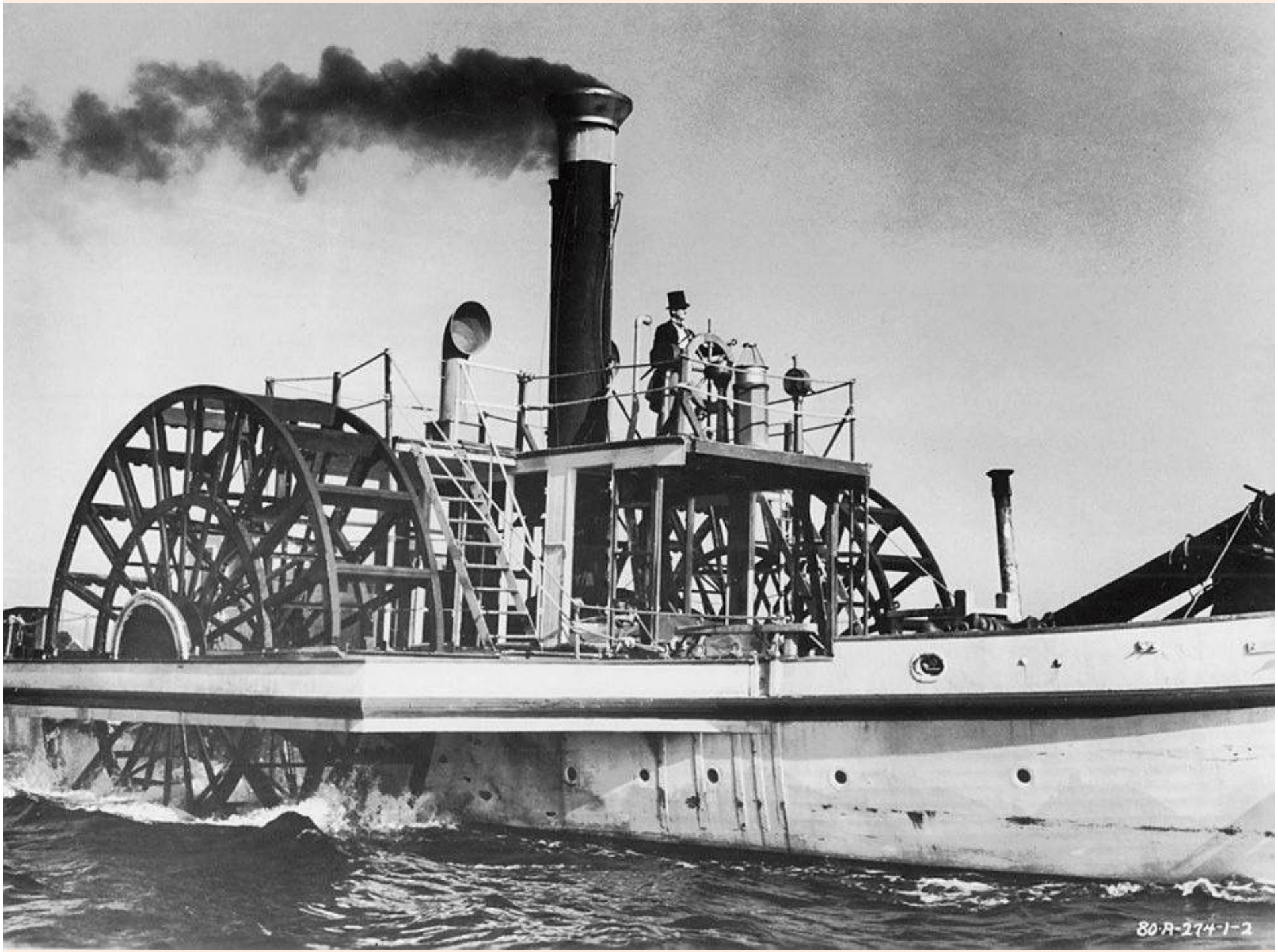


On the 18th of December, the coal gives out. Phileas Fogg buys the *Henrietta* for $60,000, and, as new owner, gives the order to burn all parts of the ship not needed to maintain the fastest possible forward motion.

12/18: the poop deck, cabins, bunks, spare deck **burned.**

12/19: the masts, rafts, and spars **burned.**

12/20: the railings, fittings, greater part of the remaining deck, and topsides **burned.**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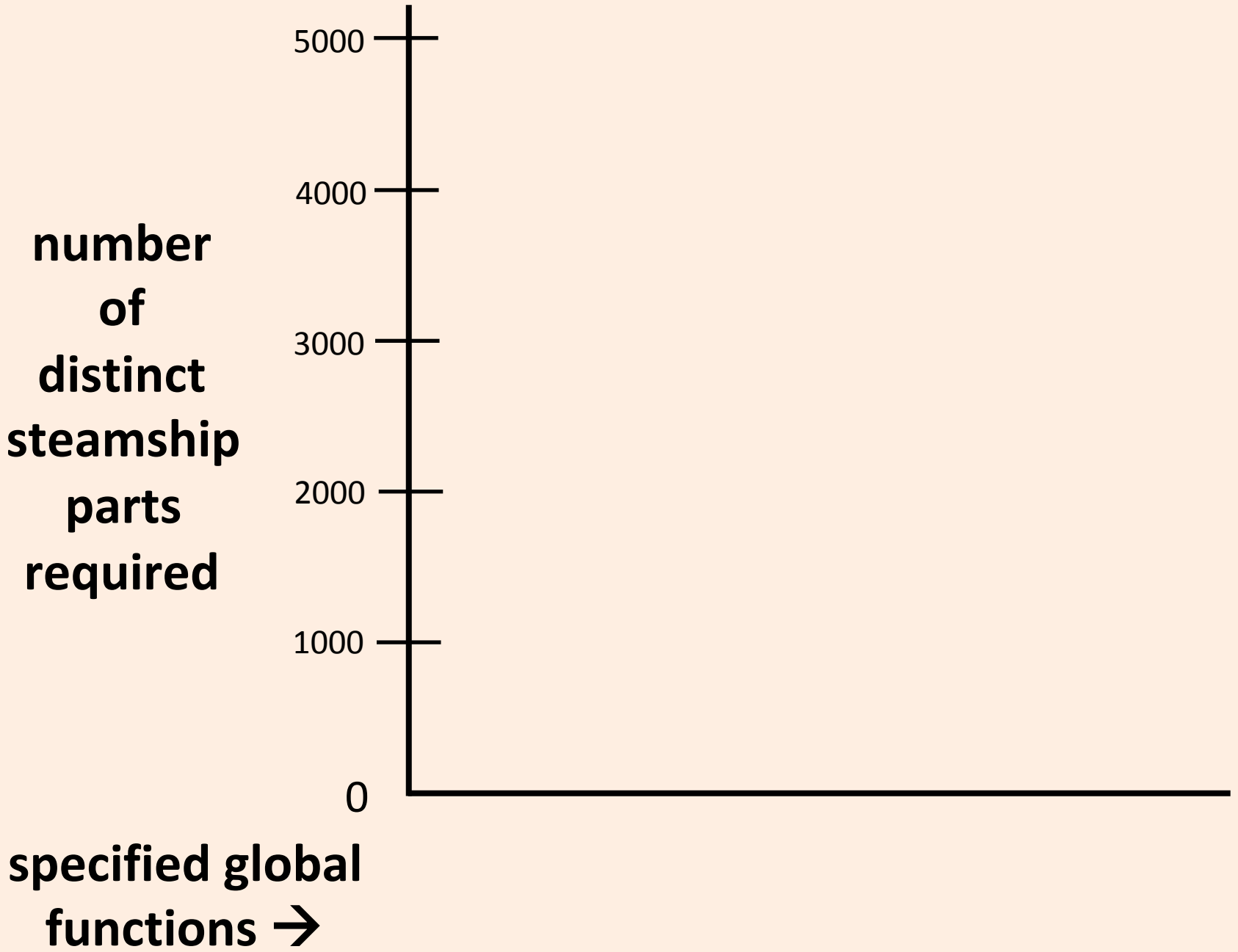
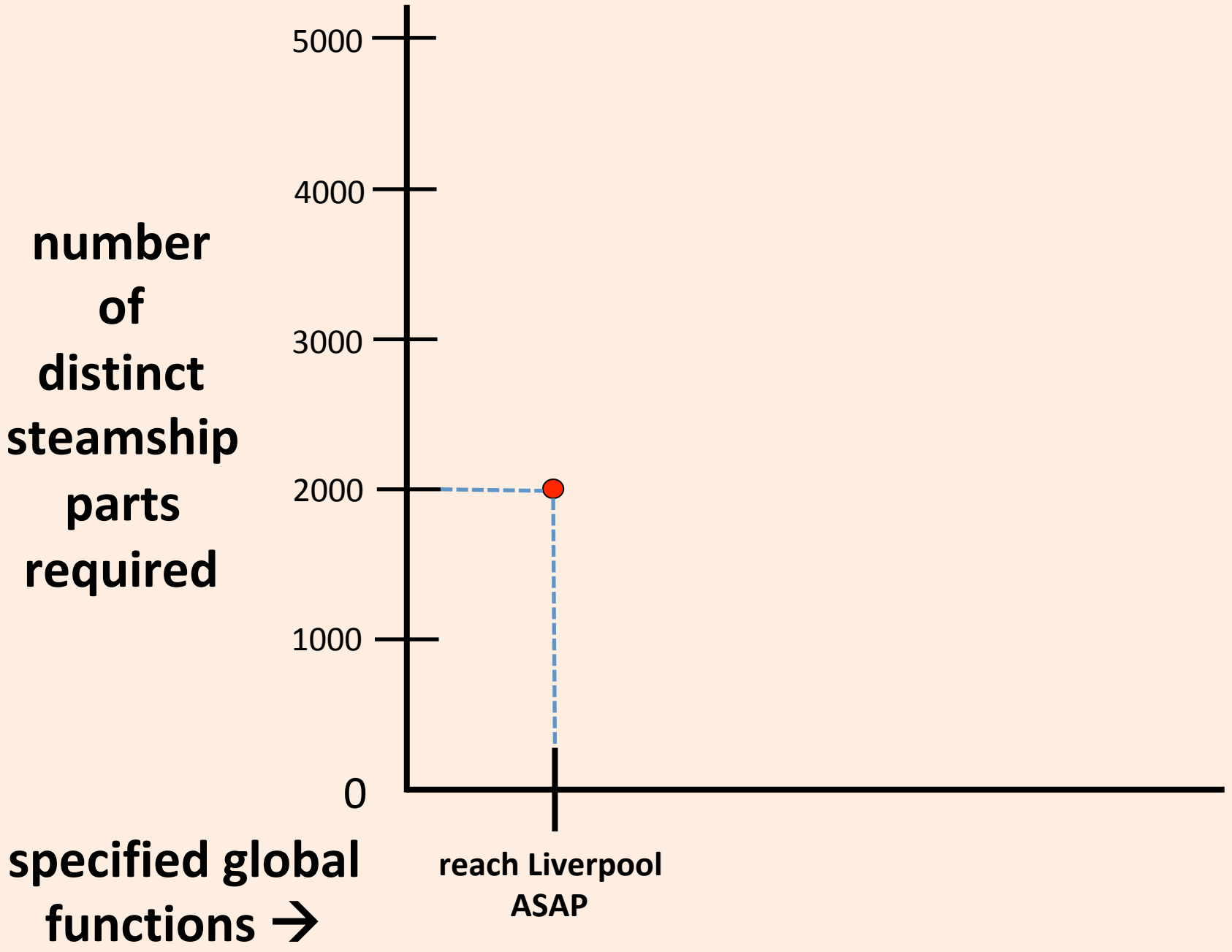
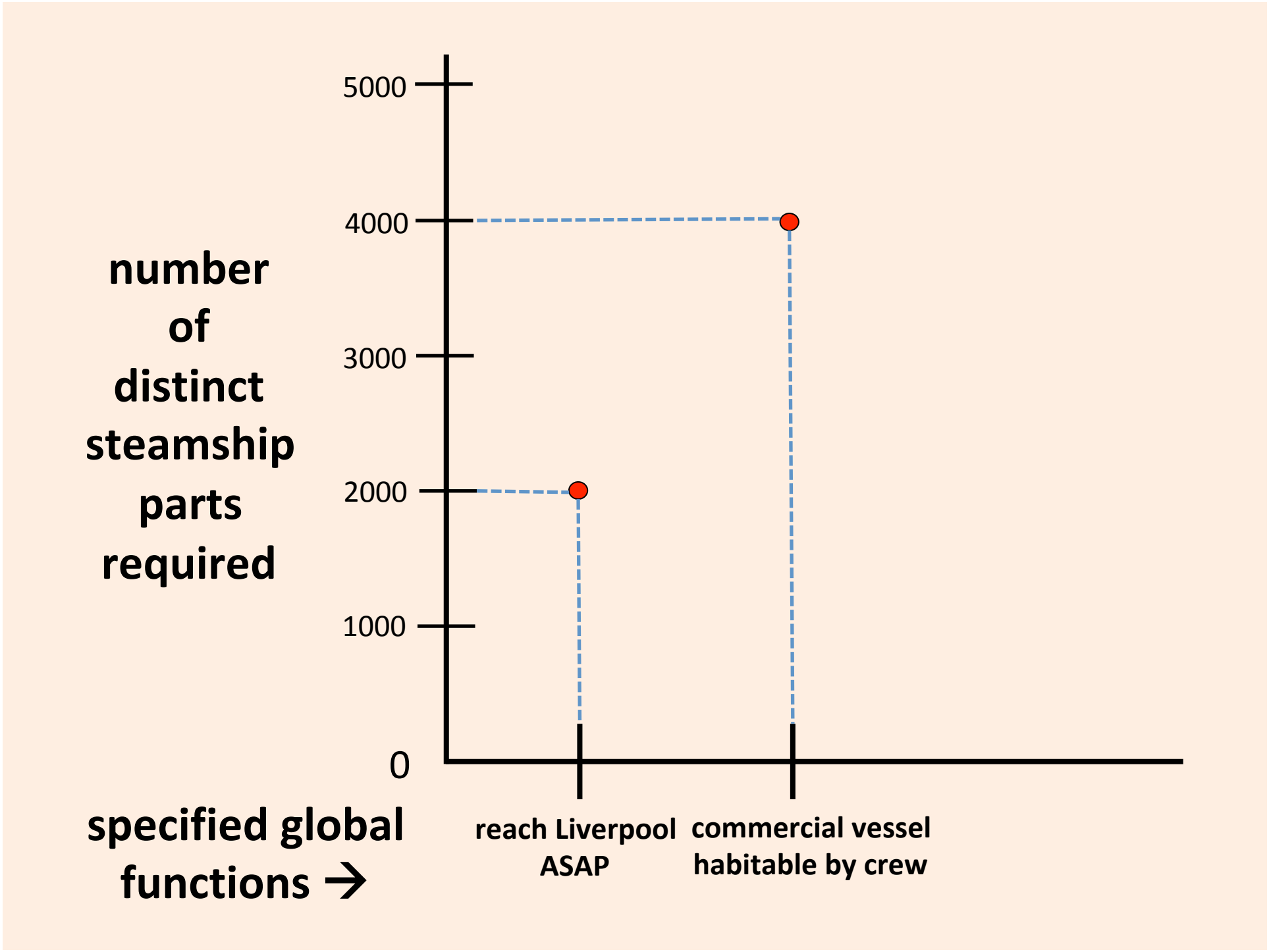
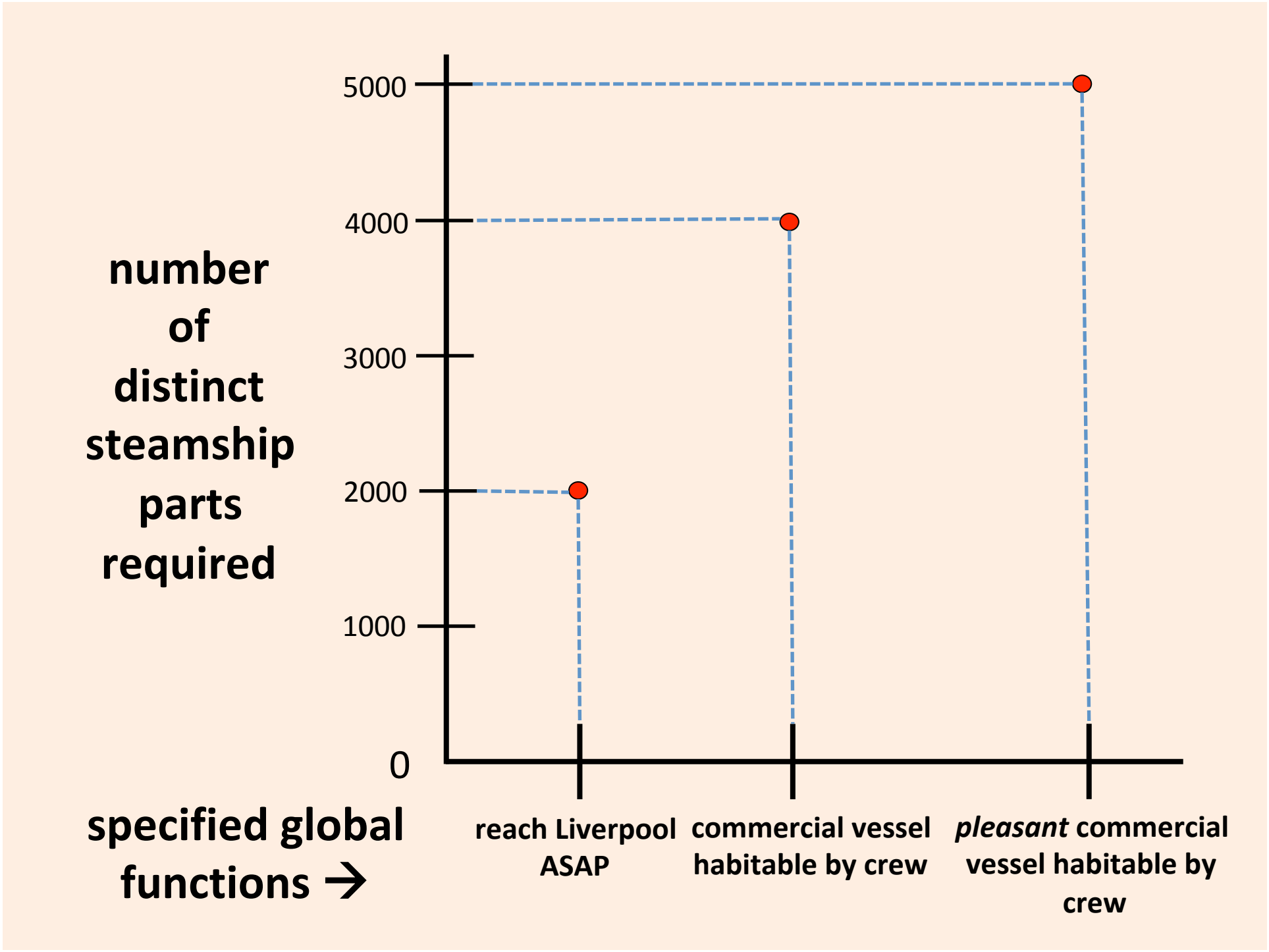
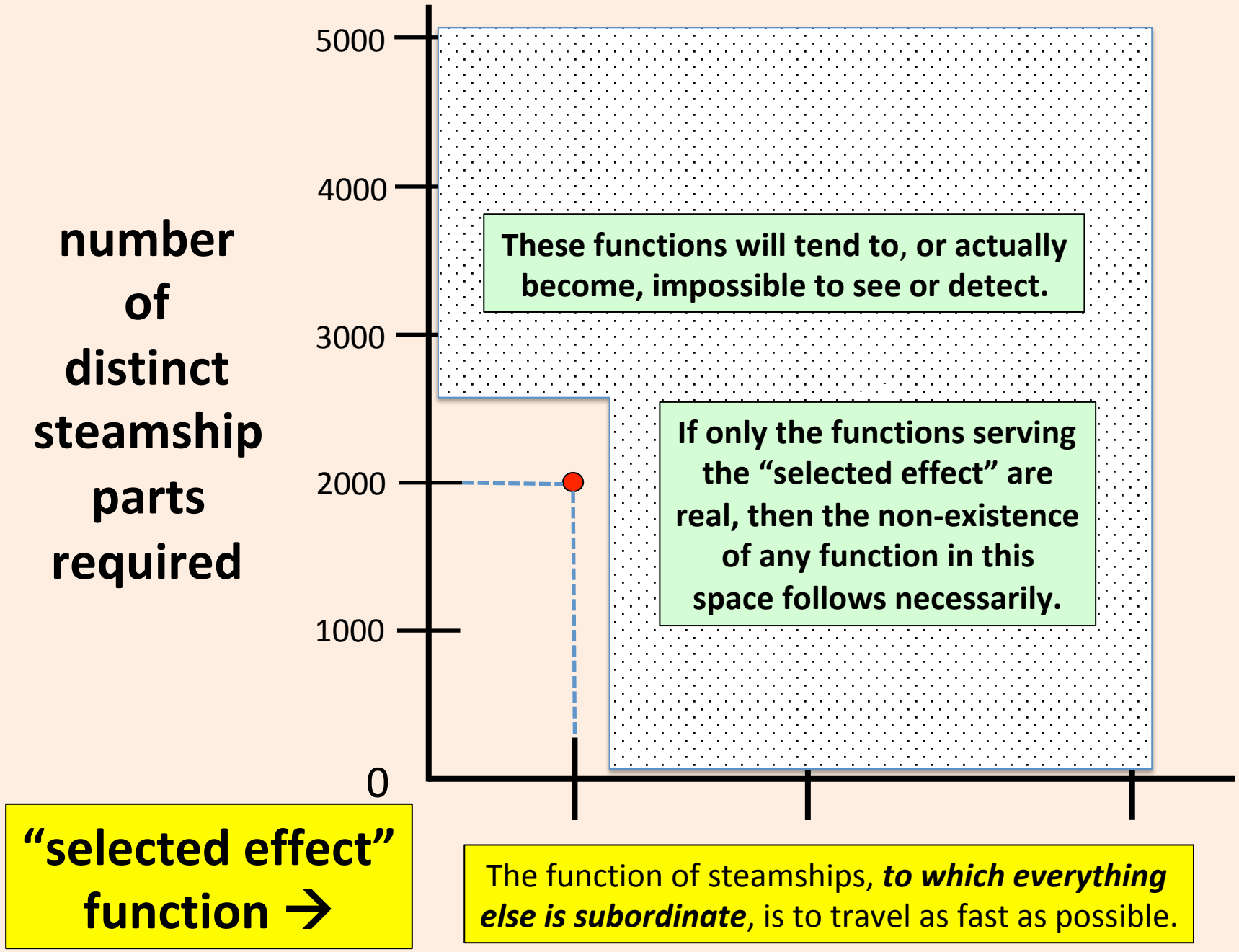
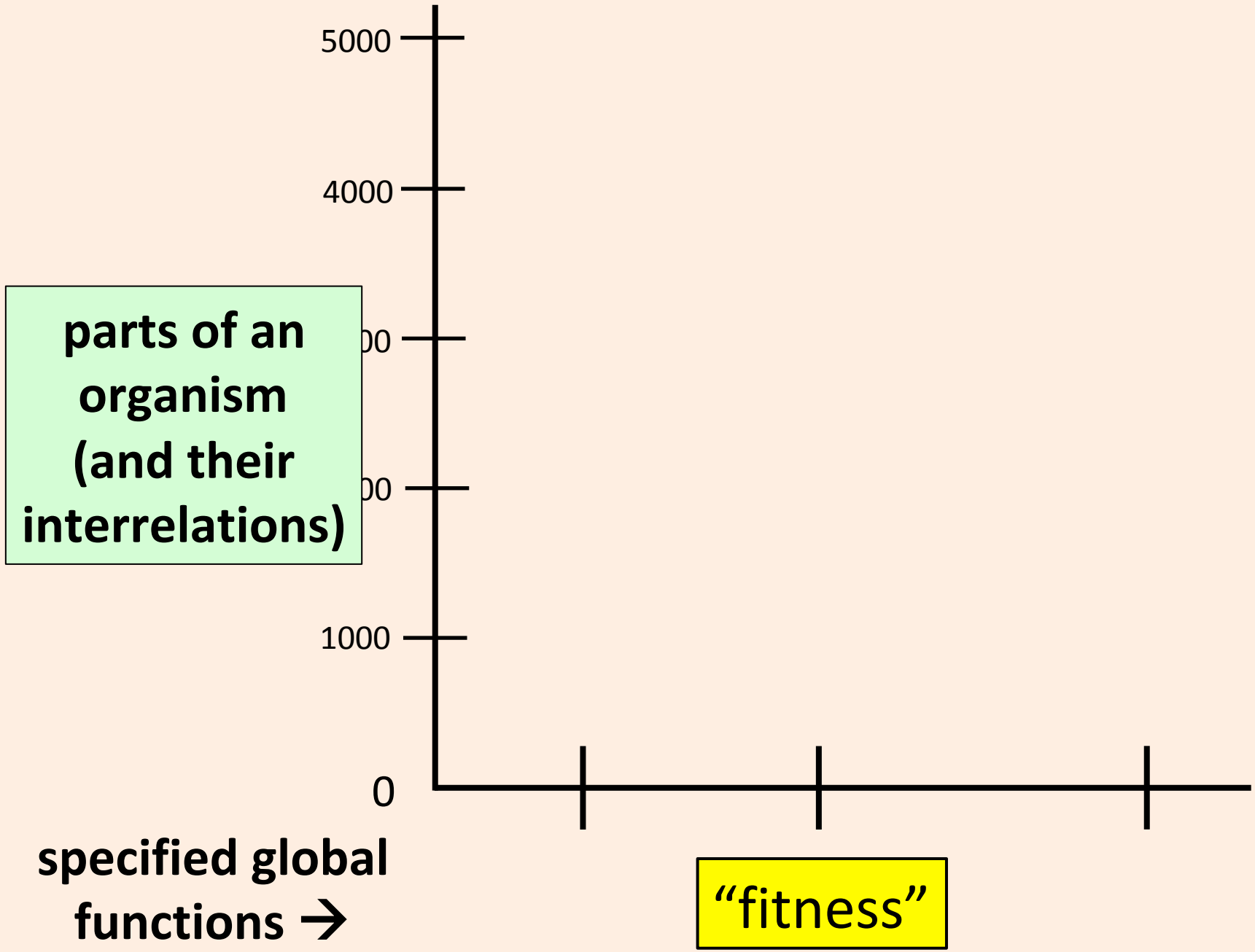

5000
4000
3000
2000
1000
0
number of distinct steamship parts required
specified global functions →

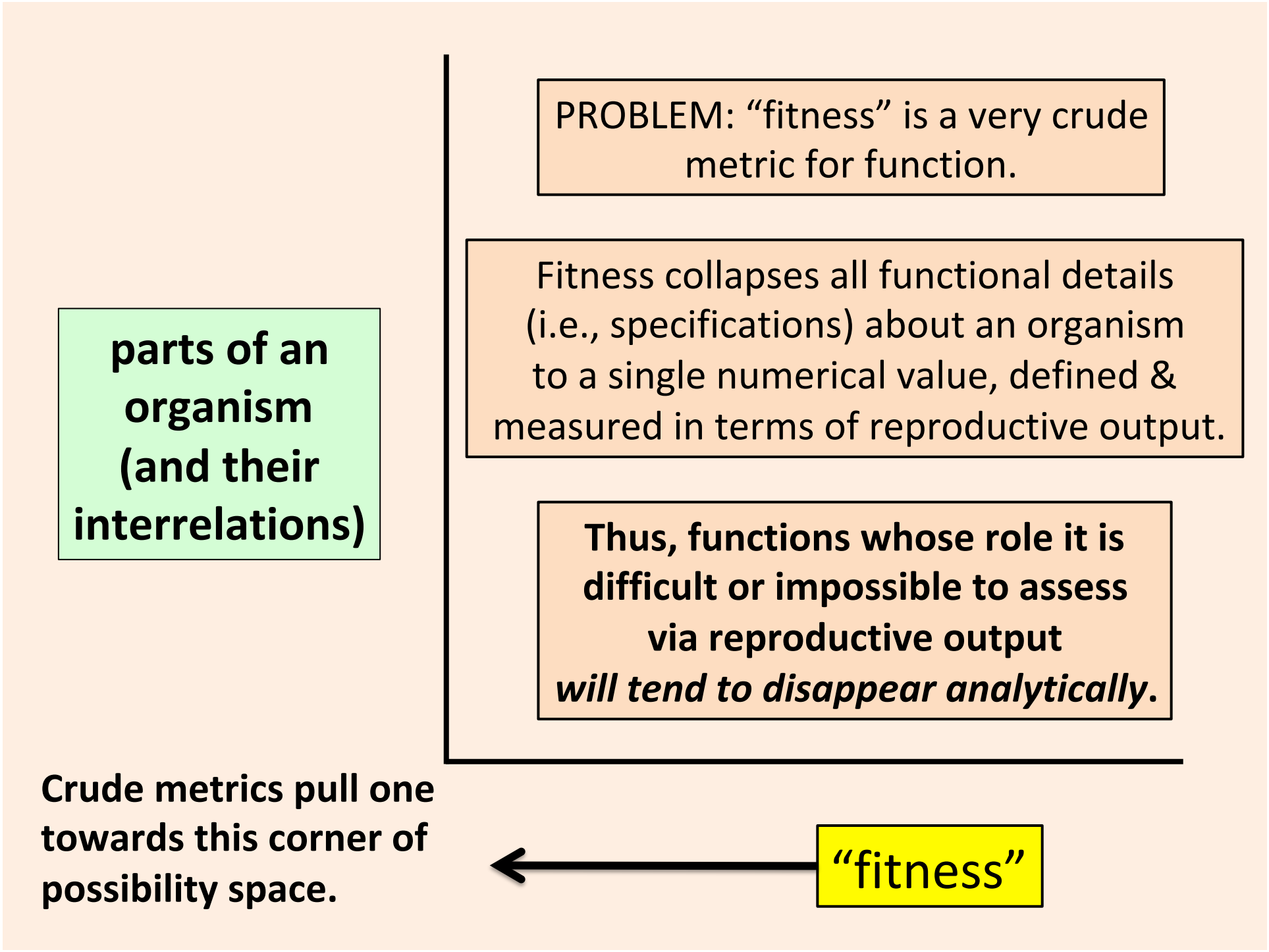

5000
4000
3000
2000
1000
0
number of distinct steamship parts required
specified global functions →
reach Liverpool ASAP


5000
4000
3000
2000
1000
0
number of distinct steamship parts required
specified global functions →
reach Liverpool ASAP
commercial vessel habitable by crew


number of distinct steamship parts required
5000
4000
3000
2000
1000
0
specified global functions →
reach Liverpool ASAP
commercial vessel habitable by crew
pleasant commercial vessel habitable by crew


number of distinct steamship parts required
5000
4000
3000
2000
1000
0
These functions will tend to, or actually become, impossible to see or detect.
If only the functions serving the "selected effect" are real, then the non-existence of any function in this space follows necessarily.
"selected effect" function →
The function of steamships, ***to which everything else is subordinate***, is to travel as fast as possible.


5000
4000
parts of an organism (and their interrelations)
1000
0
specified global functions →
“fitness”


PROBLEM: “fitness” is a very crude metric for function.
Fitness collapses all functional details (i.e., specifications) about an organism to a single numerical value, defined & measured in terms of reproductive output.
Thus, functions whose role it is difficult or impossible to assess via reproductive output will tend to disappear analytically.
parts of an organism (and their interrelations)
Crude metrics pull one towards this corner of possibility space.
“fitness”

“But Paul,” you object, “surely fitness is ***real*** – every organism has a stake in its own reproductive output.”

“Seriously, none of us would be here, listening to you today, were it not for the reproductive successes of our many ancestors.”

Listen: I like babies and all that as much as the next guy (although, arguably, not as much as my wife).

The critical question is this: *are* (or were) differences in reproductive output − fitness − truly *the cause* of biological complexity?

If so, then fitness, issuing in "selected effects," should be our preferred analytical lens for understanding function.

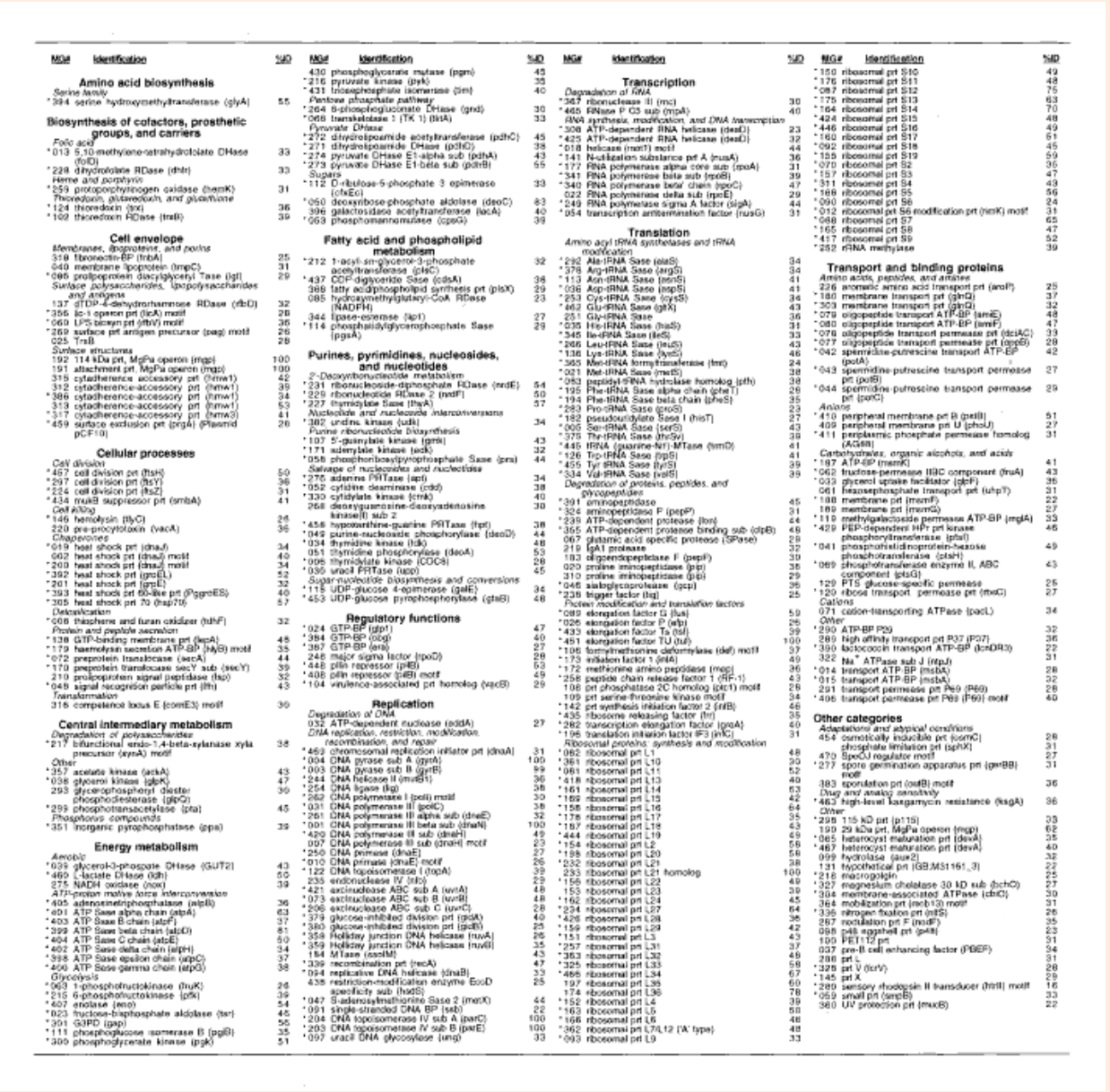
If not, however, reproduction is just another function organisms perform − essential, to be sure, but not causally primary.

It is not generally appreciated
just how severely impoverished “fitness” turns out to be, if viewed as the wellspring of biological understanding.

Absolute fitness (pop gen) is usually stipulated as 1.0, with relative frequencies of genotypes in the population falling within the interval 0.0 – 1.0.

How can anyone sensibly go from that – *a handful of numbers* – to the information needed to specify cell function, on the next slide?

The “parts list” (partial) of *Mycoplasma genitalium* (Fraser et al. 1995)



MG# Identification %ID

Amino acid biosynthesis

Serine family
* 394 serine hydroxymethyltransferase (glyA) 55

Biosynthesis of cofactors, prosthetic groups, and carriers

Folic acid
* 013 5,10-methylene-tetrahydrofolate DHase (folD) 33
* 228 dihydrofolate RDase (dhfr) 33

Heme and porphyrin
* 259 protoporphyrinogen oxidase (hemK) 31

Thioredoxin, glutaredoxin, and glutathione
* 124 thioredoxin (trx) 36
* 102 thioredoxin RDase (trxB) 39

Cell envelope

Membranes, lipoproteins, and porins
318 fibronectin-BP (fnbA)
040 membrane lipoprotein (mpC) 31
* 095 prolipoprotein diacylglyceryl Tase (lgt) 29

Surface polysaccharides, lipopolysaccharides and antigens
137 dTDP-4-dehydrorhamnose RDase (dtrD) 32
* 356 ic-1 operon prt (licA) motif 28
* 060 LPS biosyn prt (rfbV) motif 36
* 269 surface prt antigen precursor (pag) motif 29
025 TraB
Surface structures
192 114 kDa prt, MgPa operon (mgp) 100
191 attachment prt, MgPa operon (mgp) 100
315 cytadherence accessory prt (hmw1) 42
312 cytadherence-accessory prt (hmw1) 39
* 386 cytadherence-accessory prt (hmw1) 34
313 cytadherence-accessory prt (hmw1) 53
* 317 cytadherence-accessory prt (hmw3) 41
* 459 surface exclusion prt (prgA) (Plasmid pCF10) 26

Cellular processes

Cell division
* 467 cell division prt (ftsH) 50
* 297 cell division prt (ftsY) 36
* 224 cell division prt (ftsZ) 31
* 434 mukB suppressor prt (smbA) 41

Cell killing
* 146 hemolysin (tlyC) 26
220 pre-procytolixin (vacA) 36

Chaperones
* 019 heat shock prt (dnaJ) 34
002 heat shock prt (dnaJ) motif 40
* 200 heat shock prt (dnaJ) motif 34
* 392 heat shock prt (groEL) 52
* 201 heat shock prt (groES) 32
* 393 heat shock prt 60-like prt (PggroES) 40
* 305 heat shock prt 70 (hsp70) 57

Detoxification
* 008 thiophene and furan oxidizer (tdhF) 32

Protein and peptide secretion
* 138 GTP-binding membrane prt (ffcA) 48
* 179 haemolysin secretion ATP-BP (hlyB) motif 35
* 172 preprotein translocase (secA) 44
* 178 preprotein translocase secY sub (secY) 39
210 prolipoprotein signal peptidase (lsp) 32
* 046 signal recognition particle prt (ffh) 43

Transformation
316 competence locus E (comE3) motif 30

Central intermediary metabolism

Degradation of polysaccharides
* 217 bifunctional endo-1,4-beta-xylanase xyla precursor (xynA) motif 38

Other
* 357 acetate kinase (ackA) 43
* 036 glycerol kinase (glpK) 47
293 glycerophosphoryl diester phosphodiesterase (glpQ) 36
* 299 phosphotransacetylase (pta) 45

Phosphorus compounds
* 351 inorganic pyrophosphatase (ppa) 39

Energy metabolism

Aerobic
* 039 glycerol-3-phospate DHase (GUT2) 43
* 460 L-lactate DHase (ldh) 50
275 NADH oxidase (nox) 39

ATP-proton motive force interconversion
* 405 adenosinetriphosphatase (atpB) 36
* 401 ATP Sase alpha chain (atpA) 63
* 403 ATP Sase B chain (atpF) 37
* 399 ATP Sase beta chain (atpD) 81
* 404 ATP Sase C chain (atpE) 50
* 402 ATP Sase delta chain (atpH) 34
* 398 ATP Sase epsilon chain (atpC) 37
* 400 ATP Sase gamma chain (atpG) 38

Glycolysis
* 063 1-phosphofructokinase (fruK) 26
* 215 6-phosphofructokinase (pfk) 39
* 407 enolase (eno) 54
* 023 fructose-bisphosphate aldolase (fba) 45
* 301 G3PD (gap) 56
* 111 phosphoglucose isomerase B (pgiB) 35
* 306 phosphoglycerate kinase (pgk) 51
430 phosphoglycerate mutase (pgm) 45
* 216 pyruvate kinase (pyk) 35
* 431 triosephosphate isomerase (tim) 40

Pentose phosphate pathway
* 264 6-phosphogluconate DHase (gnd) 30
* 068 transketolase 1 (TK 1) (tktA) 33

Pyruvate DHase
* 272 dihydrolipoamide acetyltransferase (pdhC) 45
* 271 dihydrolipoamide DHase (pdhD) 38
* 274 pyruvate DHase E1-alpha sub (pdhA) 43
* 273 pyruvate DHase E1-beta sub (pdhB) 55

Sugars
* 112 D-ribulose-5-phosphate 3 epimerase (cfxEc) 33
* 060 deoxyribose-phosphate aldolase (deoC) 83
396 galactosidase acetyltransferase (lacA) 40
* 063 phosphomannomutase (cpeG) 39

Fatty acid and phospholipid metabolism

* 212 1-acyl-sn-glycerol-3-phosphate acetyltransferase (plsC) 32
* 437 CDP-diglyceride Sase (cdsA) 38
388 fatty acid/phospholipid synthesis prt (plsX) 29
085 hydroxymethylglutaryl-CoA RDase (NADPH) 23
344 lipase-esterase (lip1) 27
* 114 phosphatidylglycerophosphate Sase (pgsA) 29

Purines, pyrimidines, nucleosides, and nucleotides

2'-Deoxyribonucleotide metabolism
* 231 ribonucleoside-diphosphate RDase (nrdE) 54
* 229 ribonucleotide RDase 2 (nrdF) 50
* 227 thymidylate Sase (thyA) 57

Nucleotide and nucleoside interconversions
* 382 uridine kinase (udk) 34

Purine ribonucleotide biosynthesis
* 107 5'-guanylate kinase (gmk) 43
* 171 adenylate kinase (adk) 32
* 058 phosphoribosylpyrophosphate Sase (prs) 44

Salvage of nucleosides and nucleotides
* 275 adenine PRTase (apt) 34
* 052 cytidine deaminase (cdd) 38
* 330 cytidylate kinase (cmk) 40
268 deoxyguanosine-deoxyadenosine kinase(II) sub 2 30
* 458 hypoxanthine-guanine PRTase (hpt) 38
* 048 purine-nucleoside phosphorylase (deoD) 44
* 034 thymidine kinase (tdk) 48
051 thymidine phosphorylase (deoA) 53
* 095 thymidylate kinase (COG8) 28
* 036 uracil PRTase (upp) 45

Sugar-nucleotide biosynthesis and conversions
* 115 UDP-glucose 4-epimerase (galE) 34
* 453 UDP-glucose pyrophosphorylase (galU) 48

Regulatory functions

* 024 GTP-BP (gtp1) 47
* 384 GTP-BP (obg) 40
* 387 GTP-BP (era) 27
246 major sigma factor (rpoD) 29
* 448 pilin repressor (pilB) 53
* 408 pilin repressor (pilB) motif 49
* 104 virulence-associated prt homolog (vacB) 29

Replication

Degradation of DNA
052 ATP-dependent nuclease (addA) 27

DNA replication, restriction-modification, recombination, and repair
* 469 chromosomal replication initiator prt (dnaA) 31
* 004 DNA gyrase sub A (gyrA) 100
* 003 DNA gyrase sub B (gyrB) 89
* 244 DNA helicase II (rnuB1) 36
* 254 DNA ligase (lig) 38
* 262 DNA polymerase I (polI) motif 30
* 031 DNA polymerase III (polC) 38
* 261 DNA polymerase III alpha sub (dnaE) 32
* 001 DNA polymerase III beta sub (dnaN) 100
* 429 DNA polymerase III sub (dnaH) 49
007 DNA polymerase III sub (dnaH) motif 23
* 256 DNA primase (dnaE) 27
* 010 DNA primase (dnaE) motif 26
* 122 DNA topoisomerase I (topA) 39
235 endonuclease IV (nfo) 29
* 421 excinuclease ABC sub A (uvrA) 48
* 073 excinuclease ABC sub B (uvrB) 48
* 206 excinuclease ABC sub C (uvrC) 28
* 379 glucose-inhibited division prt (gidA) 40
* 380 glucose-inhibited division prt (gidB) 25
* 358 Holliday junction DNA helicase (ruvA) 26
* 359 Holliday junction DNA helicase (ruvB) 35
184 MTase (cosMI) 43
* 339 recombination prt (recA) 47
* 094 replicative DNA helicase (dnaB) 33
438 restriction-modification enzyme EcoD specificity sub (hsdS) 25
* 047 S-adenosylmethionine Sase 2 (metX) 44
* 091 single-stranded DNA BP (ssb) 22
* 204 DNA topoisomerase IV sub A (parC) 100
* 203 DNA topoisomerase IV sub B (parE) 100
* 097 uracil DNA glycosylase (ung) 33

Transcription

Degradation of RNA
* 367 ribonuclease III (mc) 30
* 465 RNase P C5 sub (rnpA) 40

RNA synthesis, modification, and DNA transcription
* 308 ATP-dependent RNA helicase (deaD) 23
* 425 ATP-dependent RNA helicase (deaD) 32
* 018 helicase (mutT) motif 44
* 141 N-utilization substance prt A (nusA) 36
* 172 RNA polymerase alpha core sub (rpoA) 31
* 341 RNA polymerase beta sub (rpoB) 39
* 340 RNA polymerase beta' chain (rpoC) 47
022 RNA polymerase delta sub (rpoE) 29
* 249 RNA polymerase sigma A factor (sigA) 44
* 054 transcription antitermination factor (nusG) 31

Translation

Amino acyl tRNA synthetases and tRNA modification
* 292 Ala-tRNA Sase (alaS) 34
* 378 Arg-tRNA Sase (argS) 34
* 113 Asn-tRNA Sase (asnS) 41
* 036 Asp-tRNA Sase (aspS) 41
* 253 Cys-tRNA Sase (cysS) 34
* 462 Glu-tRNA Sase (gltX) 43
251 Gly-tRNA Sase 36
* 035 His-tRNA Sase (hisS) 31
* 345 Ile-tRNA Sase (ileS) 33
* 266 Leu-tRNA Sase (leuS) 43
* 136 Lys-tRNA Sase (lysS) 46
* 365 Met-tRNA formyltransferase (fmt) 24
* 021 Met-tRNA Sase (metS) 38
* 282 peptidyl-tRNA hydrolase homolog (pth) 38
* 195 Phe-tRNA Sase alpha chain (pheT) 26
* 194 Phe-tRNA Sase beta chain (pheS) 35
* 283 Pro-tRNA Sase (proS) 23
* 182 pseudouridylate Sase I (hisT) 27
* 008 Ser-tRNA Sase (serS) 43
* 375 Thr-tRNA Sase (thrS) 38
* 445 tRNA (guanine-N(1)-MTase (trmD) 41
* 126 Trp-tRNA Sase (trpS) 41
* 455 Tyr-tRNA Sase (tyrS) 39
* 334 Val-tRNA Sase (valS) 39

Degradation of proteins, peptides, and glycopeptides
* 391 aminopeptidase 45
* 324 aminopeptidase P (pepP) 31
* 339 ATP-dependent protease (lon) 64
* 355 ATP-dependent protease binding sub (clpB) 46
067 glutamic acid specific protease (SPase) 28
219 IgA1 protease 32
182 oligopeptidase F (pepF) 30
020 proline iminopeptidase (pip) 35
310 proline iminopeptidase (pip) 29
* 045 sialoglycoprotease (gcp) 36
* 235 trigger factor (tig) 25

Protein modification and translation factors
* 089 elongation factor G (fus) 59
* 026 elongation factor P (efp) 26
* 433 elongation factor Ts (tsf) 39
* 451 elongation factor TU (tuf) 100
* 105 formylmethionine deformylase (def) motif 37
* 173 initiation factor 1 (infA) 49
* 172 methionine amino peptidase (map) 36
* 258 peptide chain release factor 1 (RF-1) 43
108 prt phosphatase 2C homolog (prc1) motif 28
109 prt serine-threonine kinase motif 34
* 142 prt synthesis initiation factor 2 (infB) 46
* 435 ribosome releasing factor (frr) 35
* 282 transcription elongation factor (greA) 40
* 196 translation initiation factor IF3 (infC) 31

Ribosomal proteins: synthesis and modification
* 082 ribosomal prt L1 48
* 361 ribosomal prt L10 30
* 081 ribosomal prt L11 52
* 418 ribosomal prt L13 40
* 161 ribosomal prt L14 53
* 162 ribosomal prt L15 42
* 158 ribosomal prt L16 64
* 178 ribosomal prt L17 35
* 187 ribosomal prt L18 43
* 444 ribosomal prt L19 49
* 154 ribosomal prt L2 56
* 188 ribosomal prt L20 58
* 232 ribosomal prt L21 38
293 ribosomal prt L21 homolog 100
* 156 ribosomal prt L22 49
153 ribosomal prt L23 39
* 162 ribosomal prt L24 45
* 224 ribosomal prt L27 64
* 426 ribosomal prt L28 36
* 159 ribosomal prt L29 42
* 151 ribosomal prt L3 43
* 257 ribosomal prt L31 37
* 353 ribosomal prt L32 48
* 325 ribosomal prt L33 58
* 465 ribosomal prt L34 67
197 ribosomal prt L35 60
174 ribosomal prt L36 78
* 152 ribosomal prt L4 39
* 163 ribosomal prt L5 60
* 166 ribosomal prt L6 46
* 362 ribosomal prt L7/L12 ('A' type) 48
* 093 ribosomal prt L9 33
* 150 ribosomal prt S10 49
* 176 ribosomal prt S11 48
* 087 ribosomal prt S12 75
* 175 ribosomal prt S13 63
* 164 ribosomal prt S14 70
* 424 ribosomal prt S15 48
* 446 ribosomal prt S16 49
* 160 ribosomal prt S17 51
* 092 ribosomal prt S18 45
* 185 ribosomal prt S19 59
* 070 ribosomal prt S2 36
* 157 ribosomal prt S3 47
* 311 ribosomal prt S4 43
* 166 ribosomal prt S5 56
* 090 ribosomal prt S6 24
* 012 ribosomal prt S6 modification prt (rimK) motif 31
* 088 ribosomal prt S7 65
* 165 ribosomal prt S8 47
* 457 ribosomal prt S9 52
* 252 rRNA methylase 39

Transport and binding proteins

Amino acids, peptides, and amines
226 aromatic amino acid transport prt (aroP) 25
* 180 membrane transport prt (glnQ) 37
* 303 membrane transport prt (glnQ) 32
* 079 oligopeptide transport ATP-BP (amiE) 48
* 080 oligopeptide transport ATP-BP (amiF) 47
* 076 oligopeptide transport permease prt (dciAC) 39
* 077 oligopeptide transport permease prt (oppB) 28
* 042 spermidine-putrescine transport ATP-BP (potA) 42
* 043 spermidine-putrescine transport permease prt (potB) 27
* 044 spermidine-putrescine transport permease prt (potC) 29

Anions
* 410 peripheral membrane prt B (pstB) 51
409 peripheral membrane prt U (phoU) 27
* 411 periplasmic phosphate permease homolog (AG689) 31

Carbohydrates, organic alcohols, and acids
* 187 ATP-BP (msmK) 41
* 062 fructose-permease IIBC component (fruA) 43
033 glycerol uptake facilitator (glpF) 35
061 hexosephosphate transport prt (uhpT) 31
* 188 membrane prt (msmF) 22
189 membrane prt (msmG) 27
* 118 methylgalactoside permease ATP-BP (mglA) 33
* 429 PEP-dependent HPr prt kinase phosphorylltransferase (ptsI) 46
* 041 phosphohistidinoprotein-hexose phosphotransferase (ptsH) 49
* 069 phosphotransferase enzyme II, ABC component (ptsG) 43
129 PTS glucose-specific permease 25
* 120 ribose transport permease prt (rbsC) 27

Cations
071 cation-transporting ATPase (pacL) 34

Other
* 290 ATP-BP P29 32
289 high affinity transport prt P37 (P37) 36
* 390 lactococcin transport ATP-BP (lcnDR3) 22
322 Na+ ATPase sub J (ntpJ) 31
* 014 transport ATP-BP (msbA) 28
* 015 transport ATP-BP (msbA) 32
291 transport permease prt P69 (P69) 28
* 406 transport permease prt P69 (P69) motif 40

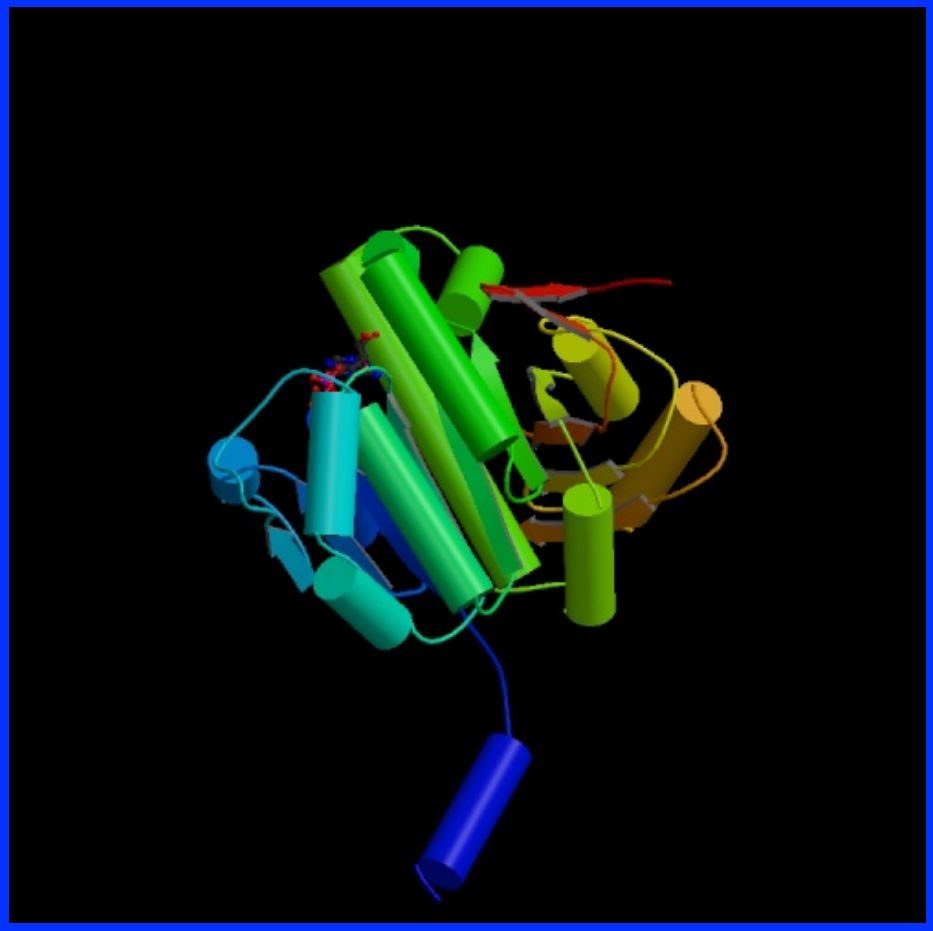
Other categories

Adaptations and atypical conditions
454 osmotically inducible prt (osmC) 28
phosphate limitation prt (sphX) 31
470 SpoOJ regulator motif 27
* 277 spore germination apparatus prt (gerBB) motif 31
383 sporulation prt (ospB) motif 36

Drug and analog sensitivity
* 463 high-level kasgamycin resistance (ksgA) 36

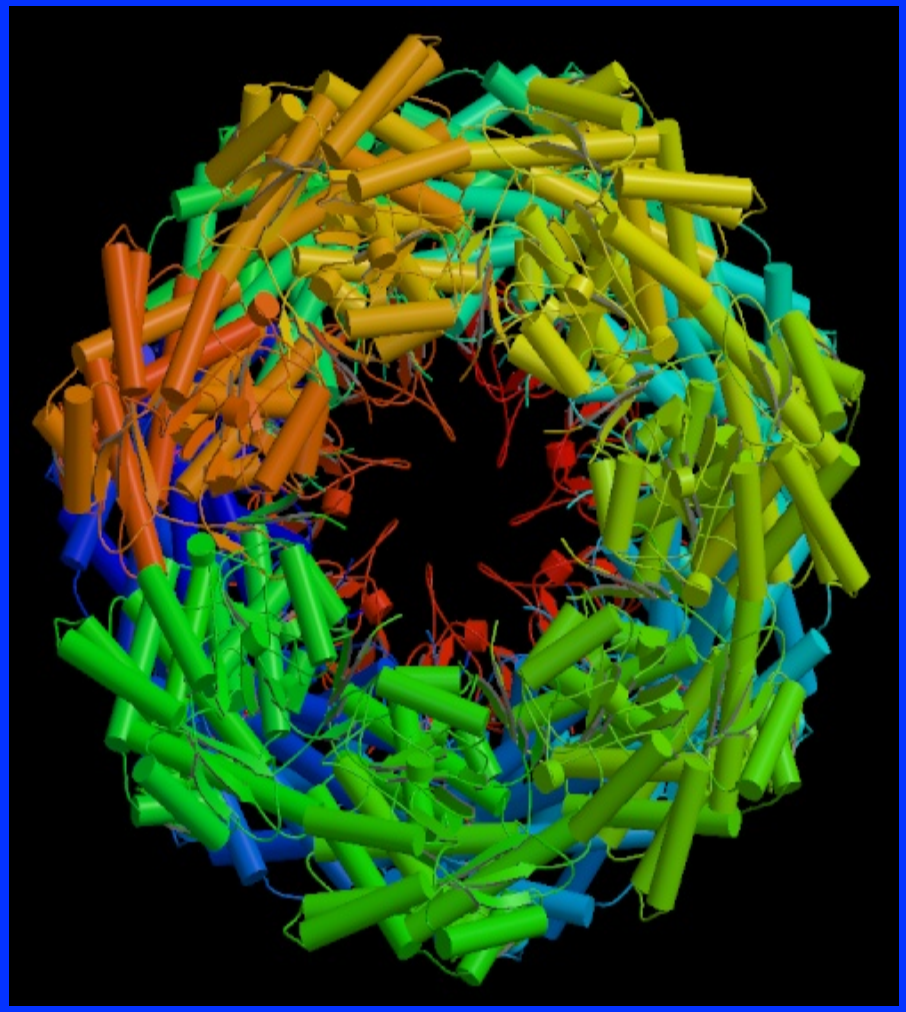
Other
* 295 115 kD prt (p115) 33
199 29 kDa prt, MgPa operon (mgp) 62
* 065 heterocyst maturation prt (devA) 35
* 467 heterocyst maturation prt (devA) 40
099 hydrolase (aue2) 32
131 hypothetical prt (GB:M31161_3) 31
* 218 macrogolgin 25
* 327 magnesium chelatase 30 kD sub (bchD) 27
* 304 membrane-associated ATPase (cbiO) 30
364 mobilization prt (mob13) motif 31
* 336 nitrogen fixation prt (nifS) 26
267 nodulation prt F (nodF) 35
098 p48 eggshell prt (p48) 23
100 PET112 prt 31
037 pre-B cell enhancing factor (PBEF) 34
298 prt L 28
* 325 prt V (tcrV) 28
* 145 prt X 28
* 289 sensory rhodopsin II transducer (htrII) motif 16
* 059 small prt (smpB) 33
380 UV protection prt (muxB) 22

Bacterial cell-division protein (ftsZ)



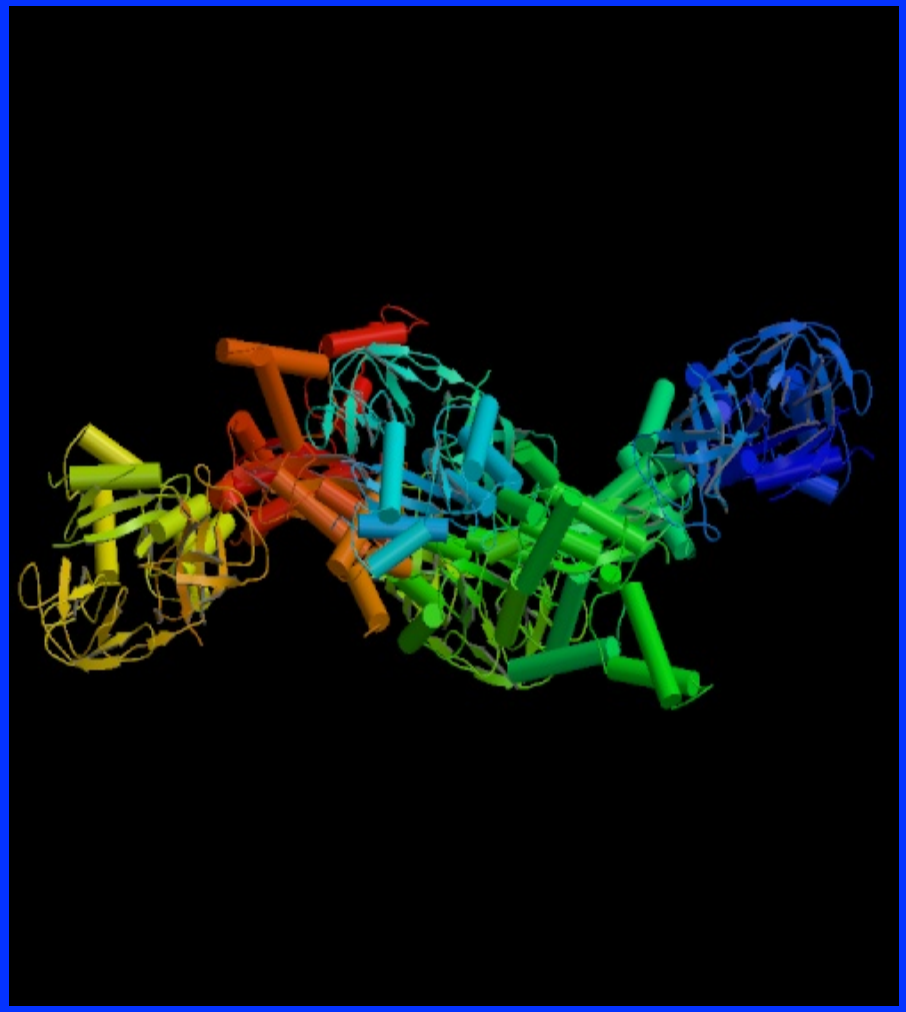
(from J. Lowe and L.A. Amos, 1998)

Chaperone (groEL)

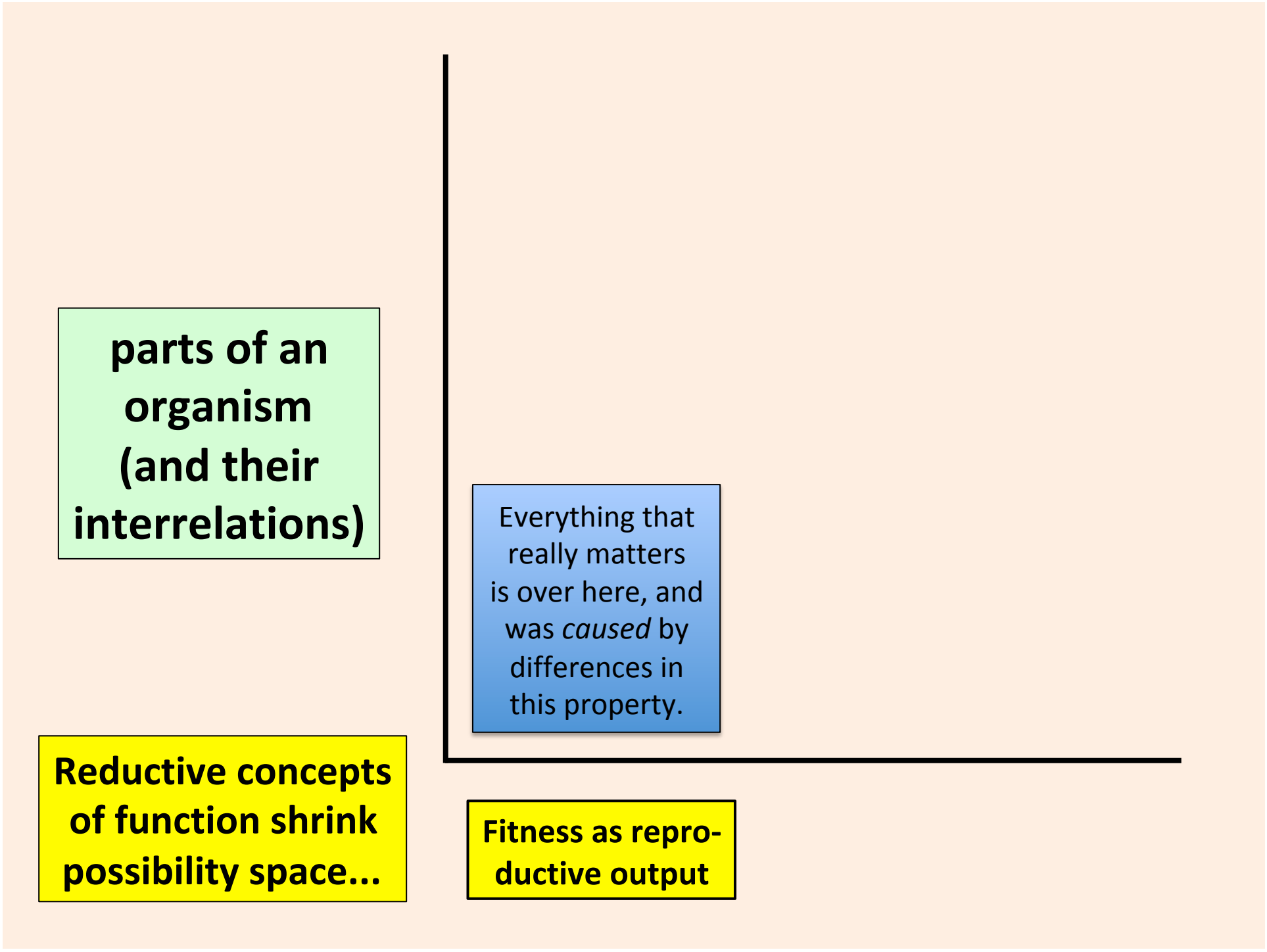


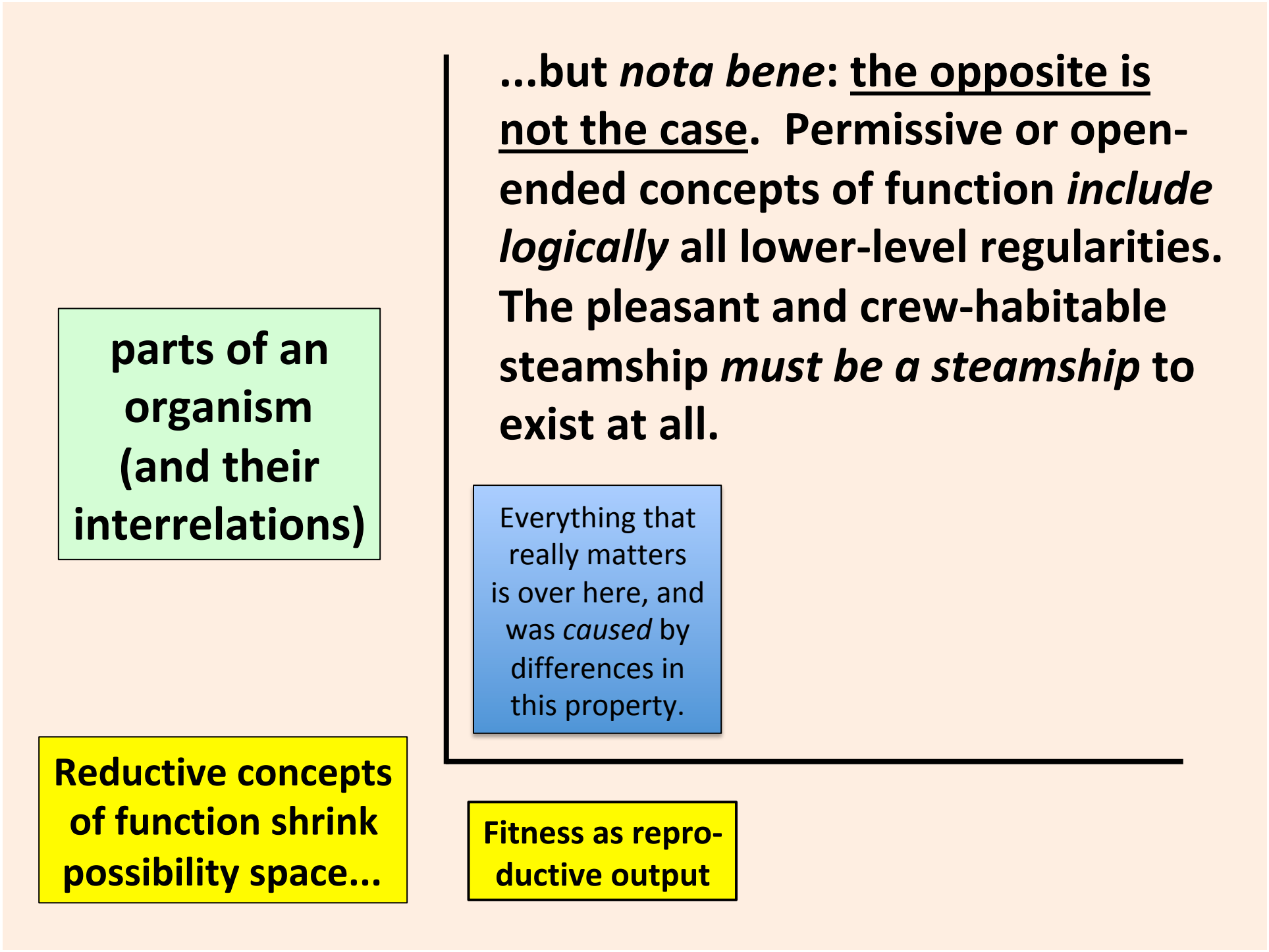
(from Z. Xu,, A. L. Horwich, and P. B. Sigler, 1997)

Elongation factor Ts (tsf)



(from Y. Wang *et al.,* 1997)


parts of an organism (and their interrelations)
Everything that really matters is over here, and was *caused* by differences in this property.
Reductive concepts of function shrink possibility space...
Fitness as repro-ductive output


...but *nota bene*: the opposite is not the case. Permissive or open-ended concepts of function *include logically* all lower-level regularities. The pleasant and crew-habitable steamship *must be a steamship* to exist at all.
parts of an organism (and their interrelations)
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Reductive concepts of function shrink possibility space...
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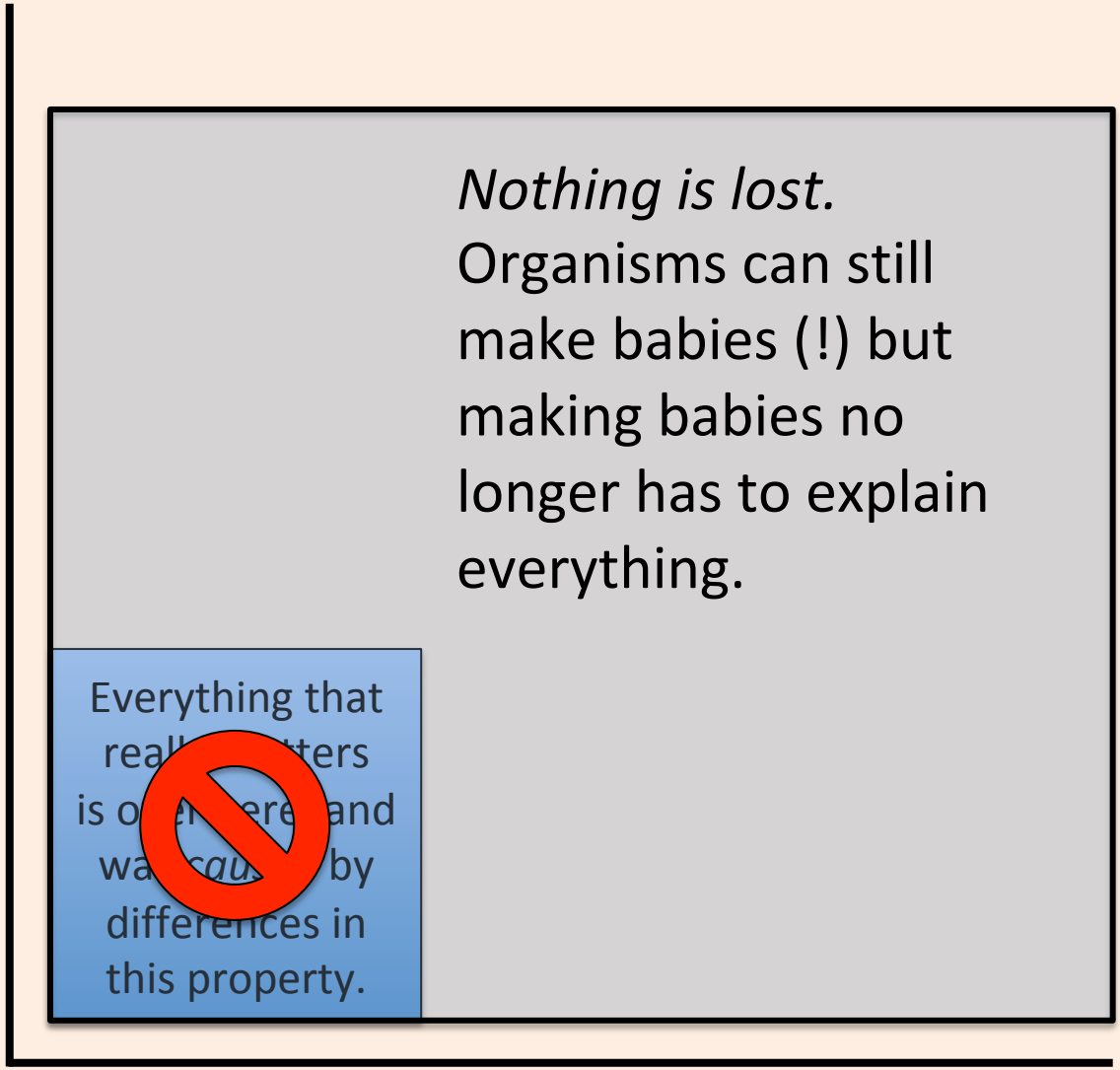


Expansive concepts of function open up possibility space...

Functions as designed systems

parts of an organism (and their interrelations)

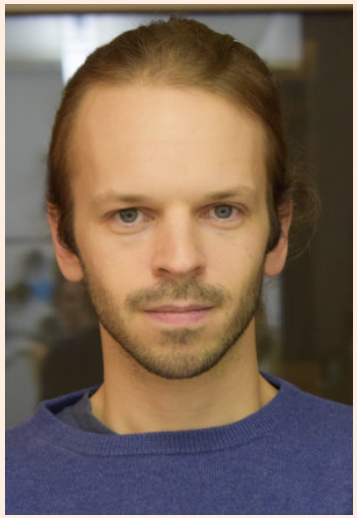
Nothing is lost.
Organisms can still make babies (!) but making babies no longer has to explain everything.

Everything that reall[illegible]tters is o[illegible]ere and wa[illegible]*caus*[illegible] by differences in this property.

In other words, reproductive output is still real, but it no longer has to carry the impossible explanatory burden of causing adaptive complexity to exist.

Expansive concepts of function open up possibility space...

Functions as designed systems



Pierre Luc Germain
University of Zurich

"Selection [a fitness-derived concept] is neither sufficient nor necessary for function. It is a very useful *proxy* to relevant functions, but an imperfect one and not the only one." (2014)

Problem is, if one has to build everything from the bottom up, fitness and selection end up very nearly exhausting your causal toolkit − and functional analysis *follows causes*.

We, as design theorists, face the very tricky problem of describing subtle or higher-level functions, in a scientific milieu where reductive analysis, and reductive criteria, pretty much run the show (even among our own crowd).

words and phrases in a text (e.g., *Moby Dick* by Herman Melville)

Text describing externally detectable actions or movements.

Reductive function: only the detectable actions matter.

"Just tell me what *happened.*"

1. Loomings

Call me Ishmael. Some years ago—never mind how long precisely—having little or no money in my purse, and nothing particular to interest me on shore, I thought I would sail about a little and see the watery part of the world. It is a way I have of driving off the spleen and regulating the circulation. Whenever I find myself growing grim about the mouth; whenever it is a damp, drizzly November in my soul; whenever I find myself involuntarily pausing before coffin warehouses, and bringing up the rear of every funeral I meet; and especially whenever my hypos get such an upper hand of me, that it requires a strong moral principle to prevent me from deliberately stepping into the street, and methodically knocking people's hats off—then, I account it high time to get to sea as soon as I can. This is my substitute for pistol and ball. With a philosophical flourish Cato throws himself upon his sword; I quietly take to the ship. There is nothing surprising in this. If they but knew it, almost all men in their degree, some time or other, cherish very nearly the same feelings towards the ocean with me.

There now is your insular city of the Manhattoes, belted round by wharves as Indian isles by coral reefs—commerce surrounds it with her surf. Right and left, the streets take you waterward. Its extreme downtown is the battery, where that noble mole

is washed by waves, and cooled by breezes, which a few hours previous were out of sight of land. Look at the crowds of water-gazers there.

Circumambulate the city of a dreamy Sabbath afternoon. Go from Corlears Hook to Coenties Slip, and from thence, by Whitehall, northward. What do you see?—Posted like silent sentinels all around the town, stand thousands upon thousands of mortal men fixed in ocean reveries. Some leaning against the spiles; some seated upon the pier-heads; some looking over the bulwarks of ships from China; some high aloft in the rigging, as if striving to get a still better seaward peep. But these are all landsmen; of week days pent up in lath and plaster—tied to counters, nailed to benches, clinched to desks. How then is this? Are the green fields gone? What do they here?

But look! here come more crowds, pacing straight for the water, and seemingly bound for a dive. Strange! Nothing will content them but the extremest limit of the land; loitering under the shady lee of yonder warehouses will not suffice. No. They must get just as nigh the water as they possibly can without falling in. And there they stand—miles of them—leagues. Inlanders all, they come from lanes and alleys, streets and avenues—north, east, south, and west. Yet here they all unite. Tell me, does the magnetic virtue of the needles of the compasses of all those ships attract them thither?

Once more. Say you are in the country; in some high land of lakes. Take almost any path you please, and ten to one it carries you down in a dale, and leaves you there by a pool in the stream. There is magic in it. Let the most absent-minded of men be plunged in his deepest reveries—stand that man on his legs, set his feet a-going, and he will infallibly lead you to water, if water there be in all that region. Should you ever be athirst in the great American

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OK, we can dump all this text, if "visible actions" are the only thing that matters.

Call me Ishmael. Some years ago—[redacted], I thought I would sail [redacted] and see the watery part of the world. [redacted]

There now is your insular city of the Manhattoes, [redacted]

[redacted]. Look at the crowds of water-gazers there.

Circumambulate the city [redacted]. Go from Corlears Hook to Coenties Slip, and from thence, by Whitehall, northward. What do you see?—[redacted] thousands of [redacted] men fixed in ocean reveries. Some leaning against the spiles; some seated upon the pier-heads; some looking over the bulwarks of ships from China; some high aloft in the rigging,

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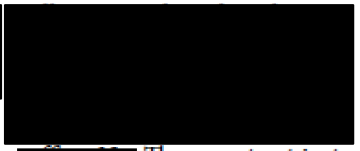

[redacted] They must get just as nigh the water as they possibly can without falling in. And there they stand—[redacted] Inlanders all,

[redacted] Yet here they all unite.

[redacted] Say you are in the country; in some high land of lakes. Take almost any path you please, [redacted] it carries you down in a dale, and leaves you there by a pool in the stream. [redacted] Let [redacted] men be plunged in his deepest reveries—stand that man on his legs, set his feet a-going, and he will infallibly lead you to water, [redacted] Should you ever be athirst in the great American

Ever wonder why the Cliff Notes summary of any novel is so much *shorter* than the novel itself?

Does that mean the blacked-out text here has *no function*?

Call me Ishmael. Some years ago—[redacted] I thought I would sail [redacted] and see the watery part of the world. [redacted]

[redacted]

There now is your insular city of the Manhattoes, [redacted]

[redacted]

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[redacted]

But look! here come more

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[redacted] Say you are in the country; in some high land of lakes. Take almost any path you please, [redacted] it carries you down in a dale, and leaves you there by a pool in the stream. [redacted] Let [redacted] men be plunged in his deepest reveries—stand that man on his legs, set his feet a-going, and he will infallibly lead you

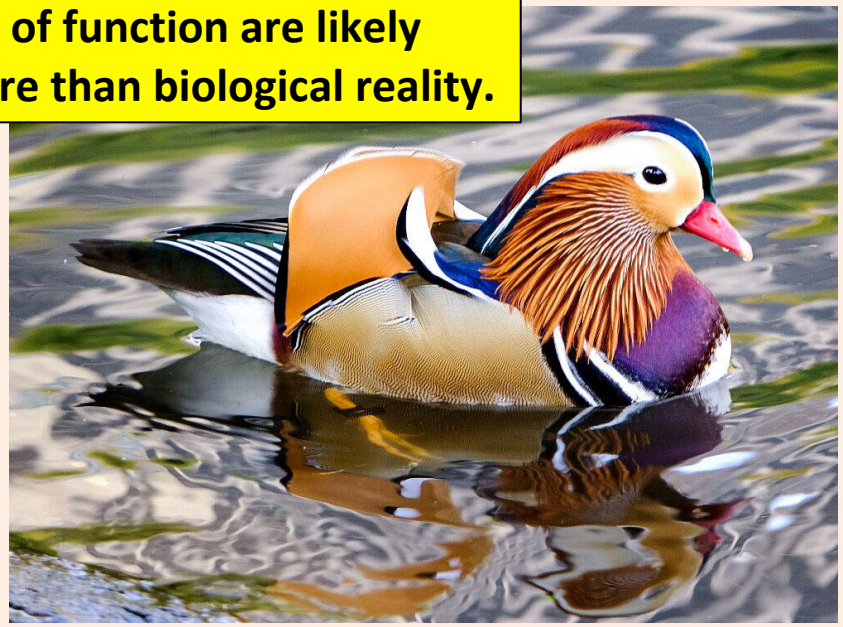
Of course not. But its functions are not obvious under the most reductive criteria (e.g., “visible actions”).

“X has no function” claims are inherently sterile and impossible to sustain evidentially.

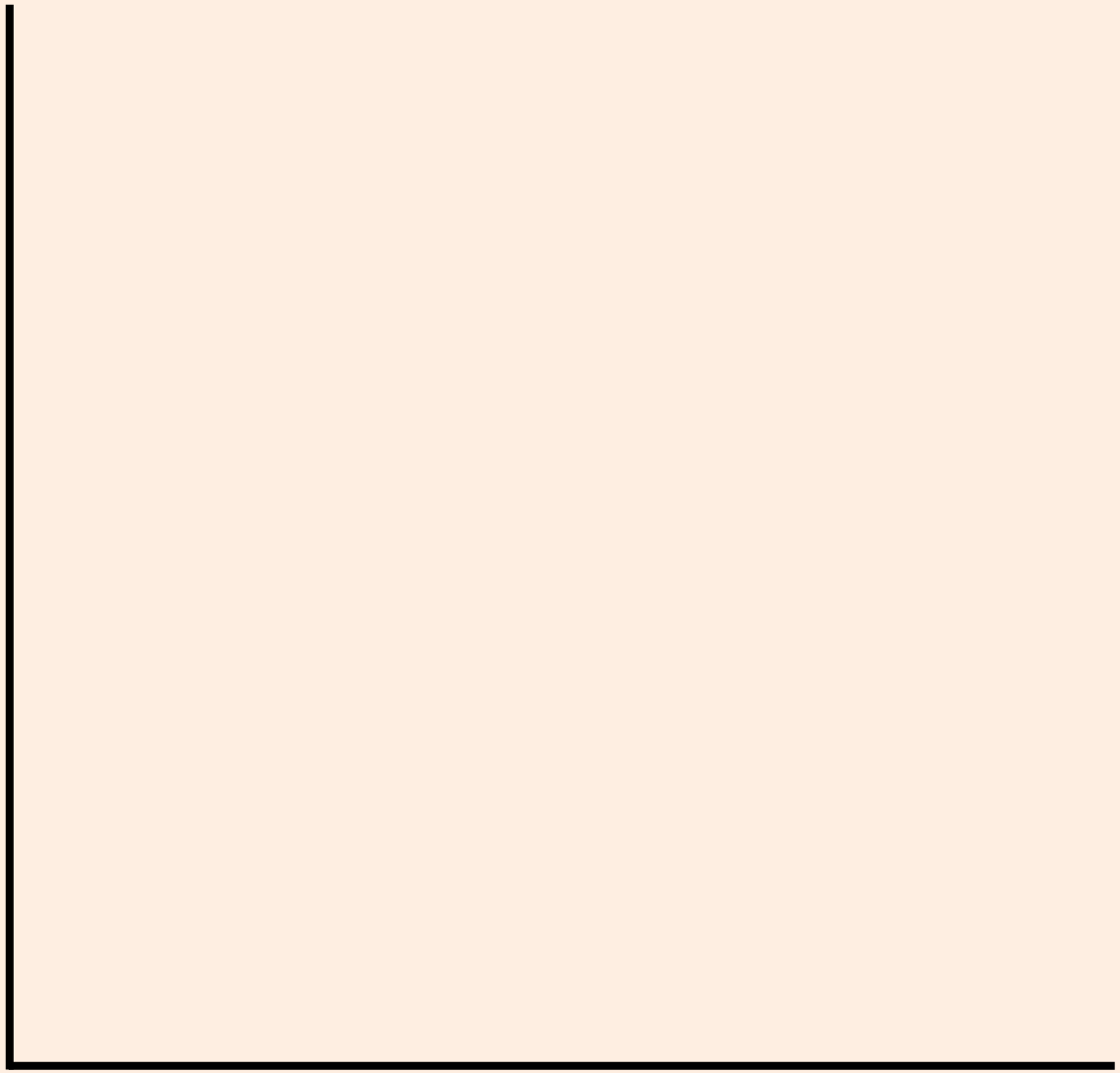
So we should take heart: our evolutionary colleagues have their faces smack up against the “no function” wall. From there, they have nowhere to go (quite literally).

BUT – you knew that was coming – we will be stuck right there with them, if we use concepts such as “selected effect,” which are grounded, not in biological reality, but naturalistic assumptions.

We do not make organisms – we find them as they are. Thus, our criteria of function are likely to reflect our ignorance far more than biological reality.

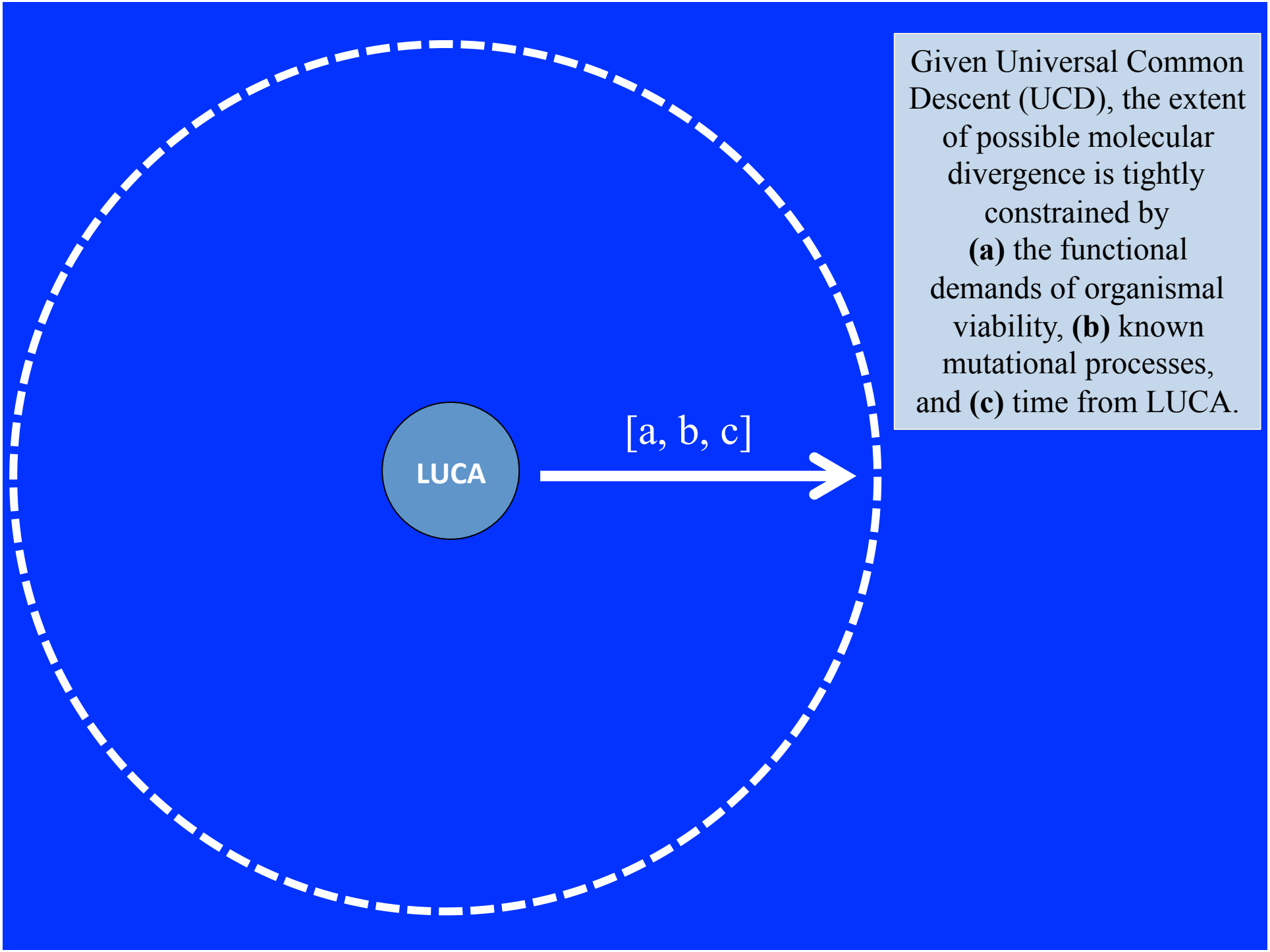


parts of an organism (and their interrelations)



fitness

universal common descent



Given Universal Common Descent (UCD), the extent of possible molecular divergence is tightly constrained by **(a)** the functional demands of organismal viability, **(b)** known mutational processes, and **(c)** time from LUCA.

design possibilities

Given Universal Common Descent (UCD), the extent of possible molecular divergence is tightly constrained by **(a)** the functional demands of organismal viability, **(b)** known mutational processes, and **(c)** time from LUCA.

But this "divergence radius" will comprise only an extremely small neighborhood ***within the possible sequence space accessible to an intelligent designer.***