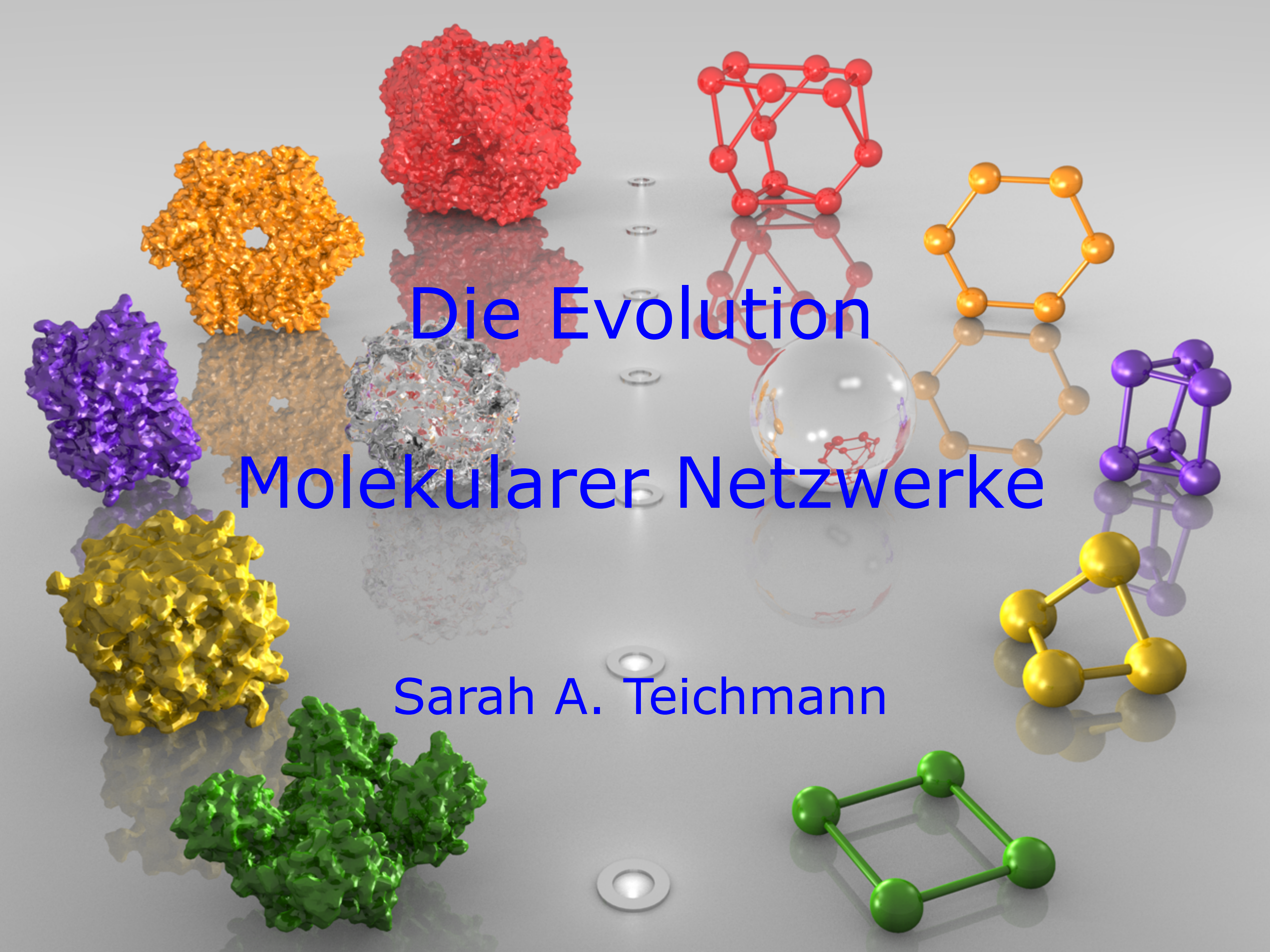
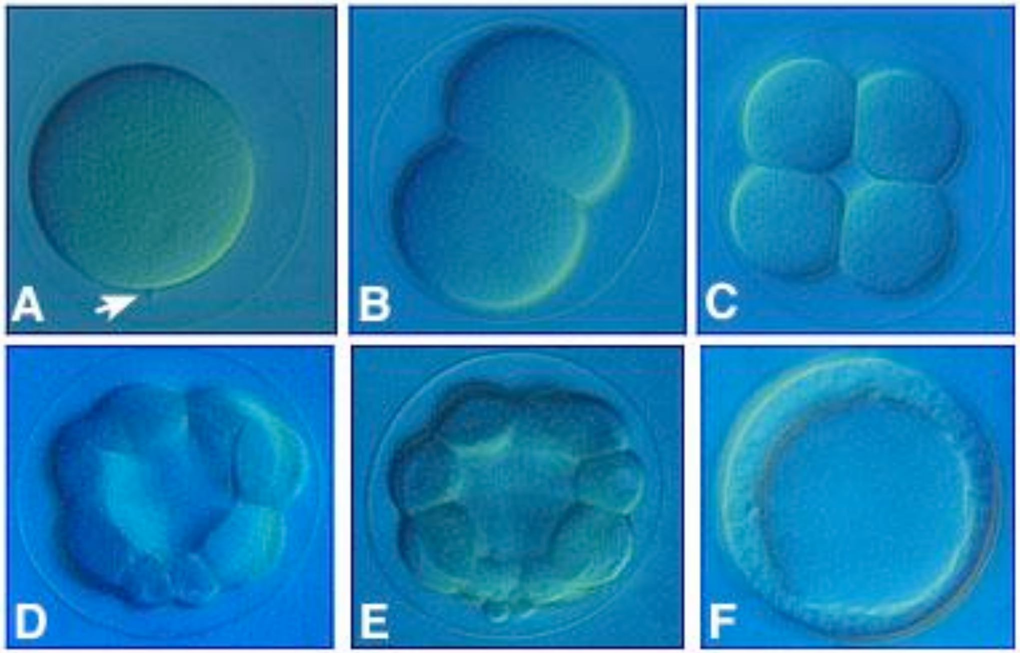
Die Evolution

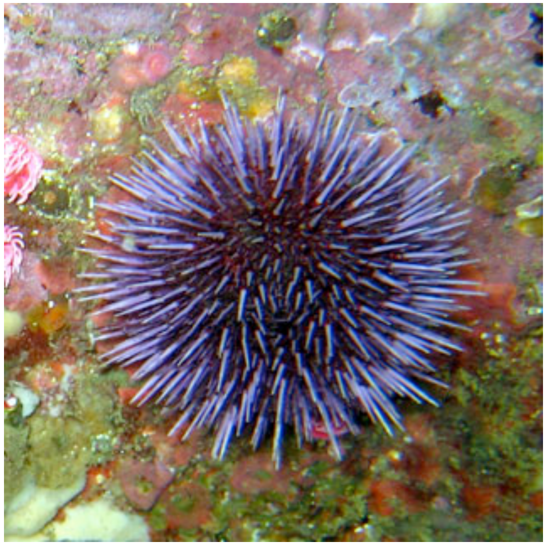
Molekularer Netzwerke

Sarah A. Teichmann

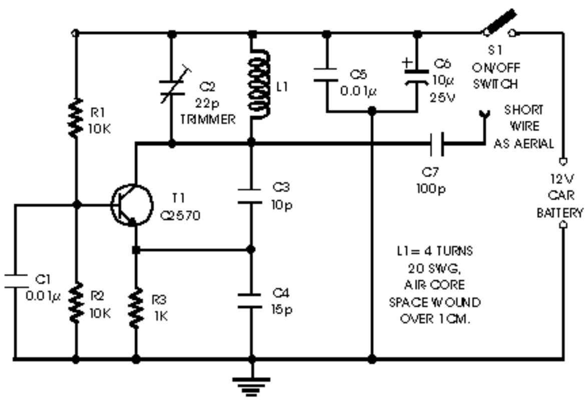


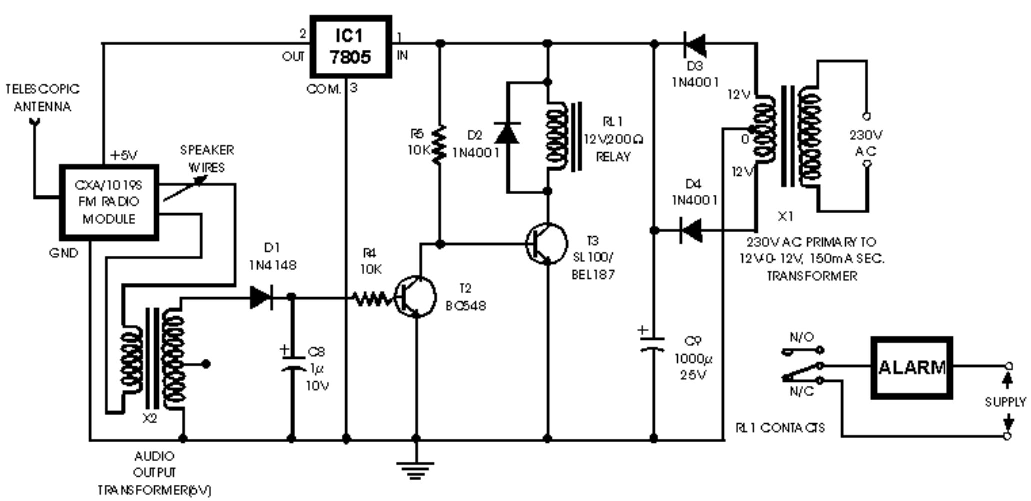
Embryonale Entwicklung des Seeigels (*Strongylocentrotus purpuratus*)



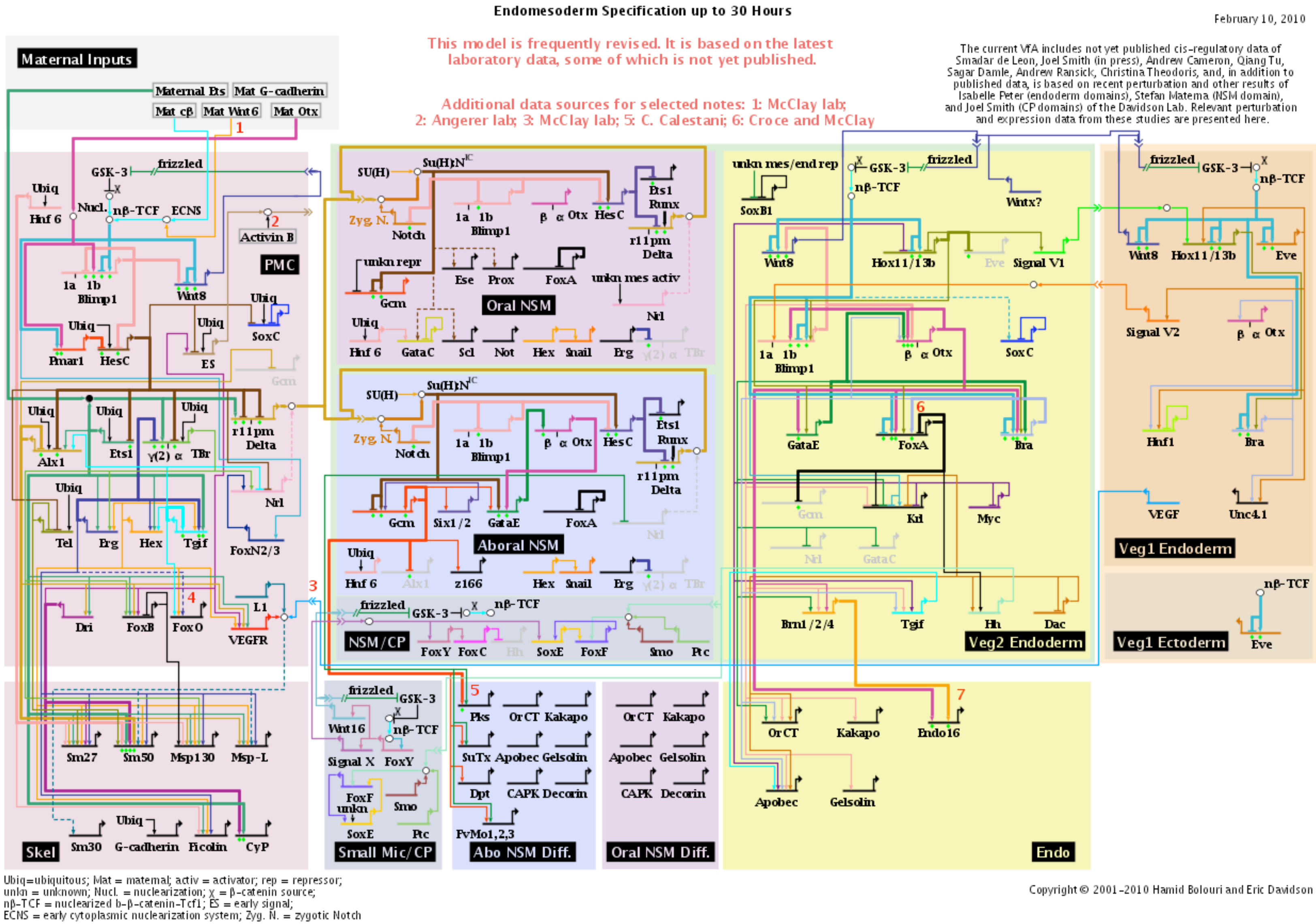


Systembiologie:
Biologen als molekulare Ingenieure

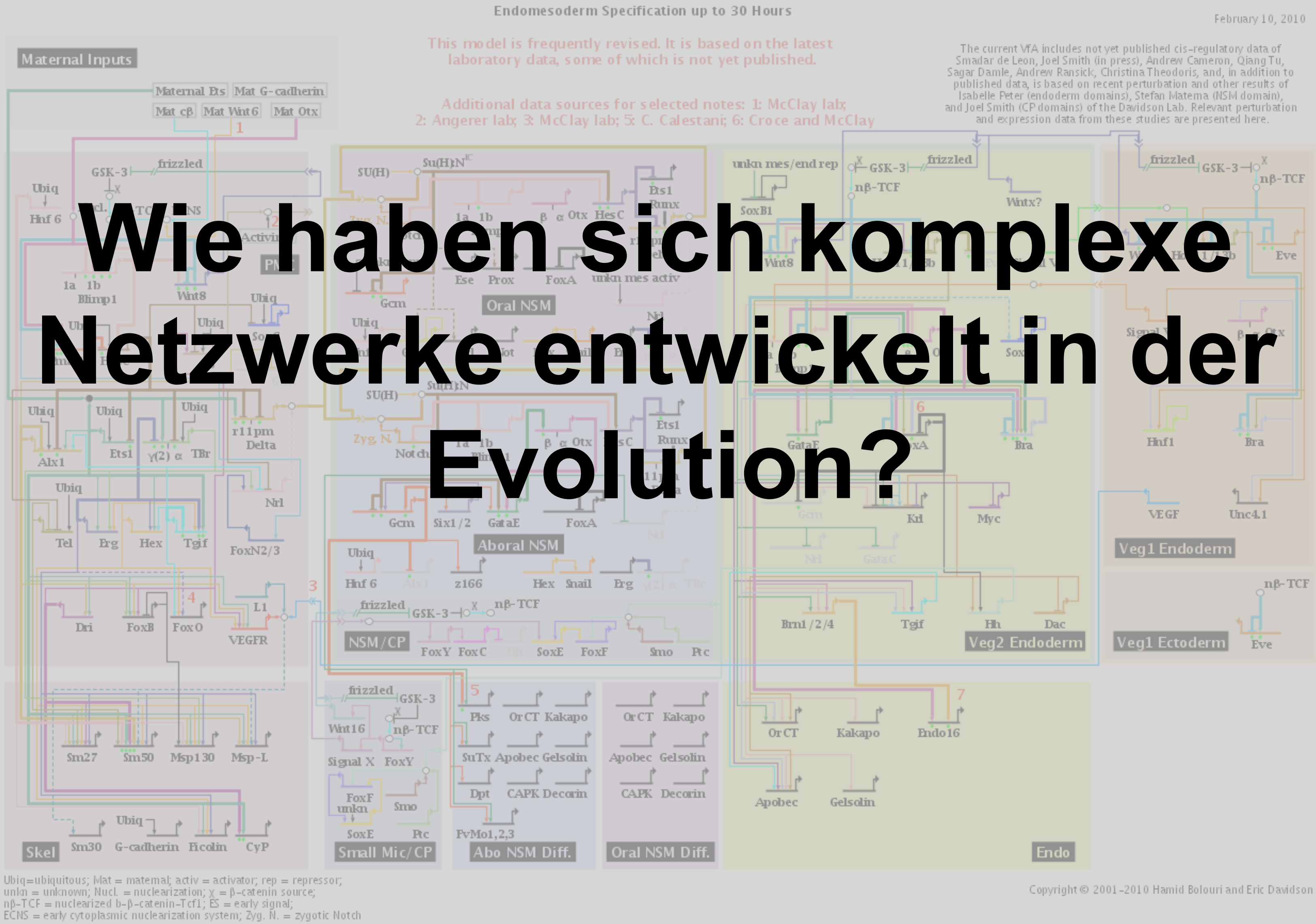


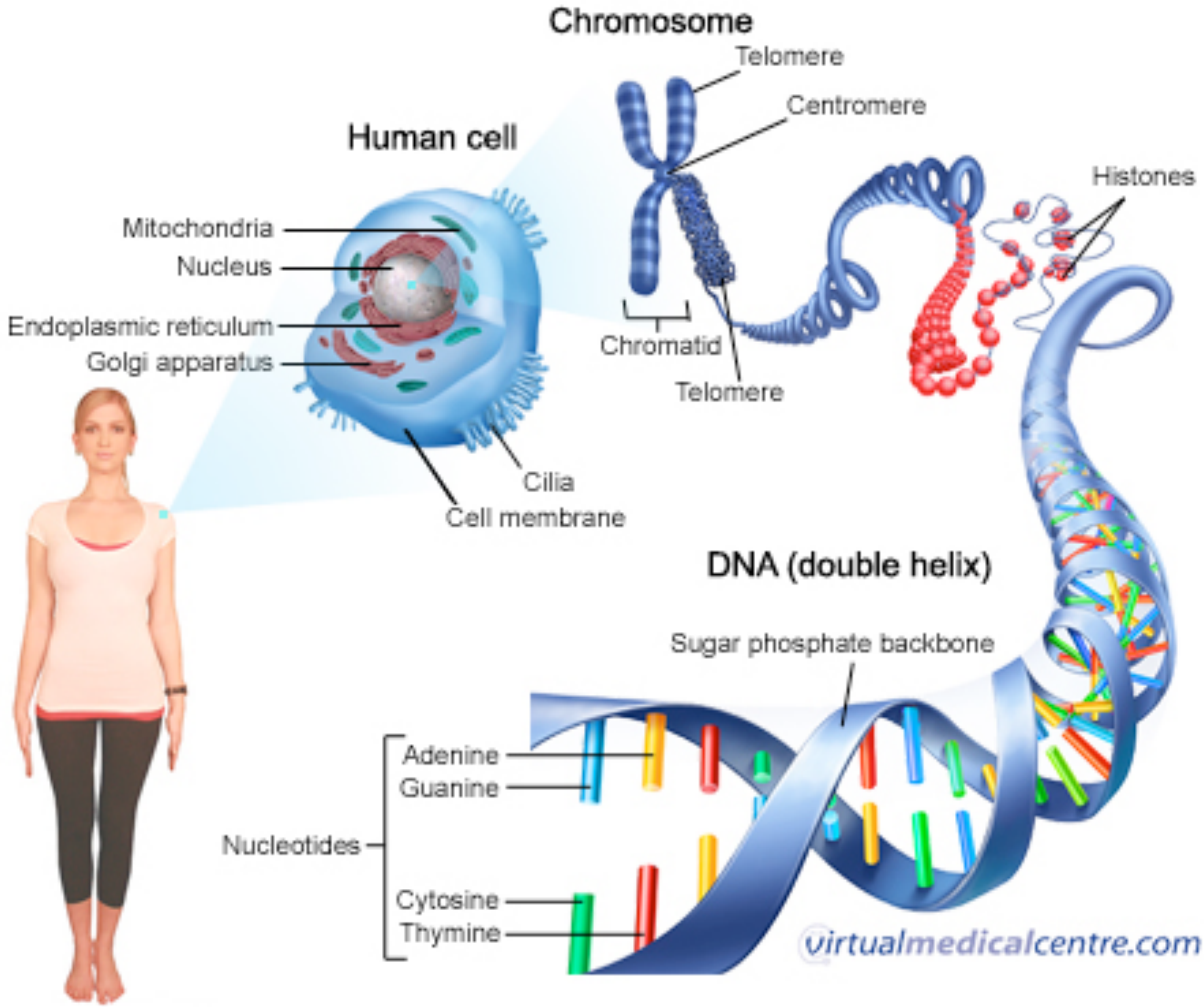


“Schaltkreise” der embryonalen Entwicklung

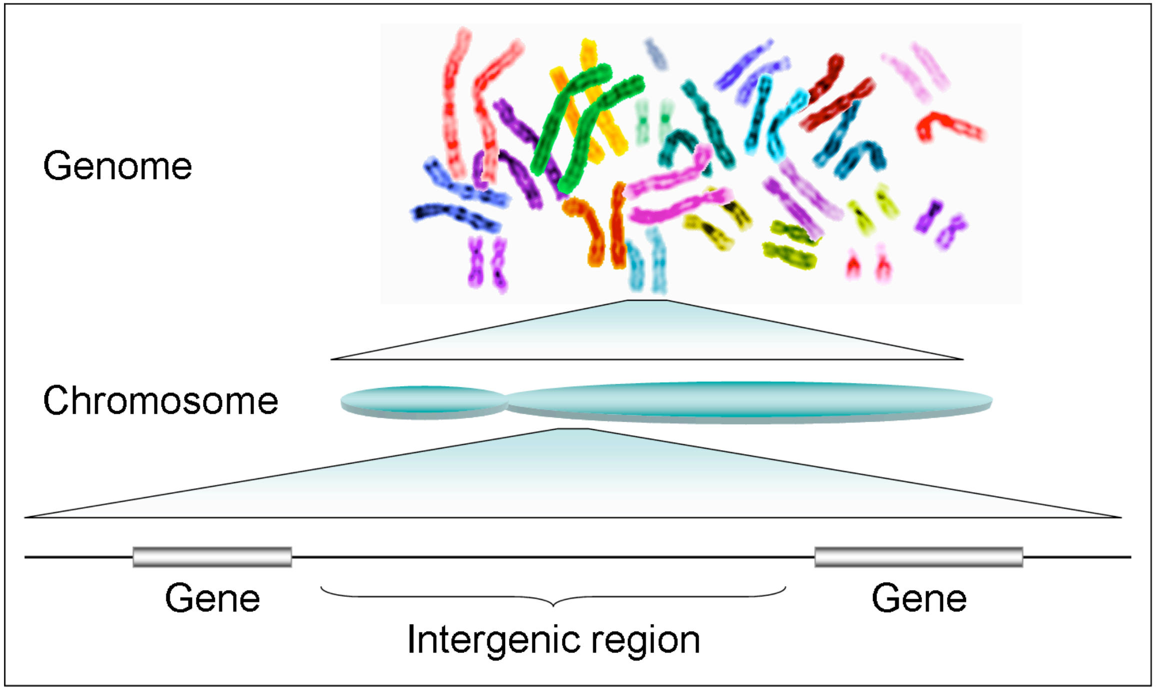


Wie haben sich komplexe Netzwerke entwickelt in der Evolution?



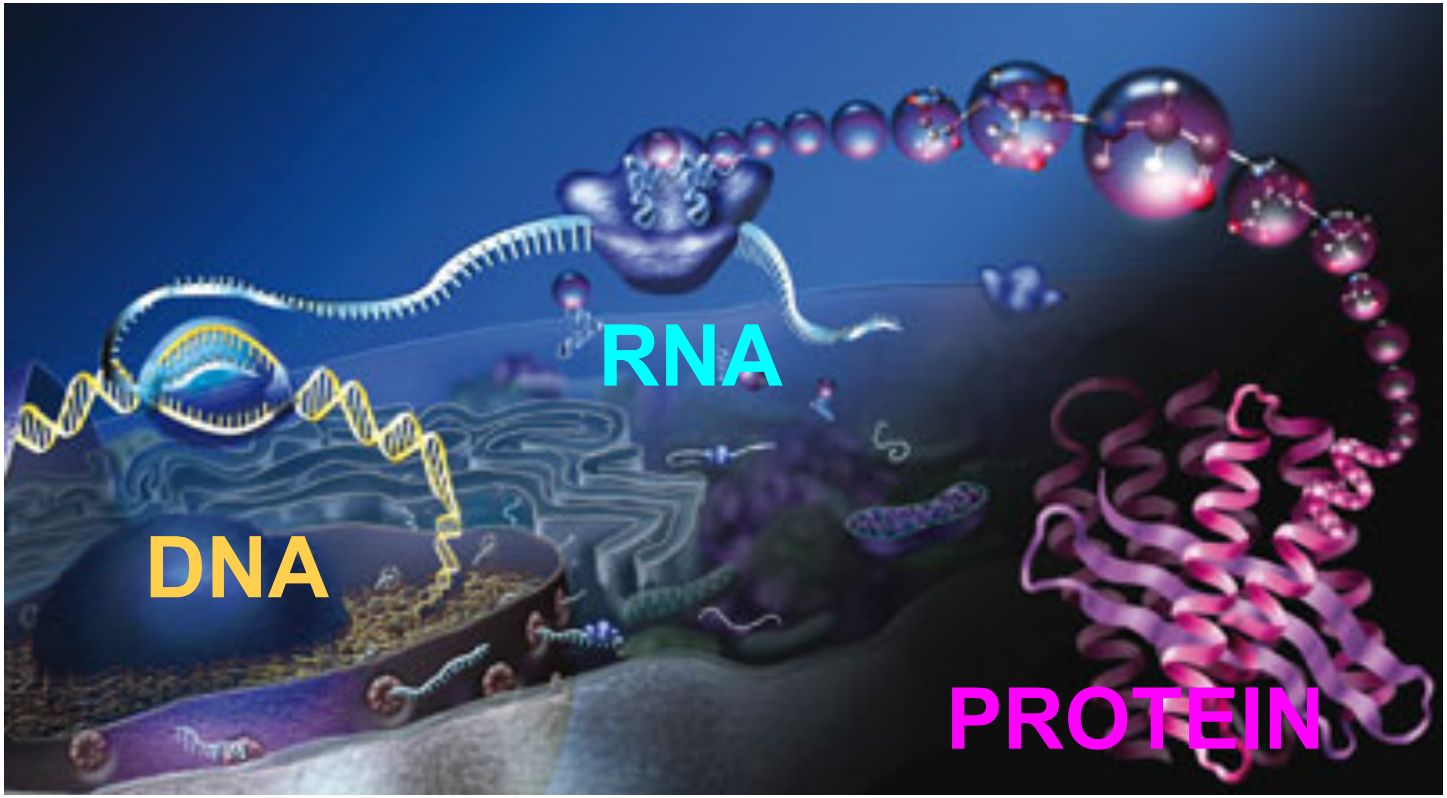

Chromosome
Telomere
Centromere
Human cell
Histones
Mitochondria
Nucleus
Endoplasmic reticulum
Golgi apparatus
Chromatid
Telomere
Cilia
Cell membrane
DNA (double helix)
Sugar phosphate backbone
Adenine
Guanine
Nucleotides
Cytosine
Thymine
virtualmedicalcentre.com

Evolutionsvorgaenge in der DNA

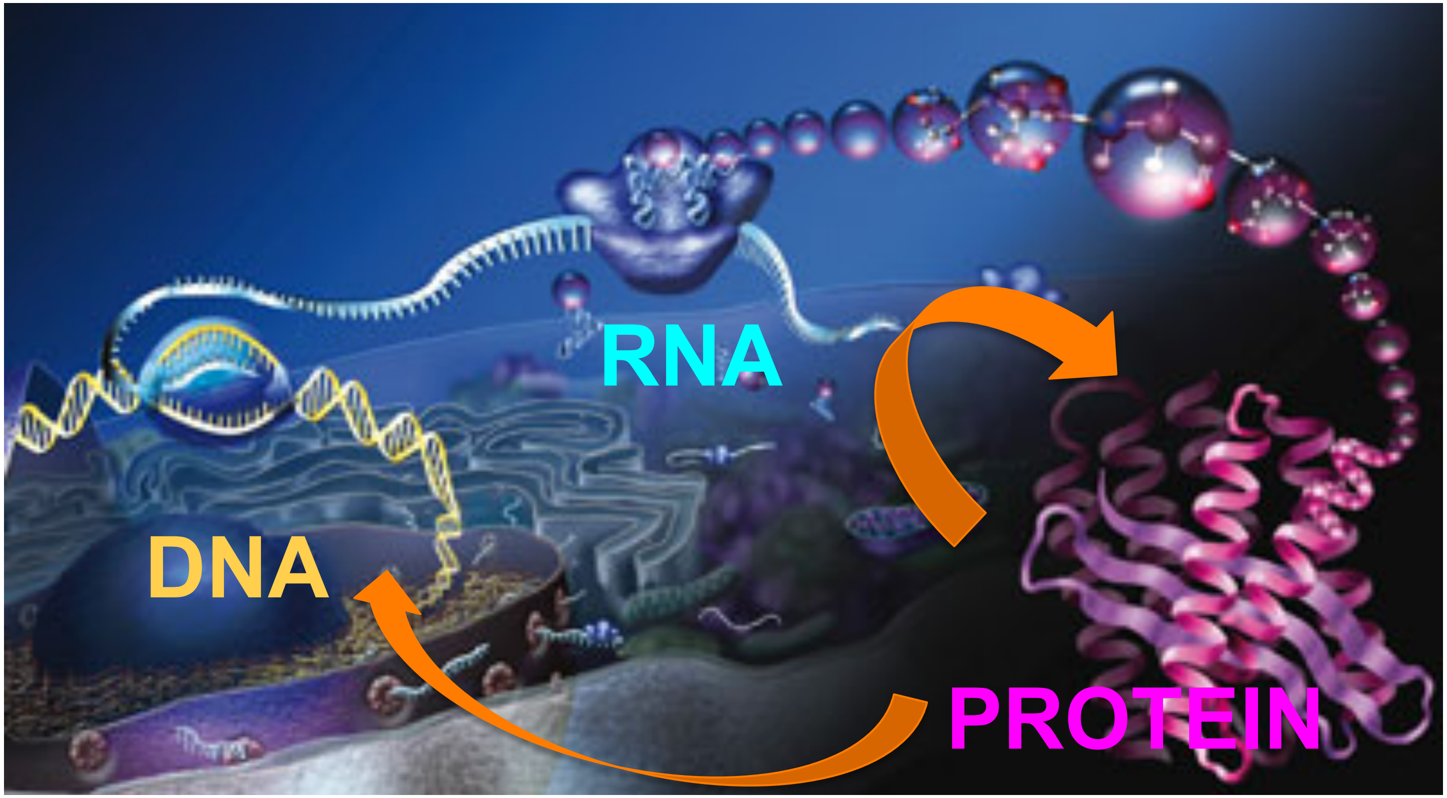


1. Mutation: Divergenz oder Konservierung der Sequenz
2. Duplikation: Kopieren der Gene
3. Genfusion: Zusammenfuegen von 2 Genen

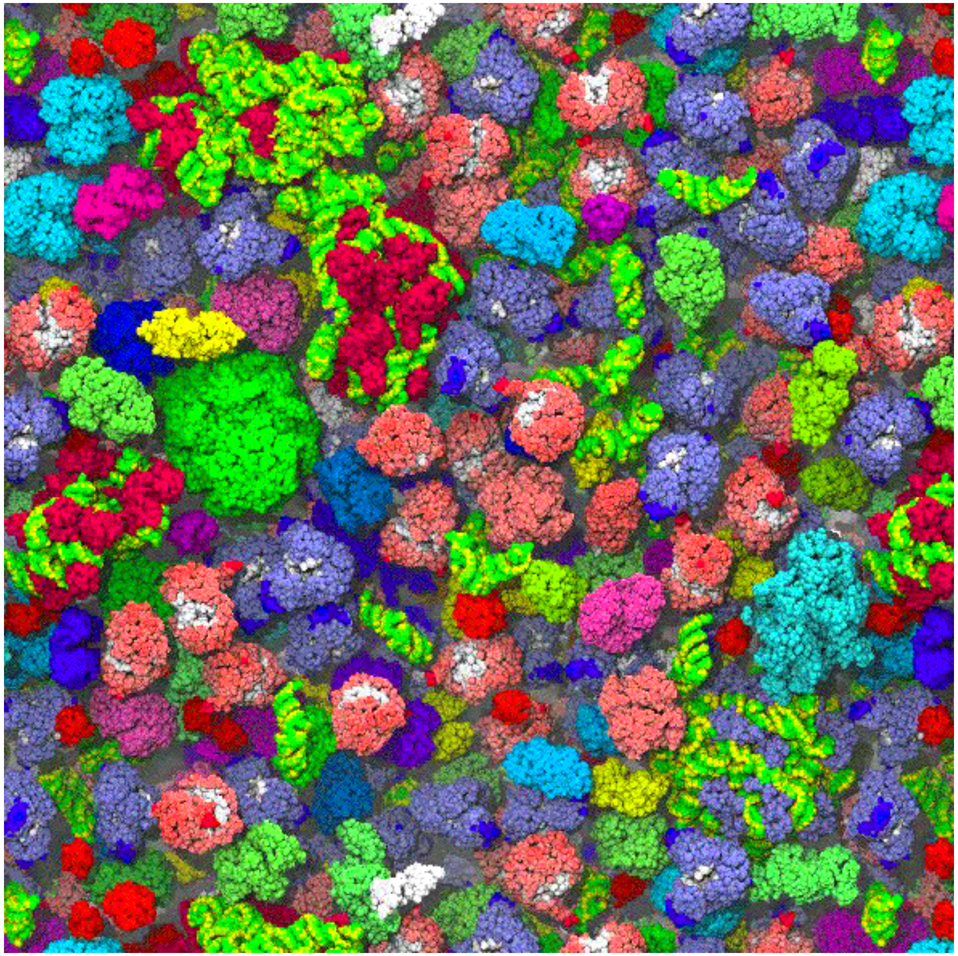
Das zentrale Dogma der Molekularbiologie



Das zentrale Dogma der Molekularbiologie



Das Innenleben einer Zelle

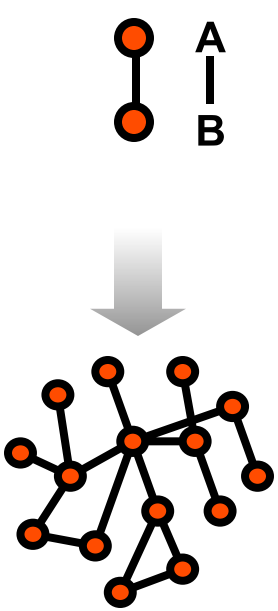


McGuffee & Elcock, *PLoS Comp Biol*, 2010

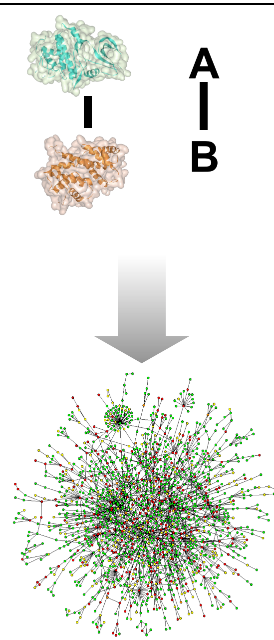
Netzwerke in der Biologie

Netzwerk	Proteinbindung	Metabolite	Genexpression
Knoten	*Proteine*	*Kleine Molekuele*	*Transcriptionsfaktor Targetgen*
Kanten	*Direkte Bindung*	*Enzymatische Katalyse*	*Genregulation*

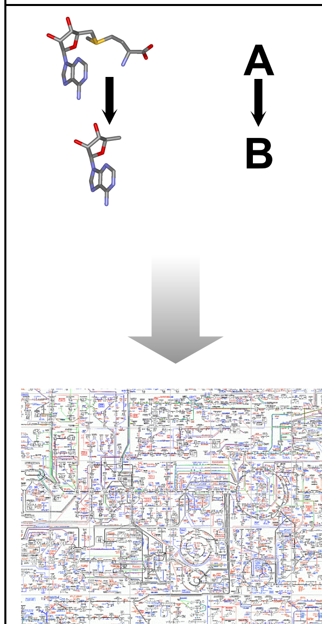
Interaktion



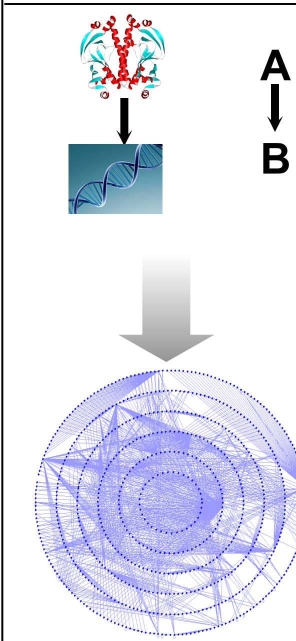
Protein-Protein



Protein-Metabolite



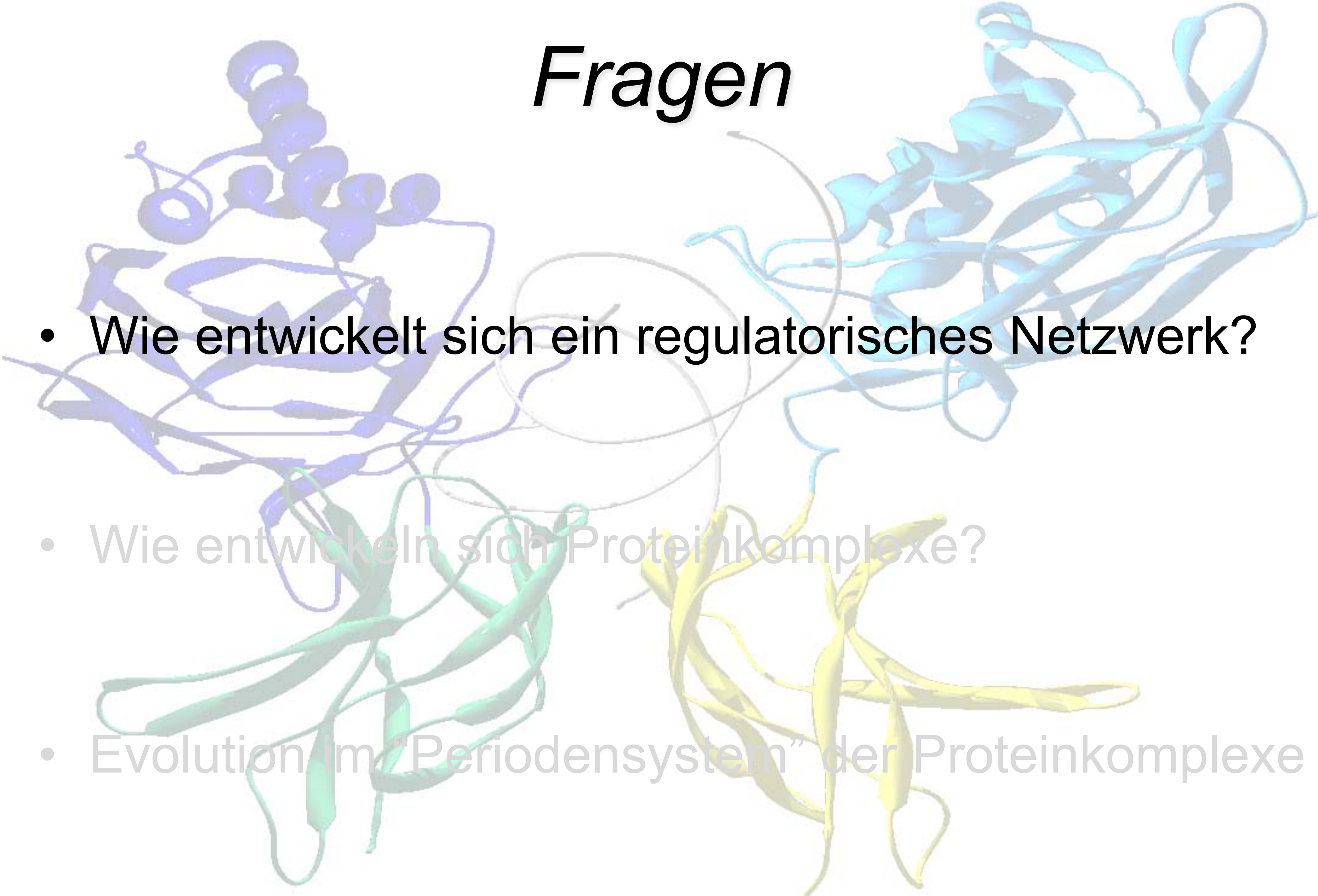
Protein-DNA



Fragen

- Wie entwickelt sich ein regulatorisches Netzwerk?
- Wie entwickeln sich Proteinkomplexe?
- Evolution im “Periodensystem” der Proteinkomplexe

Fragen



- Wie entwickelt sich ein regulatorisches Netzwerk?
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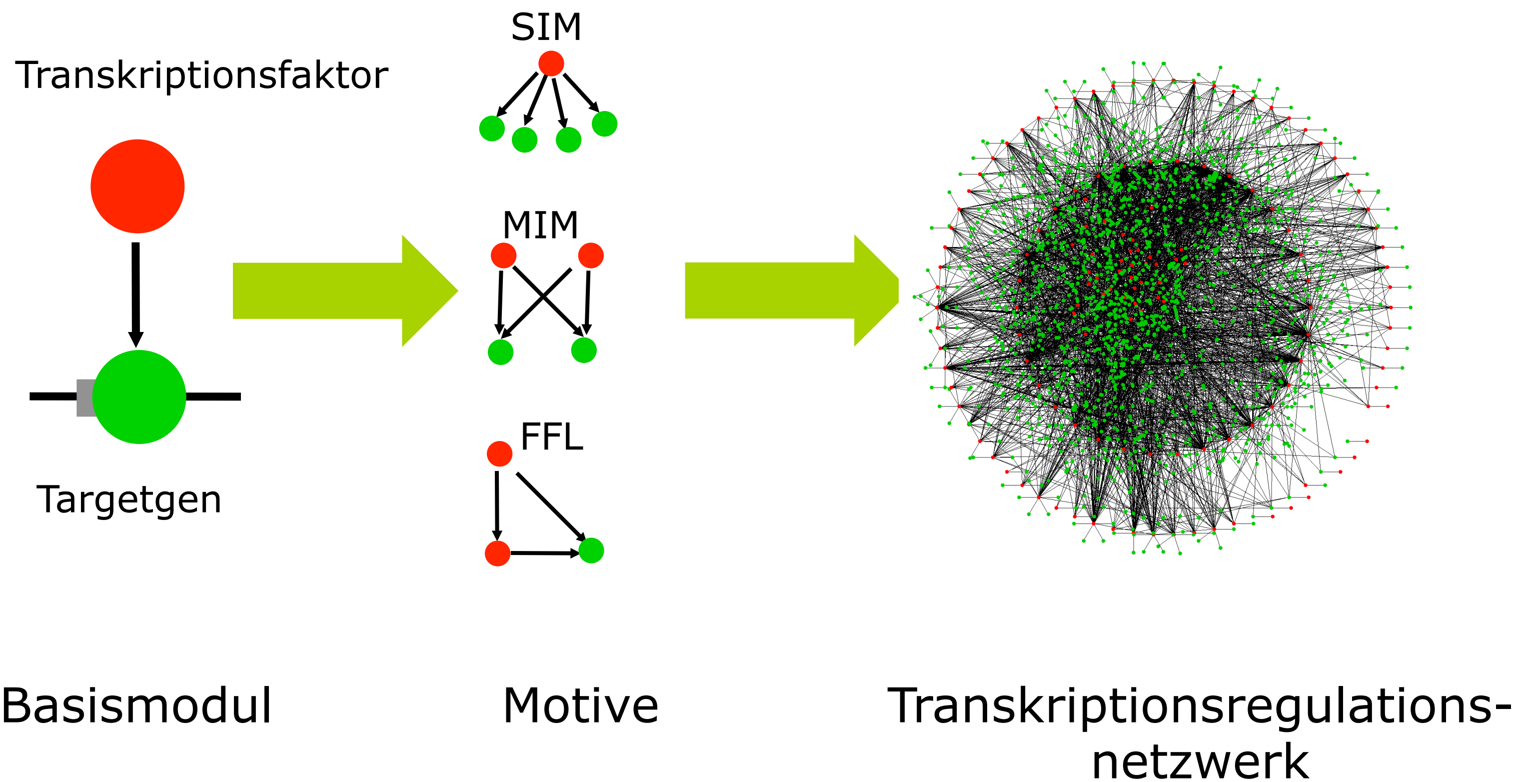
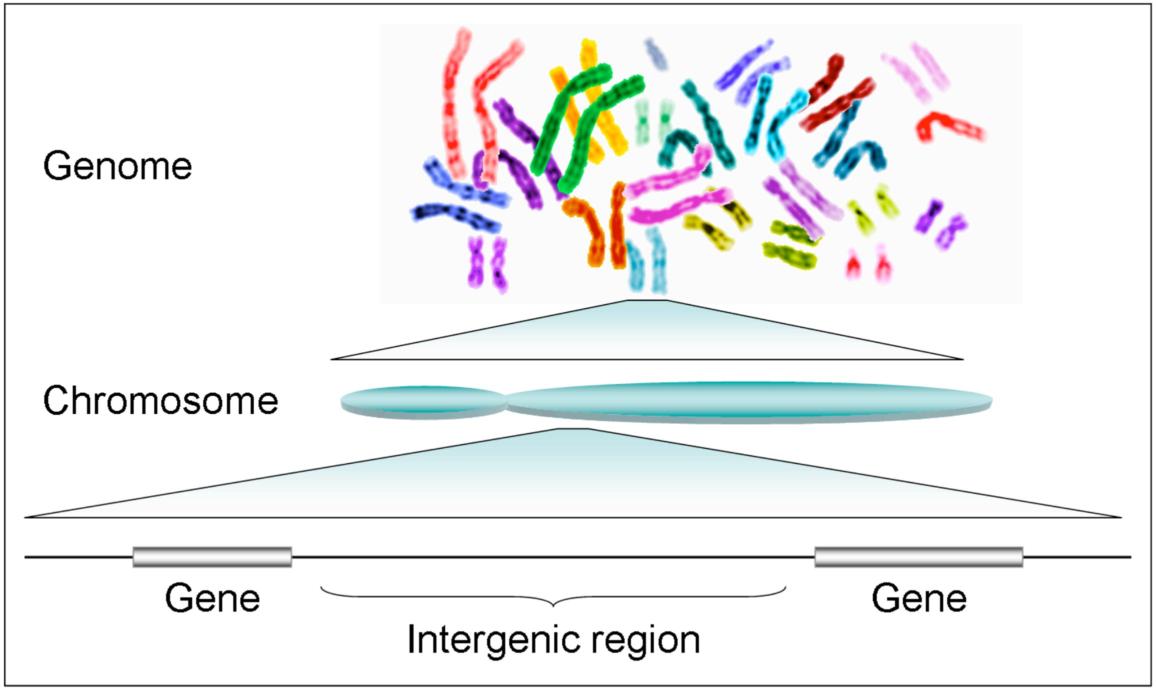
Organisation des Netzwerks der Genregulation



Babu et al. (2004) *Curr. Op. Struc. Biol*, 14, 283-291

Evolutionsvorgaenge in der DNA



1. Mutation: Divergenz oder Konservierung der Sequenz

2. Duplikation: Kopieren der Gene

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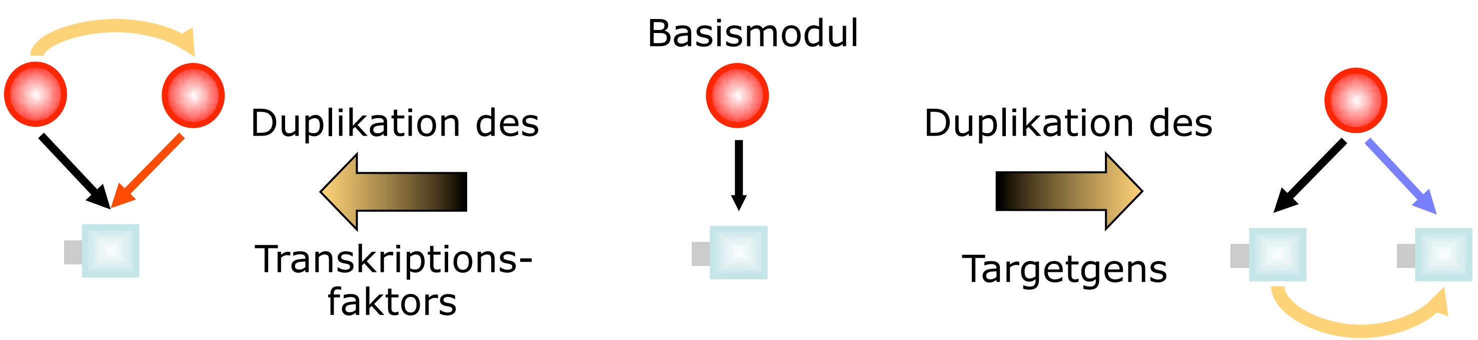
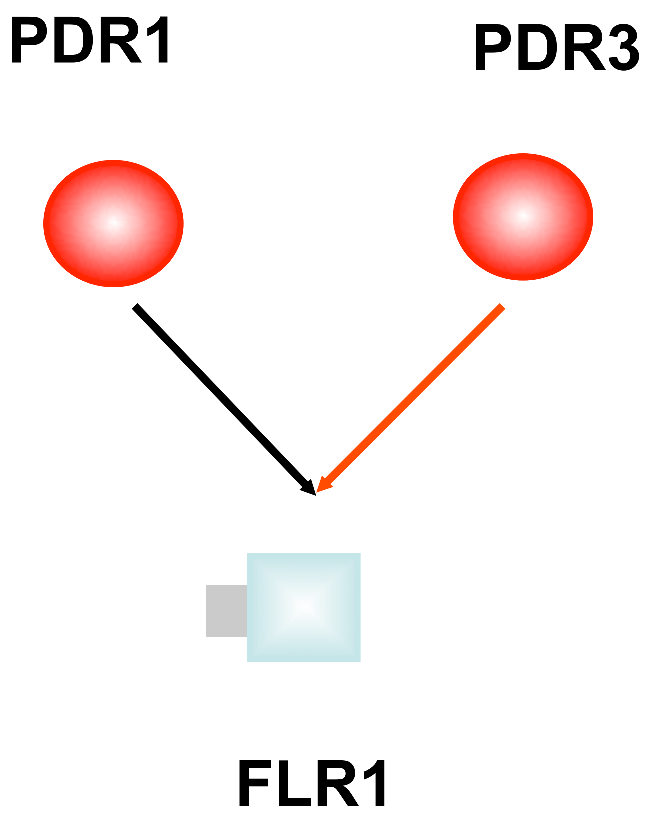
Duplikation des Basismoduls und Vererbung der Interaktion



Beispiel: Transkriptionsfaktorduplikation im Hefegenom

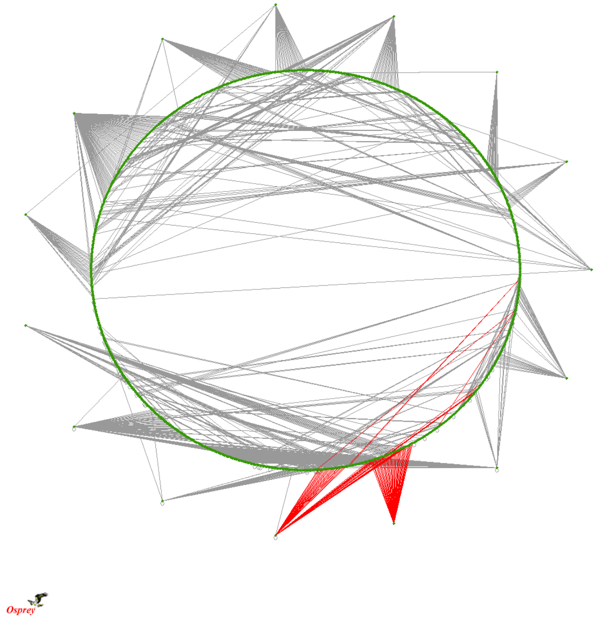


Wie haufig treten Transkriptionsfaktorduplikationen auf?

E. coli

128 Interaktionen aus 1233 insgesamt

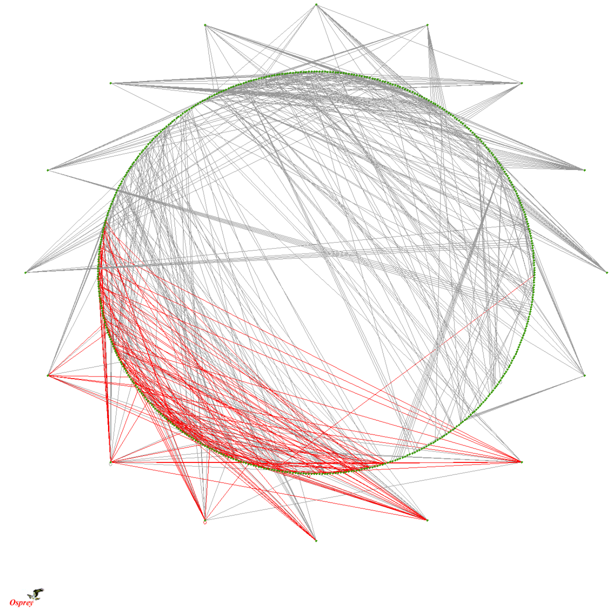
~ 10%



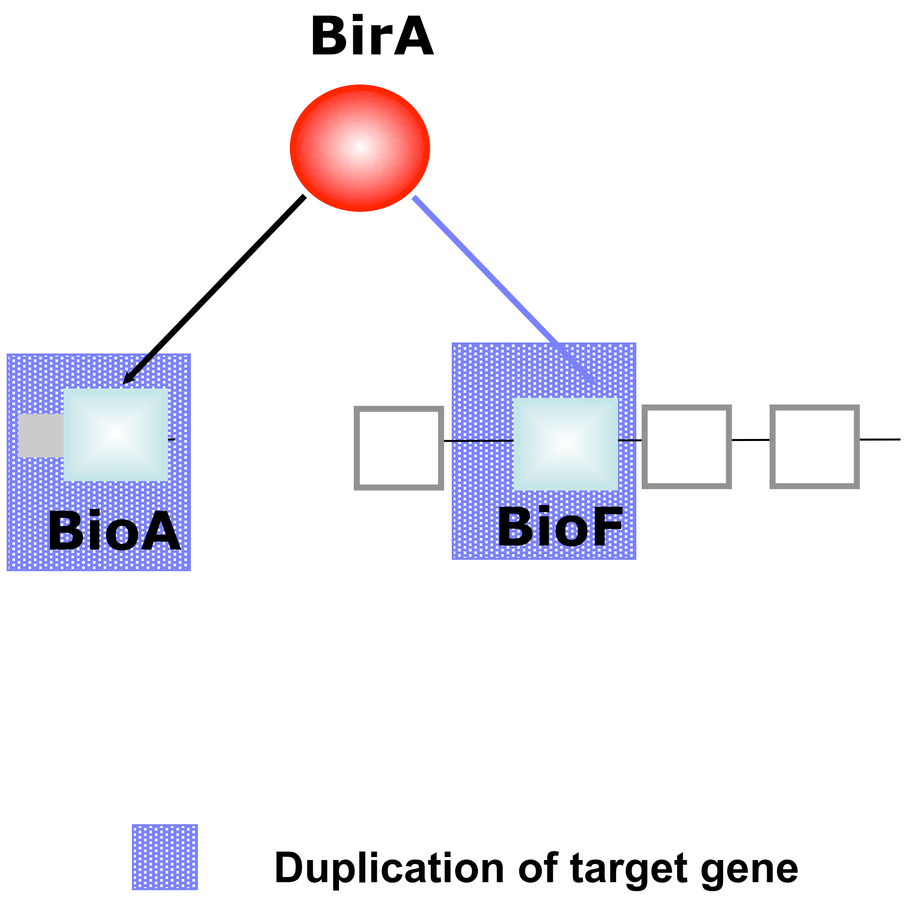
Hefe

188 Interaktionen aus 851 insgesamt

~ 22%



Beispiel: Targetgenduplikation in *E. coli*

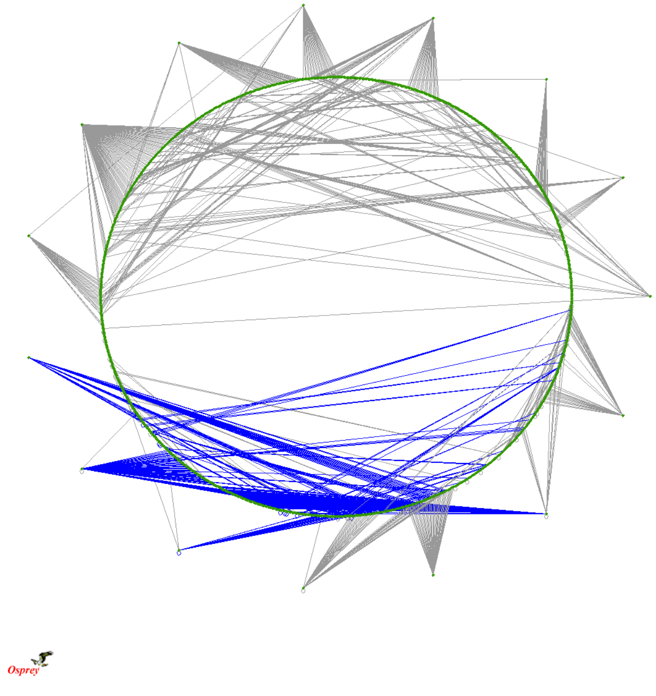


Wie haufig treten Targetgenduplikationen auf?

E. coli

272 Interaktionen aus 1233 insges.

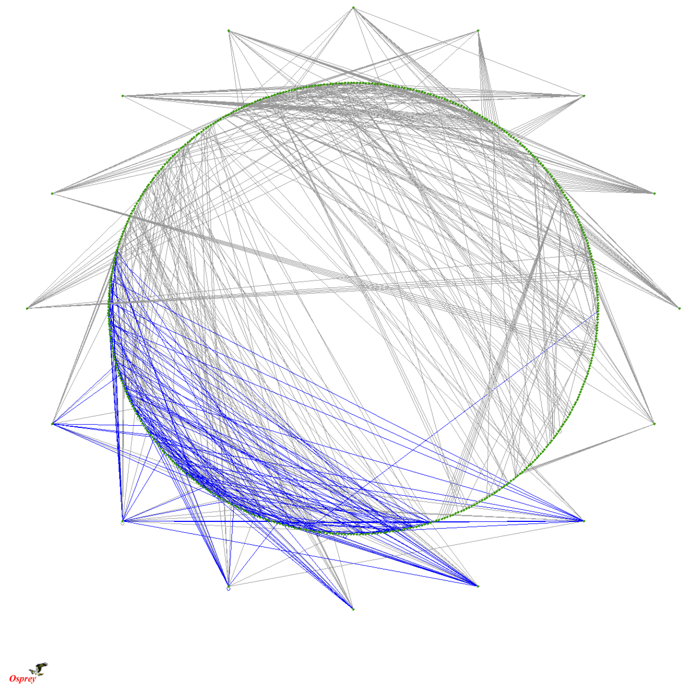
~ 22%



Hefe

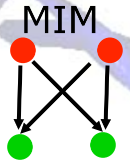
166 Interaktionen aus 851 insges.

~ 20%



Fragen

- Wie entwickelt sich ein regulatorisches Netzwerk?



Genduplikation als Motor der Evolution

- Wie entwickeln sich Proteinkomplexe?

- Evolution im "Periodensystem" der Proteinkomplexe

Fragen

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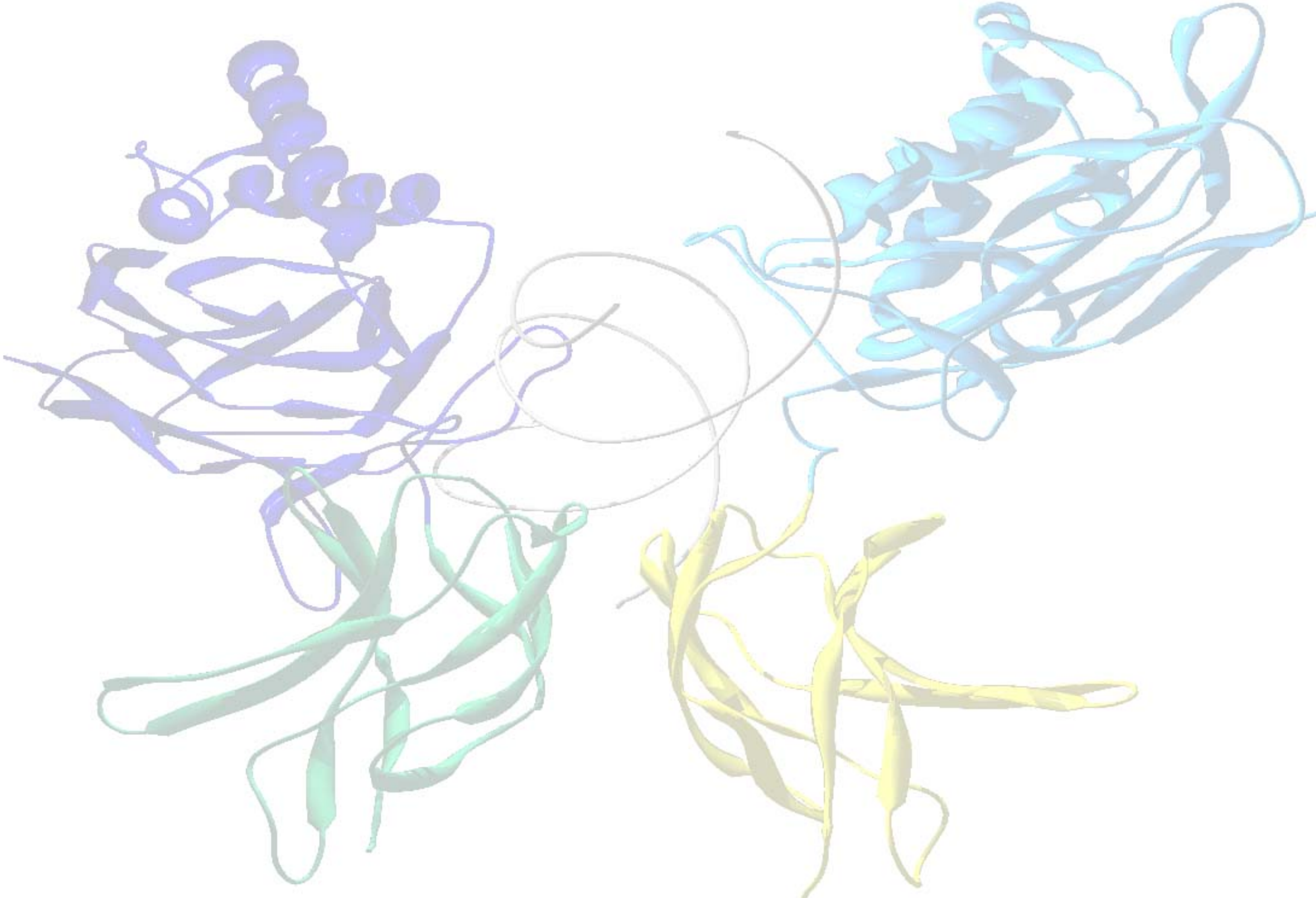
- Wie entwickeln sich Proteinkomplexe?



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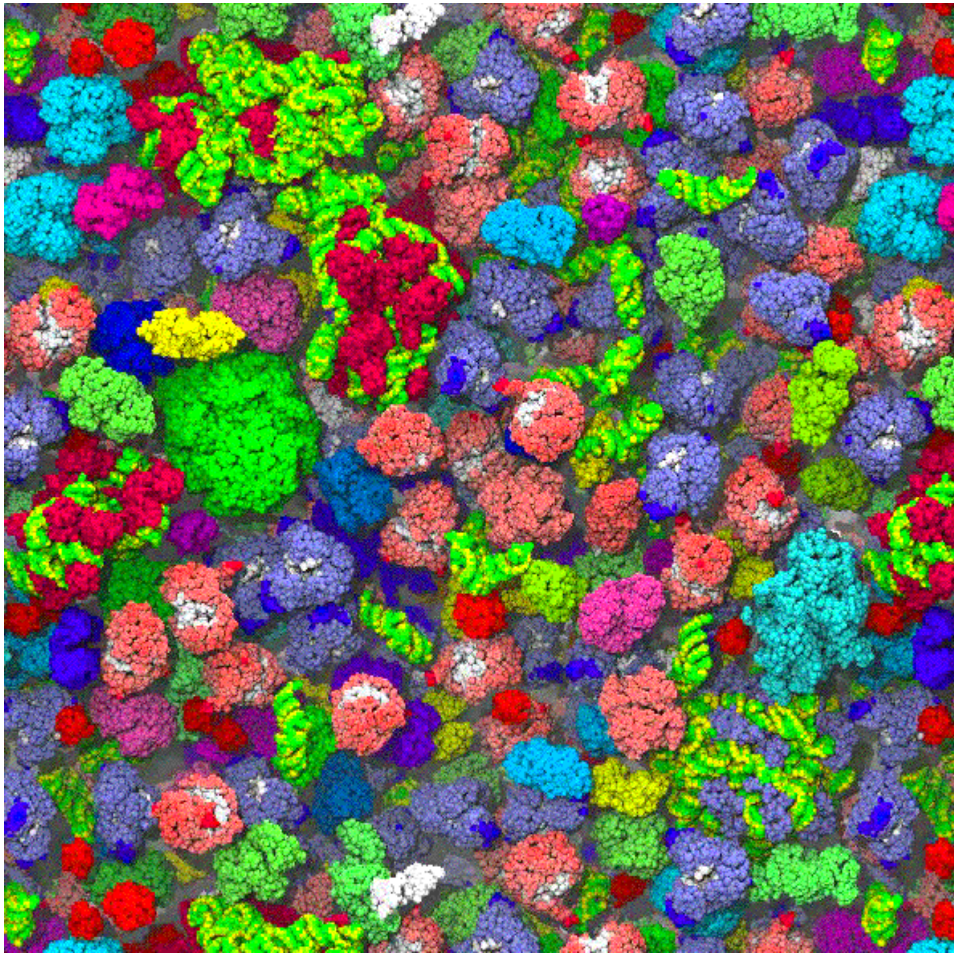
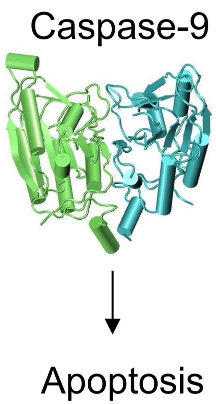


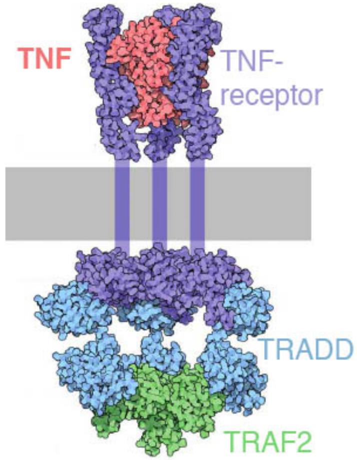
McGuffee & Elcock, *PLoS Comp Biol*, 2010

Two types of protein complexes

- Homomers



- Heteromers



Two types of protein complexes

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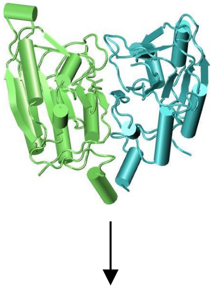
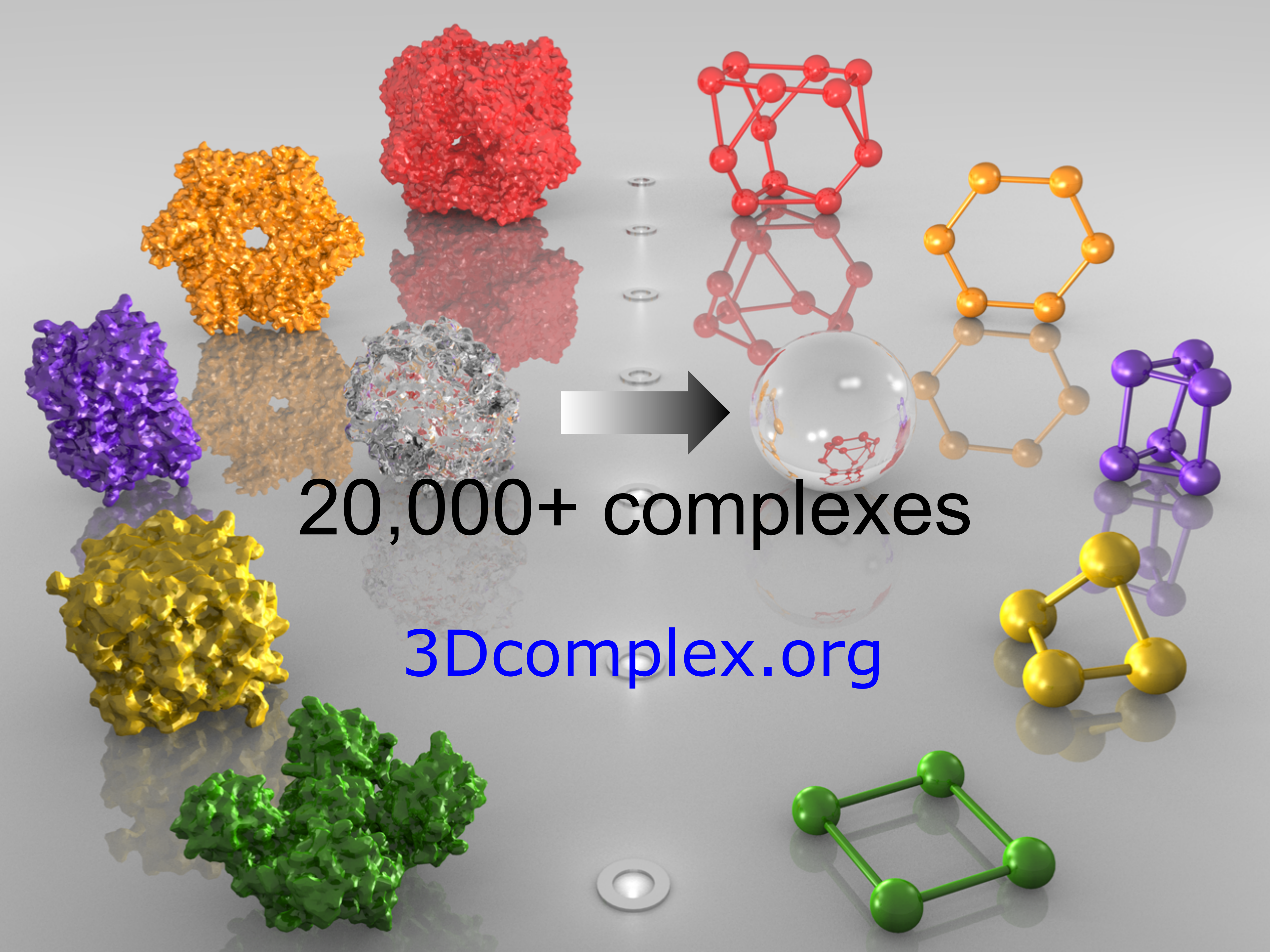
Caspase-9

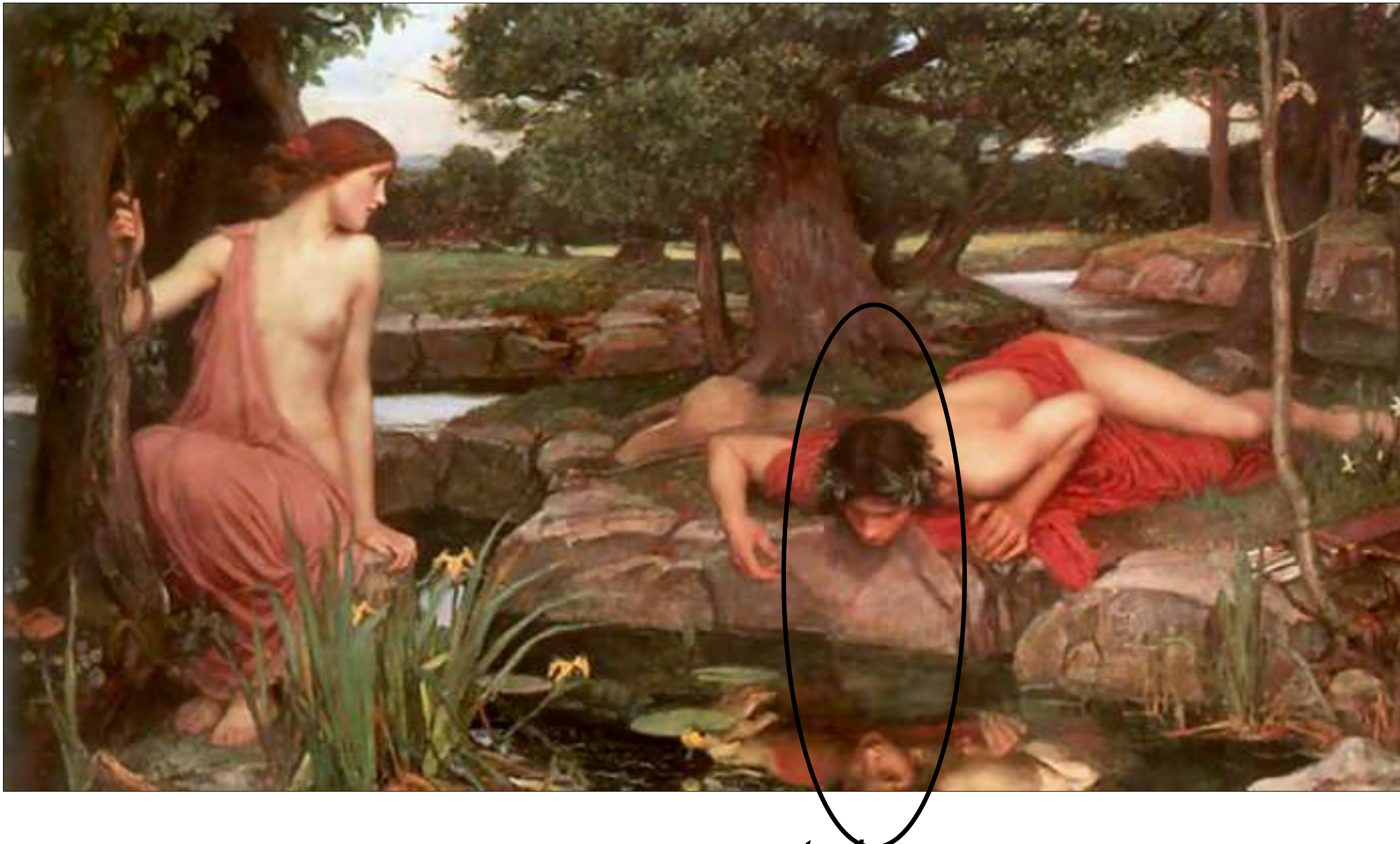


Apoptosis


20,000+ complexes
3Dcomplex.org

Molecular Narcissism:

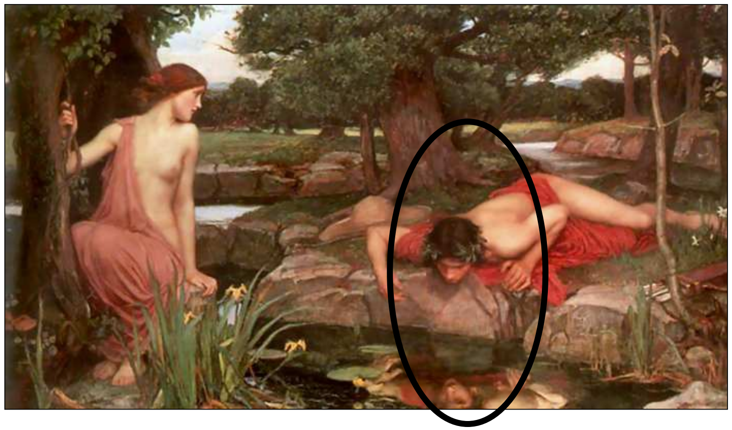
2/3 of proteins form homomers



Levy, E.D. *et al*. (2006) *PLoS Comp Biol*., **2**, e155.

Symmetrie

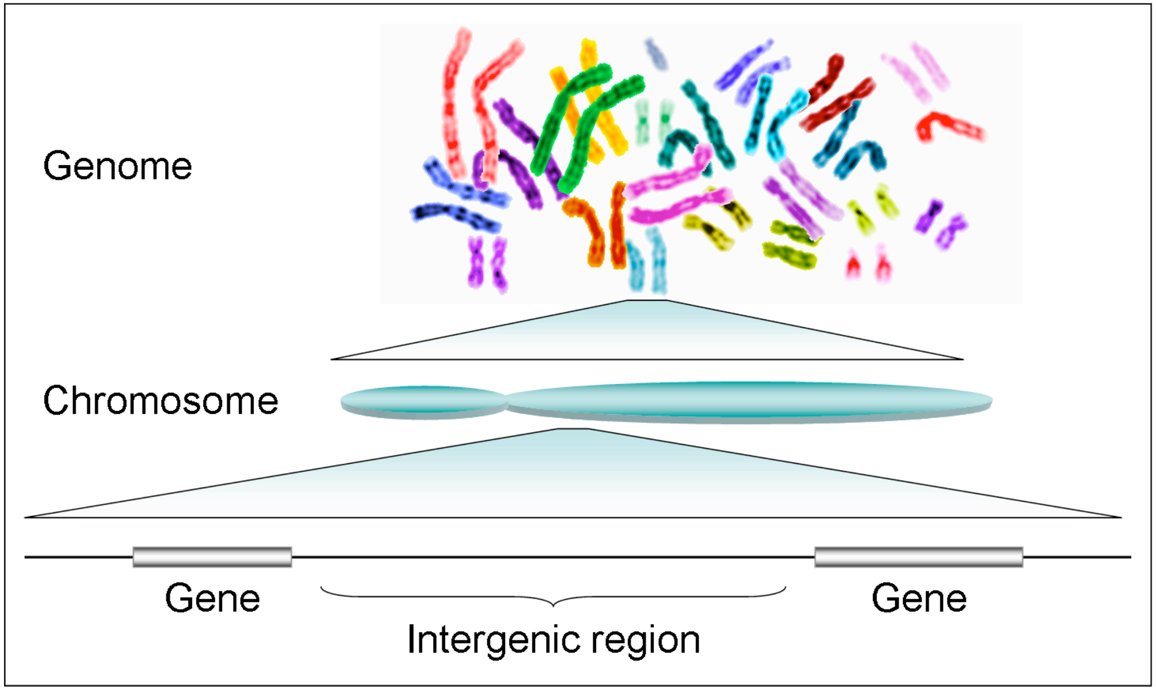
Reflektion



Rotation

Evolution der Symmetrie

Evolutionsvorgaenge in der DNA



1. **Mutation: Divergenz oder Konservierung der Sequenz**
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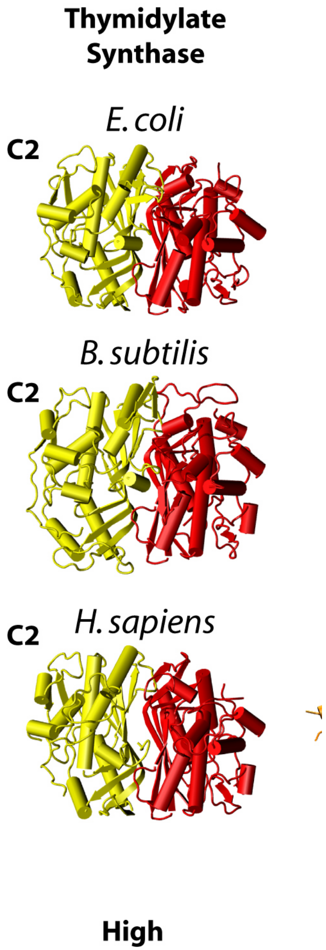
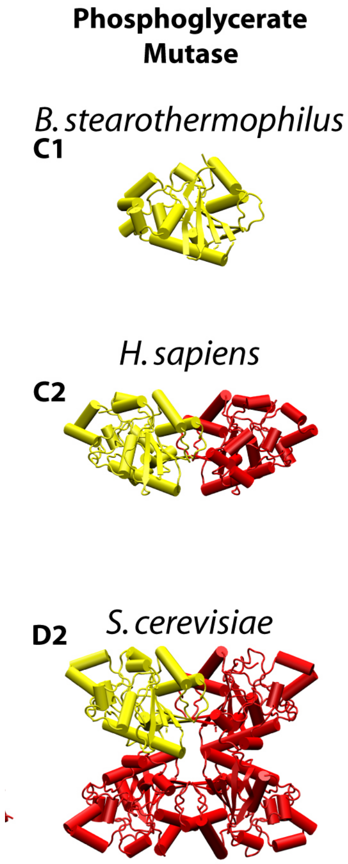
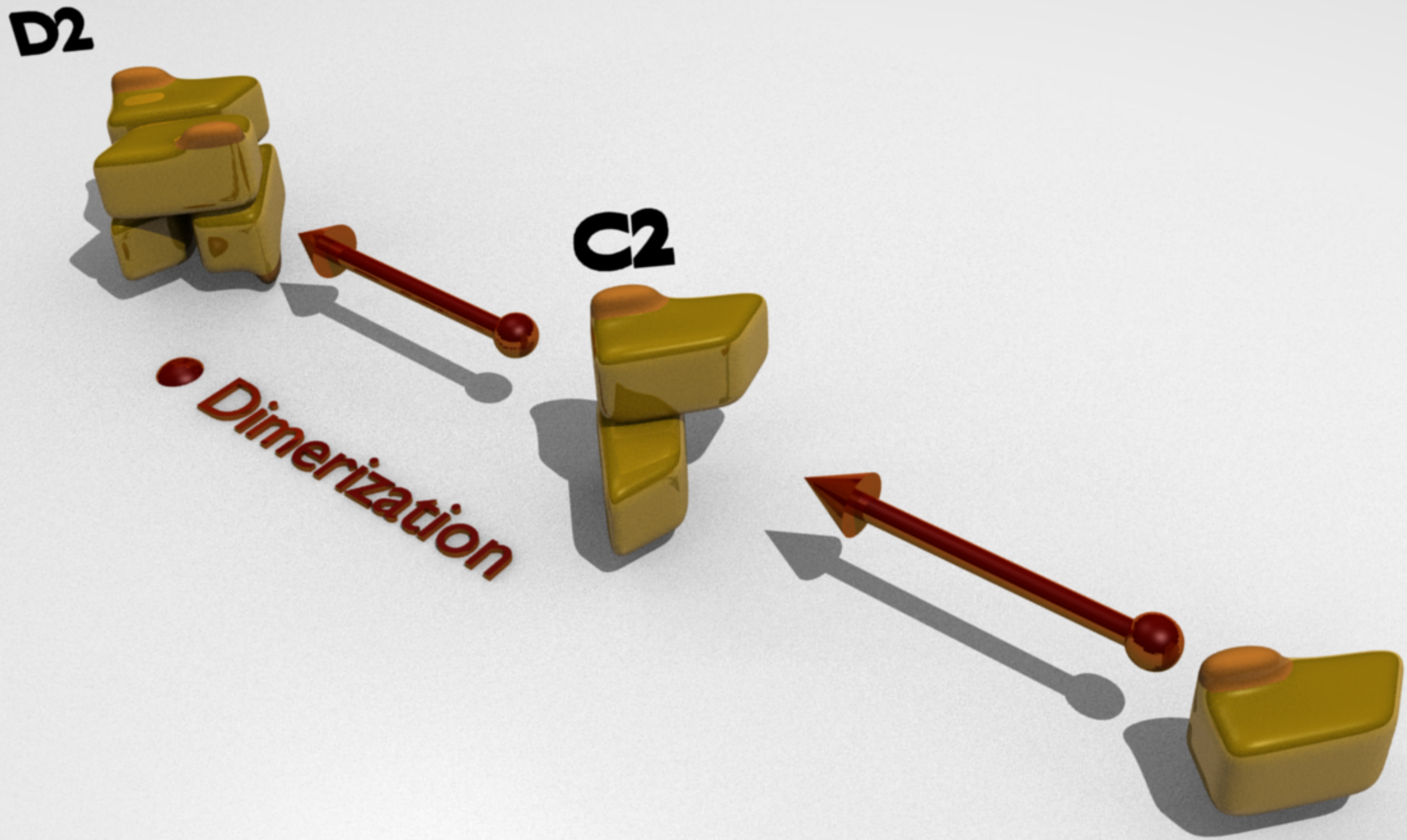
Konserviertheit oder Divergenz der Strukturen?



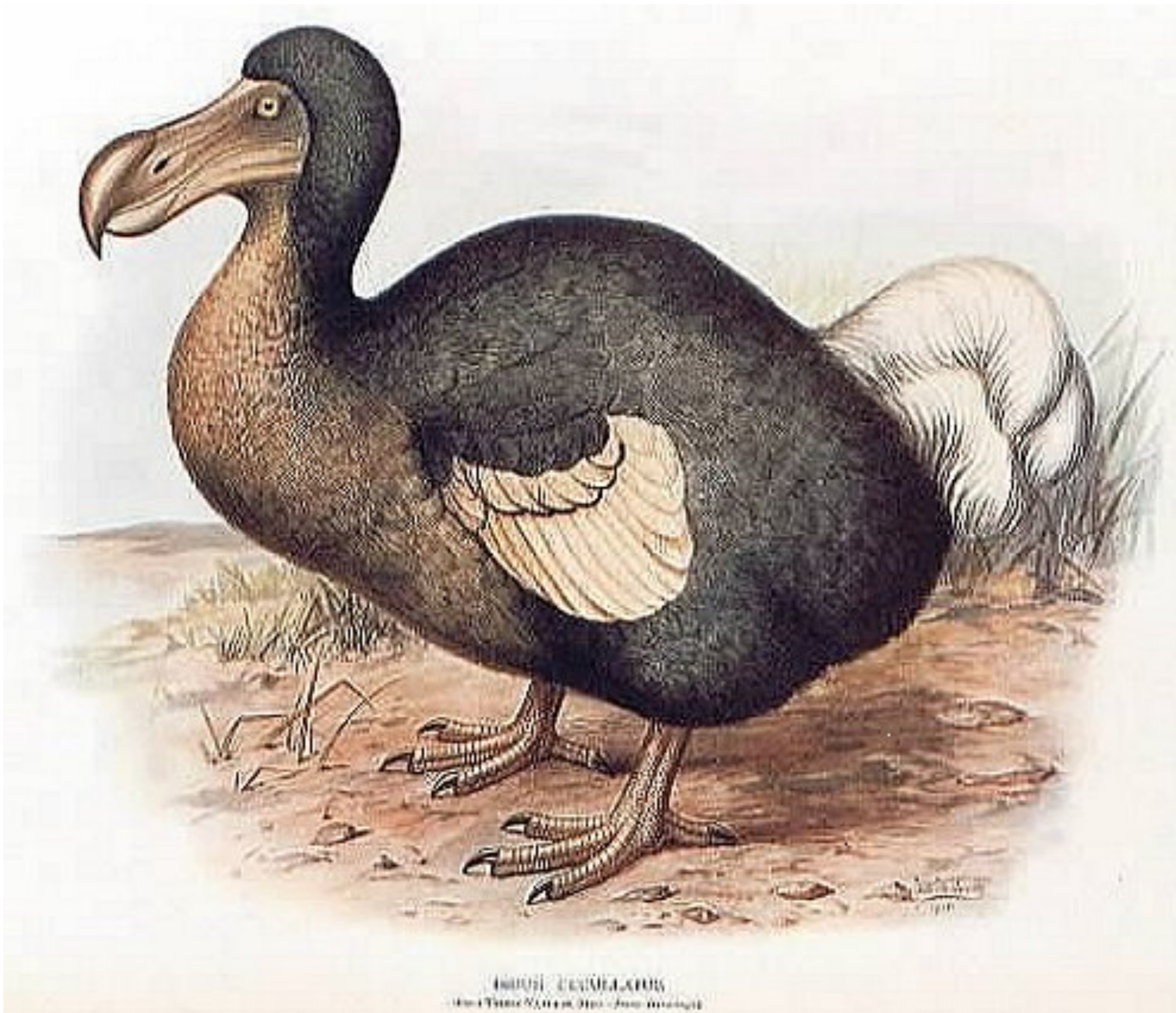
Konserviertheit oder Divergenz der Strukturen?

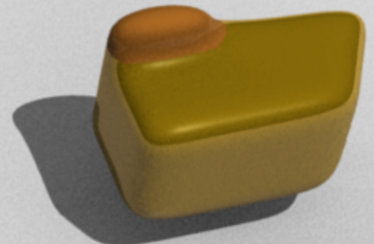


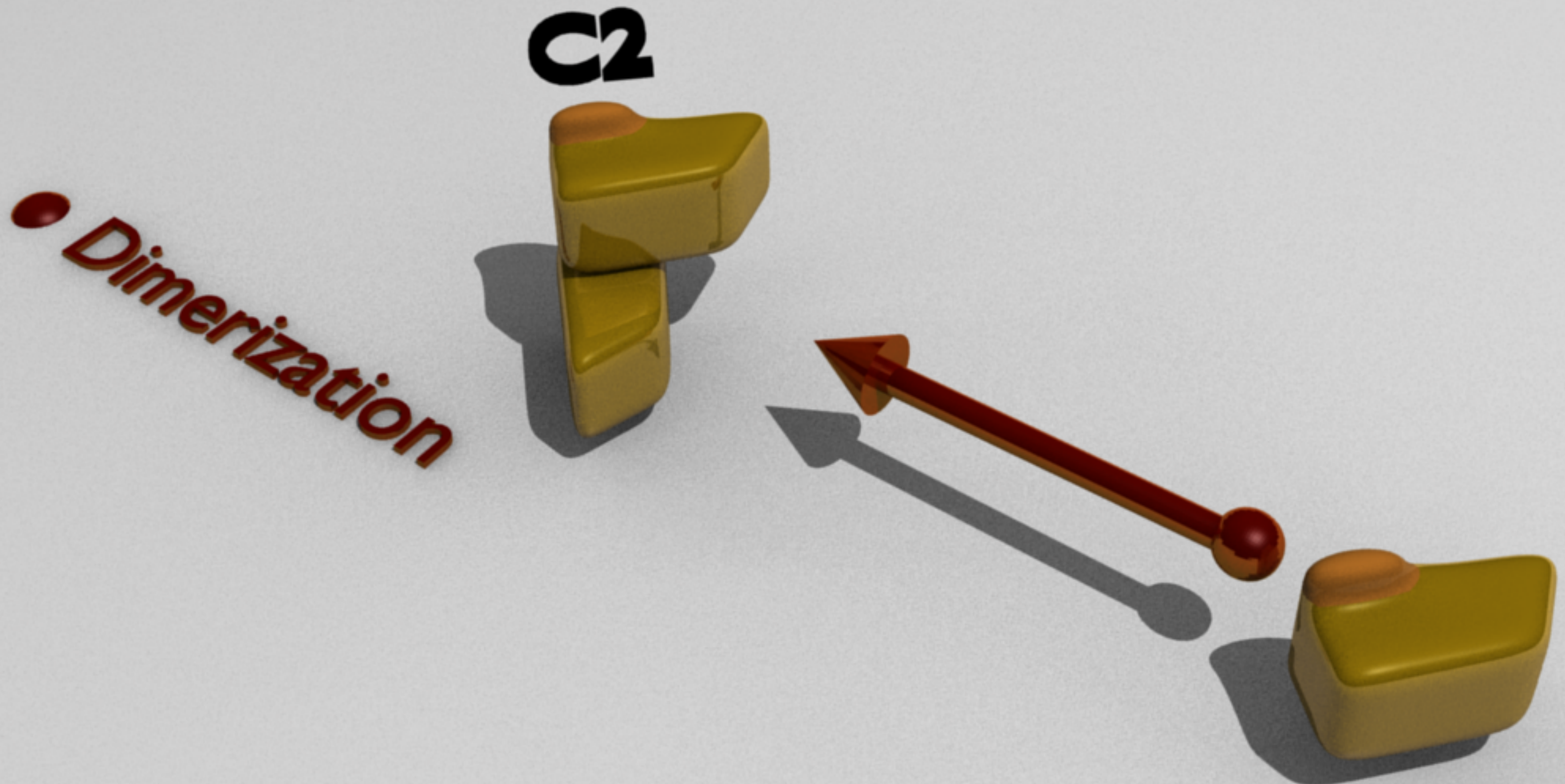
Evolutionspfad: Monomer-Dimer-Tetramer

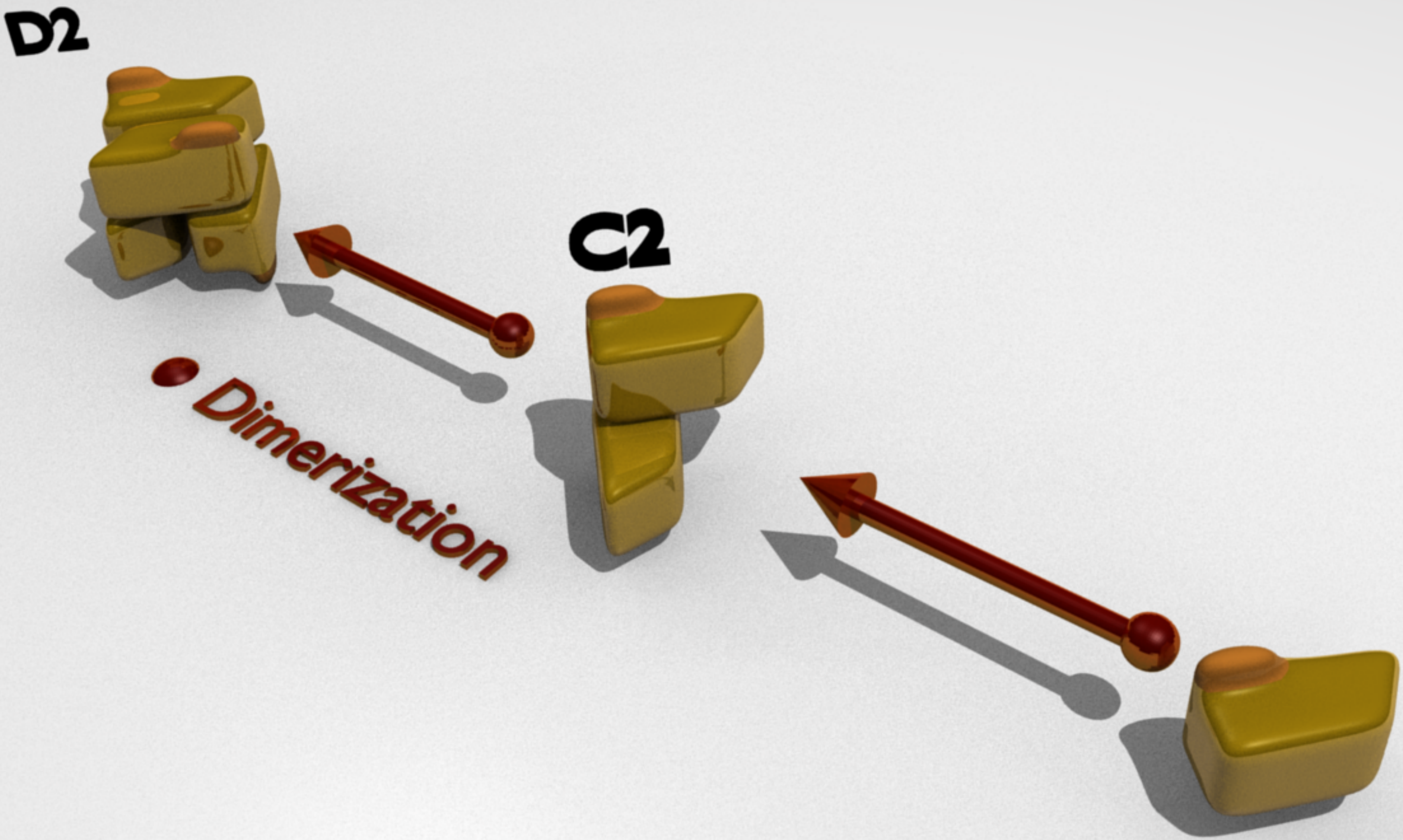


Warum diese Wege? Unnuetzes Evolutionsrelikt?



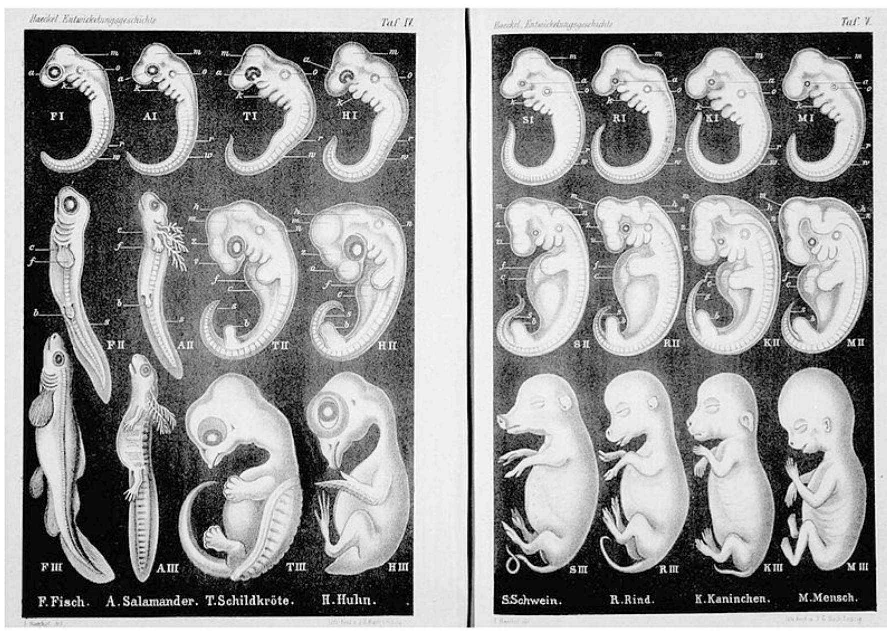



C2
Dimerization


D2
C2
Dimerization

Proteinkomplexe:

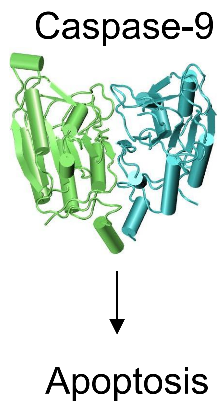
Assemblierungsweg spiegelt die Evolution wider



Levy, E.D., Erba, E.B., Robinson, C.V. & Teichmann, S.A. (2008). *Nature*, 453, 1262-5.

Two types of protein complexes

- Homomers



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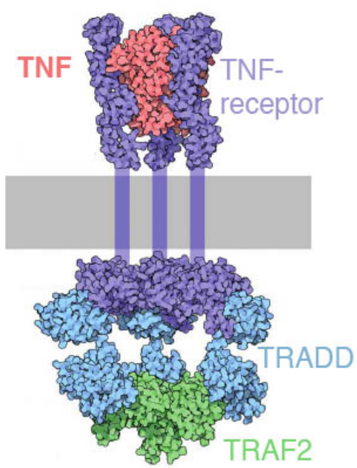
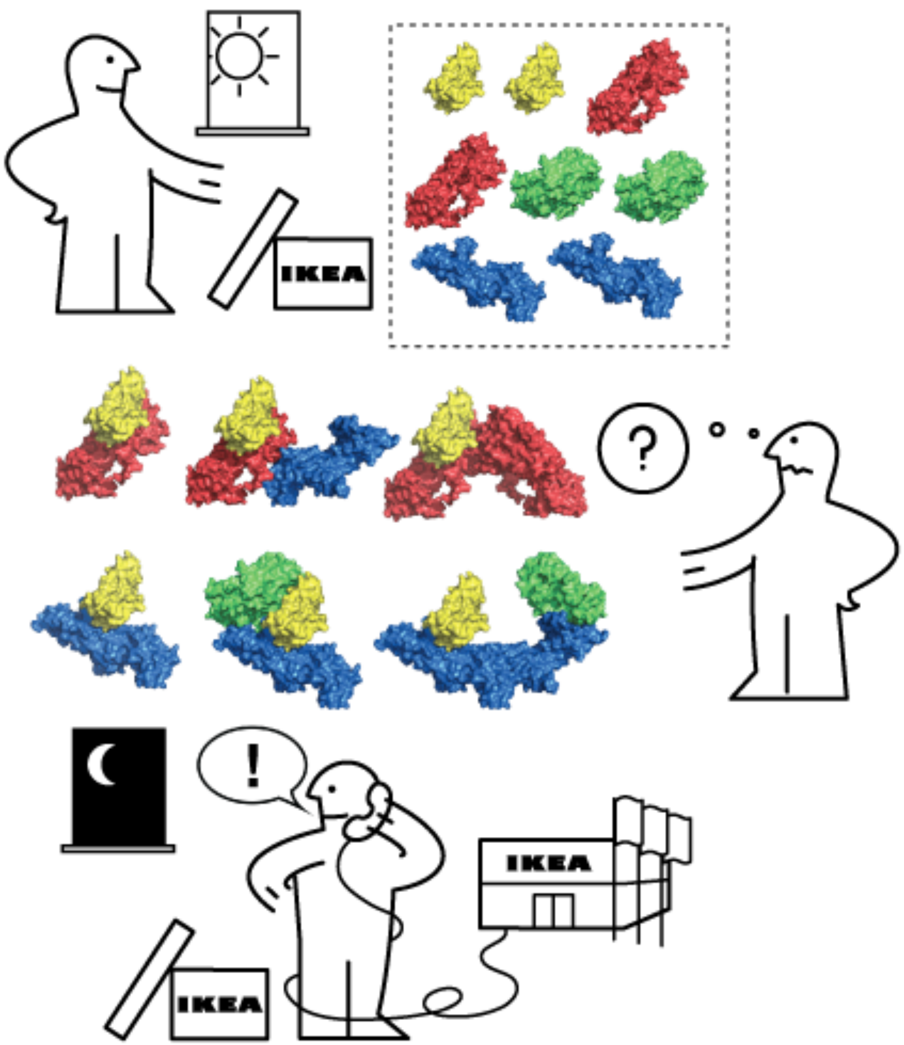


The order of assembly is important

Random assembly



Joe Marsh

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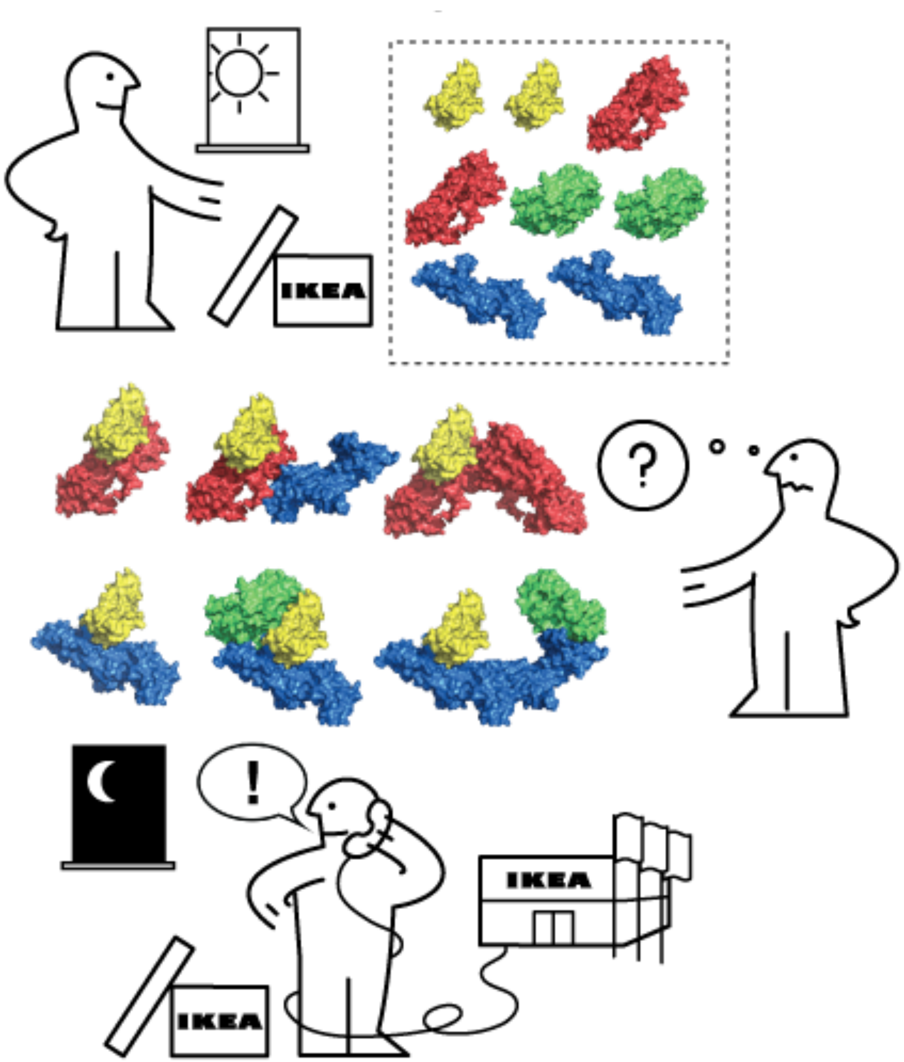
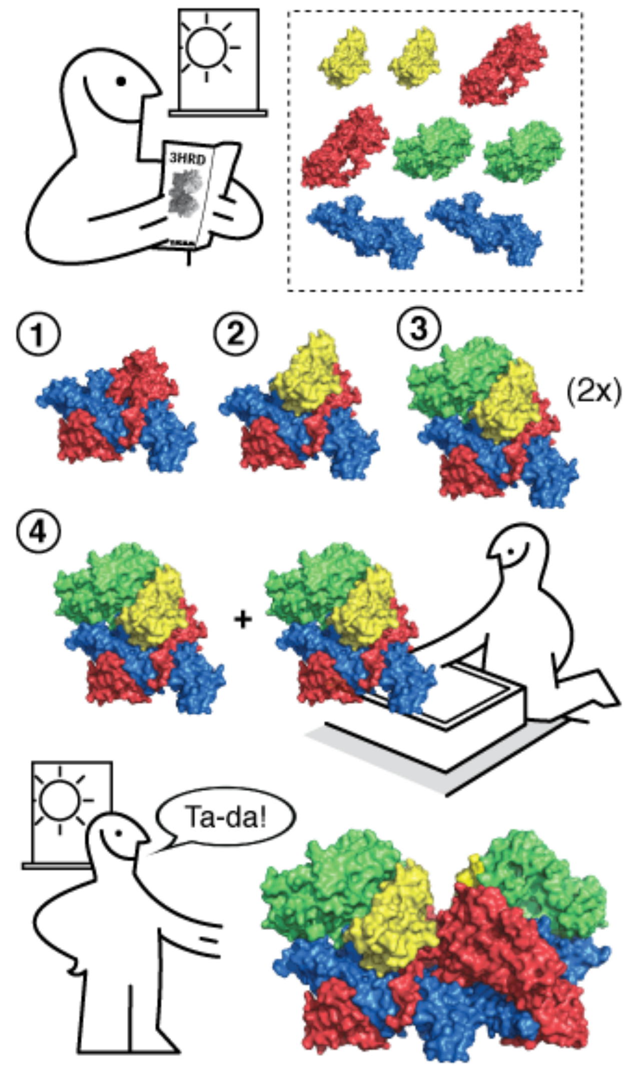
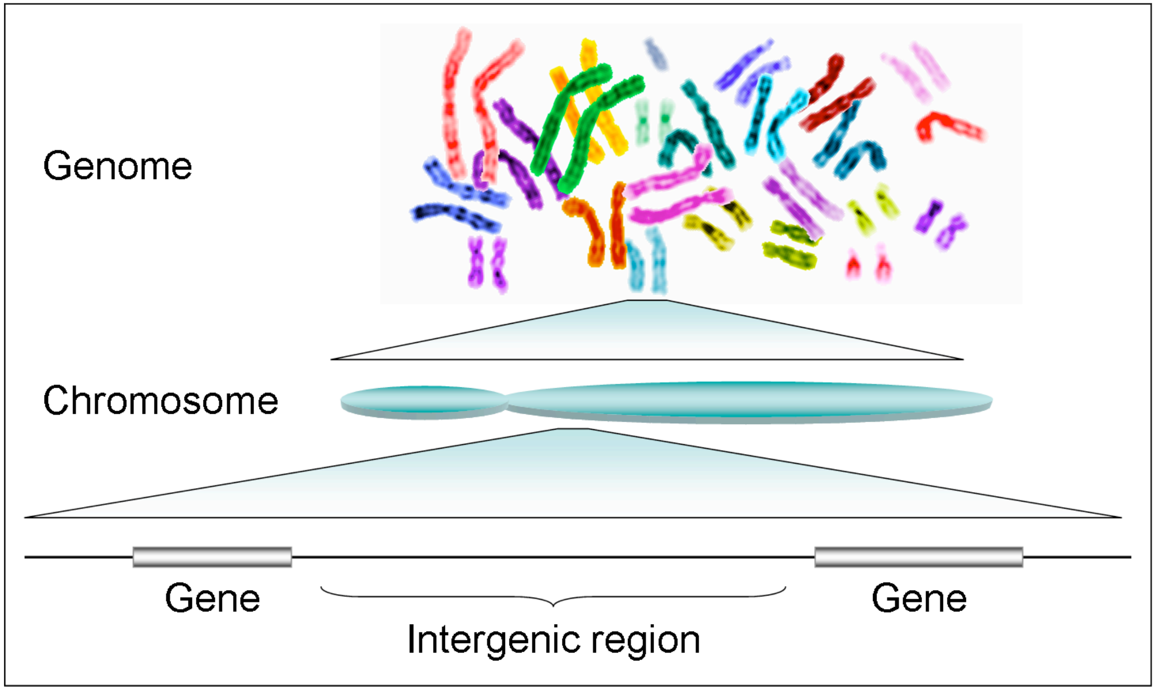


Ordered assembly



Joe Marsh

Evolutionsvorgaenge in der DNA



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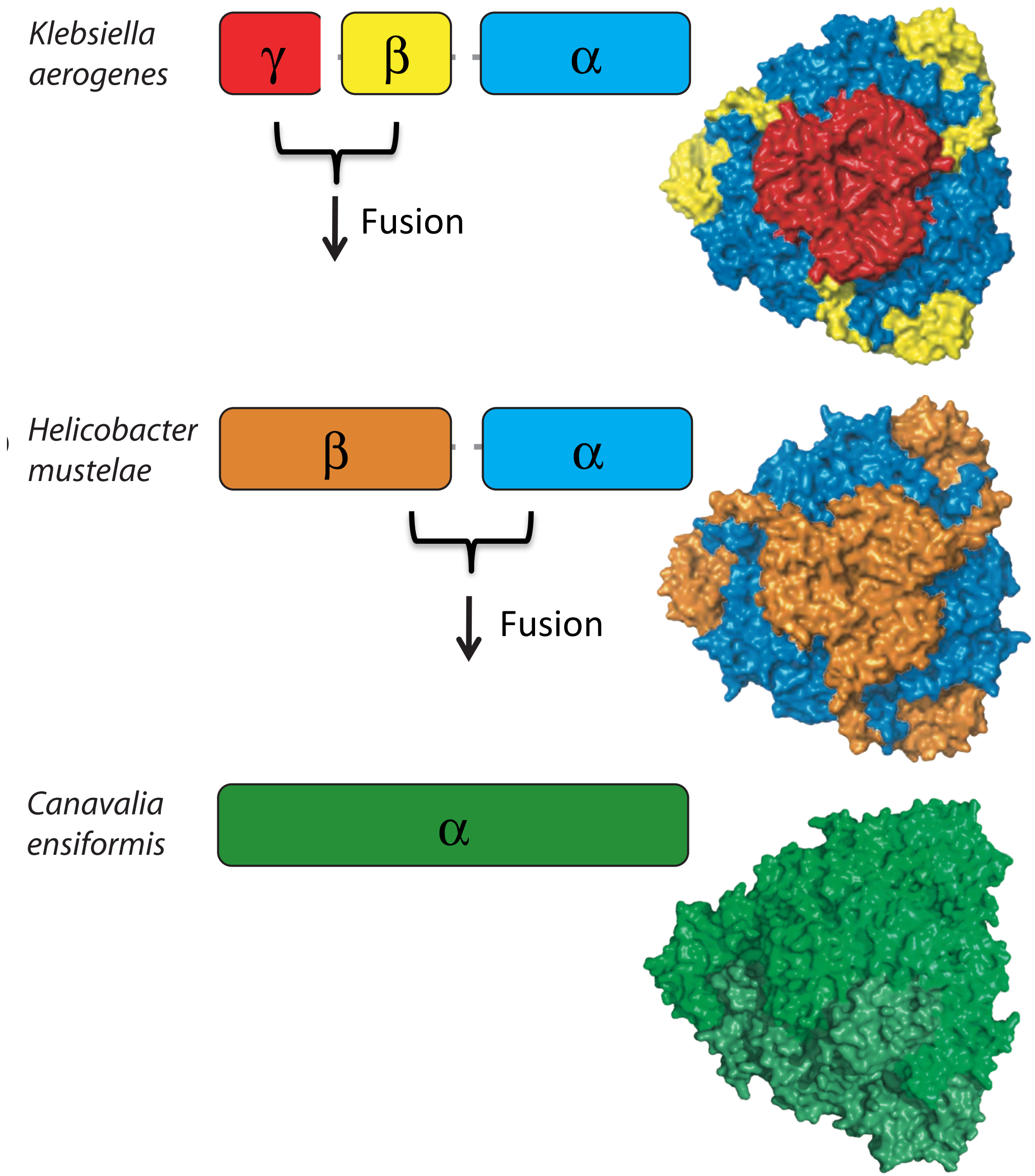
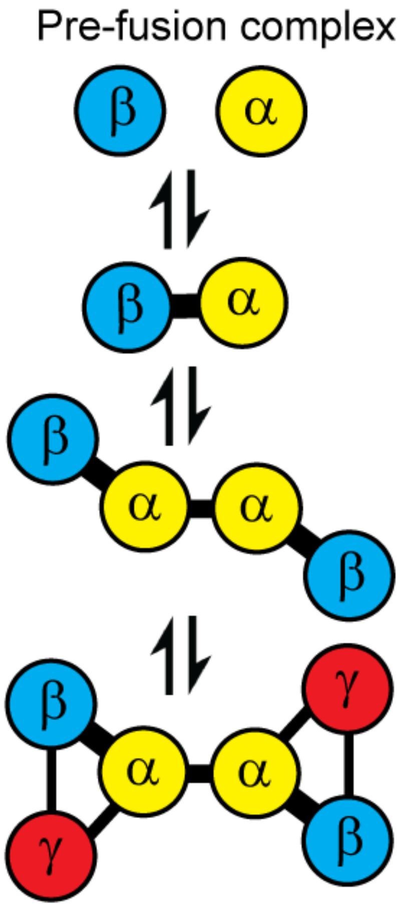
Probing assembly conservation:

Gene fusion and fission

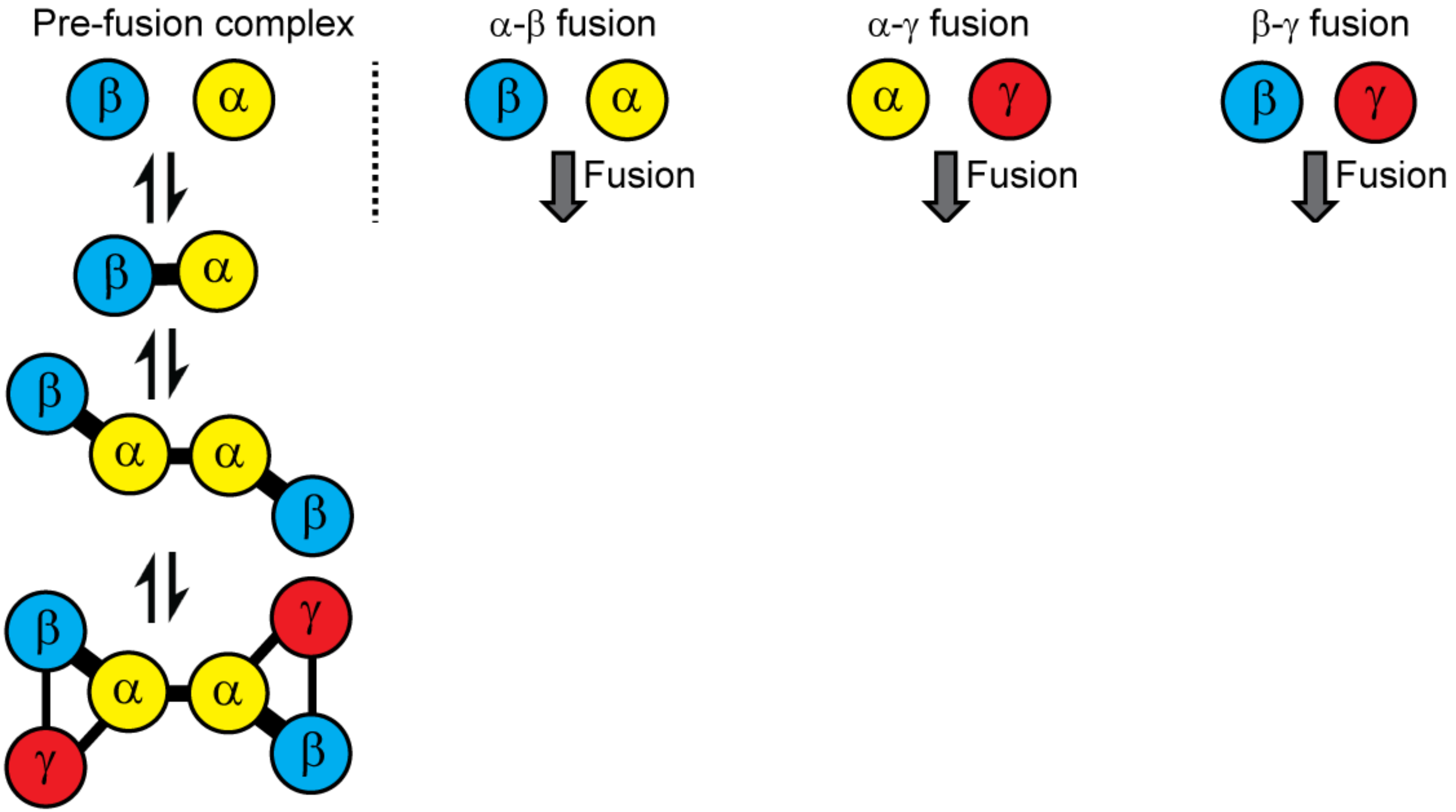


Marsh, J., Hernandez, H., Hall, Z., Ahnert, S., Perica, T., Robinson, C.V., Teichmann, S.A. (2013) *Cell*, 153, 461-70 .

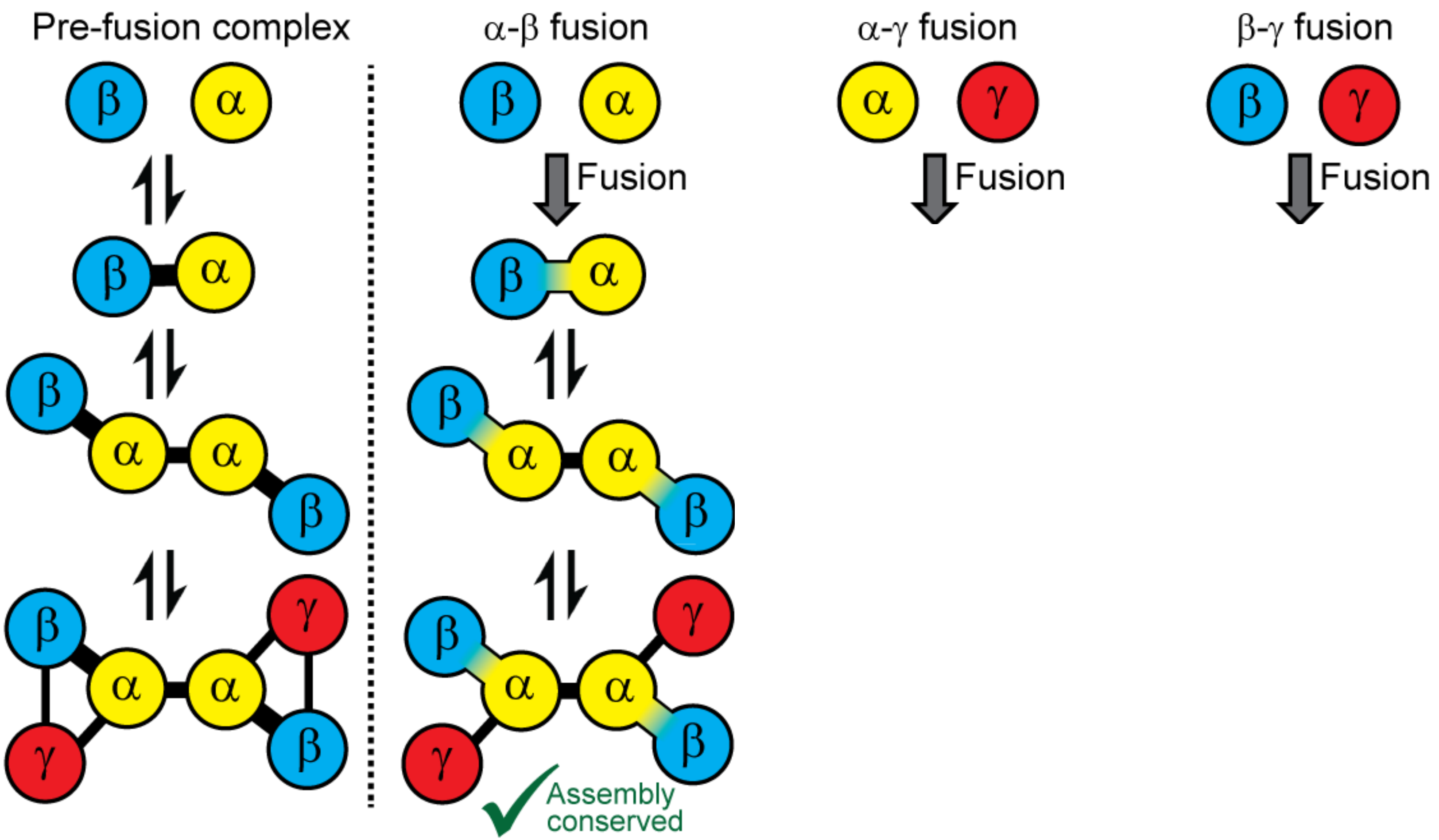
Probing assembly conservation with gene fusion events



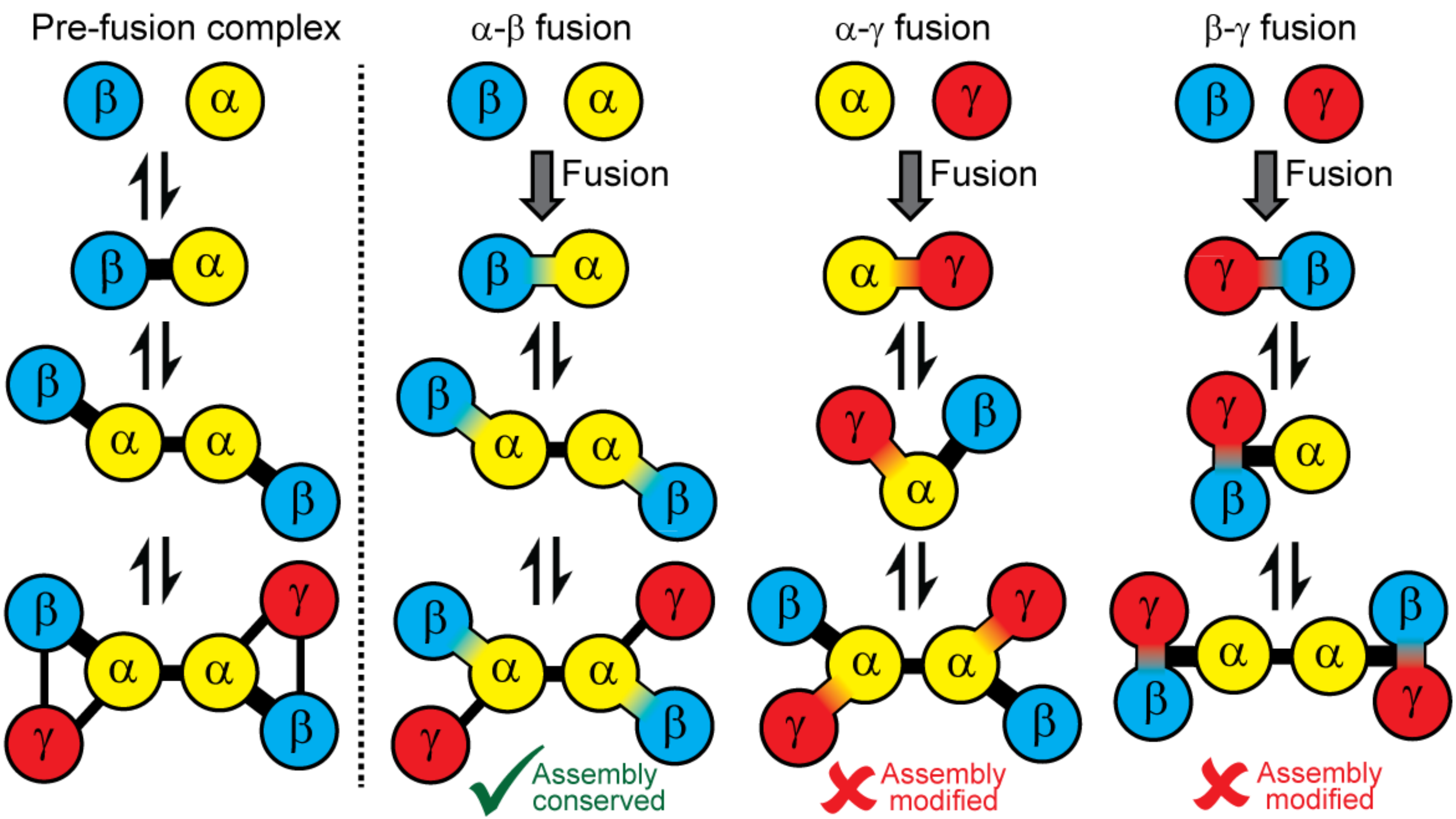
Probing assembly conservation with gene fusion events



Probing assembly conservation with gene fusion events



Probing assembly conservation with gene fusion events



Fragen

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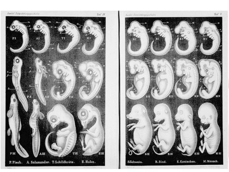

Evolution widerspiegelt Assemblierungsweg

Fragen

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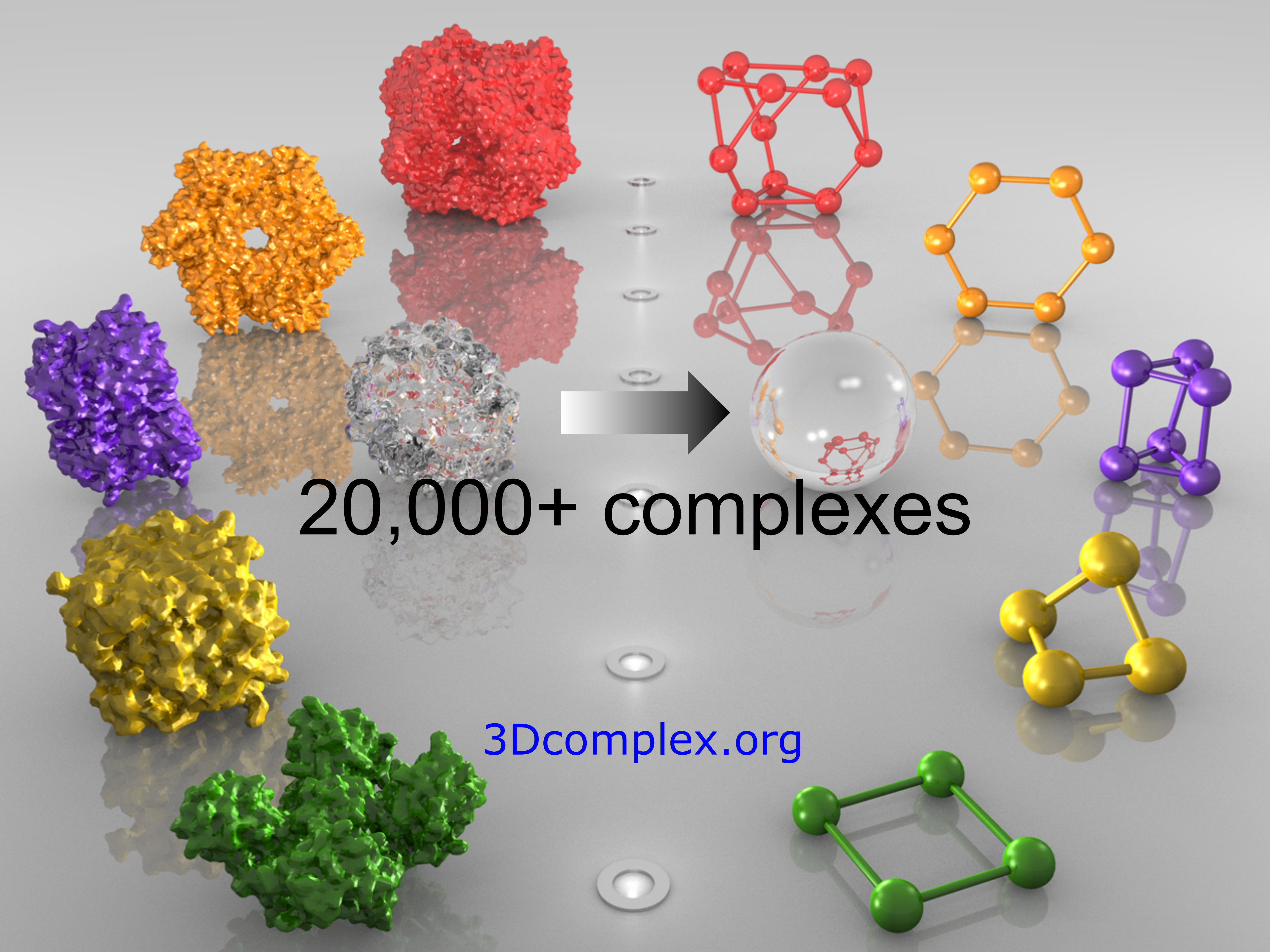
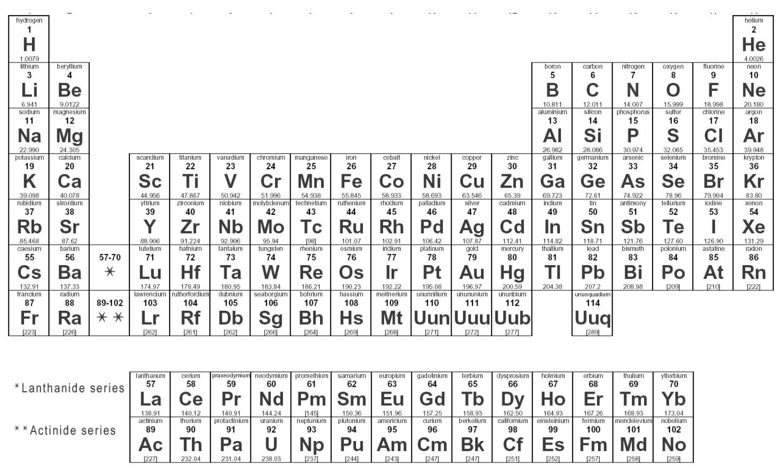
- Evolution im “Periodensystem” der Proteinkomplexe

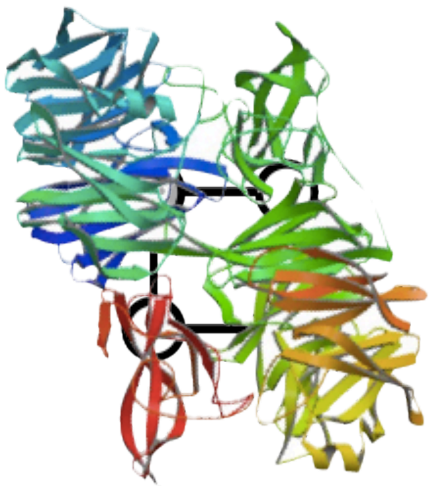

20,000+ complexes
3Dcomplex.org

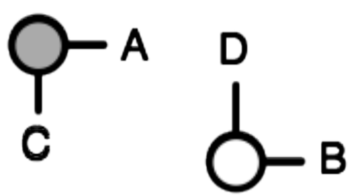
Klassifizierung der Proteinkomplexe

20,000+ Komplexe



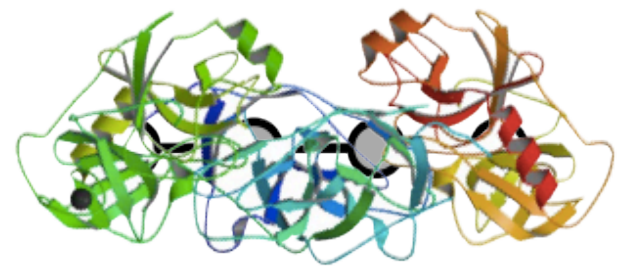
KODIERUNG DES ASSEMBLIERUNGSWEGS

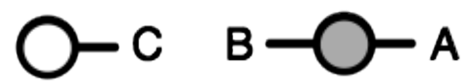




A-B C-D

$$(2,2) \quad \begin{pmatrix} 0 & 2 \\ 2 & 0 \end{pmatrix}$$

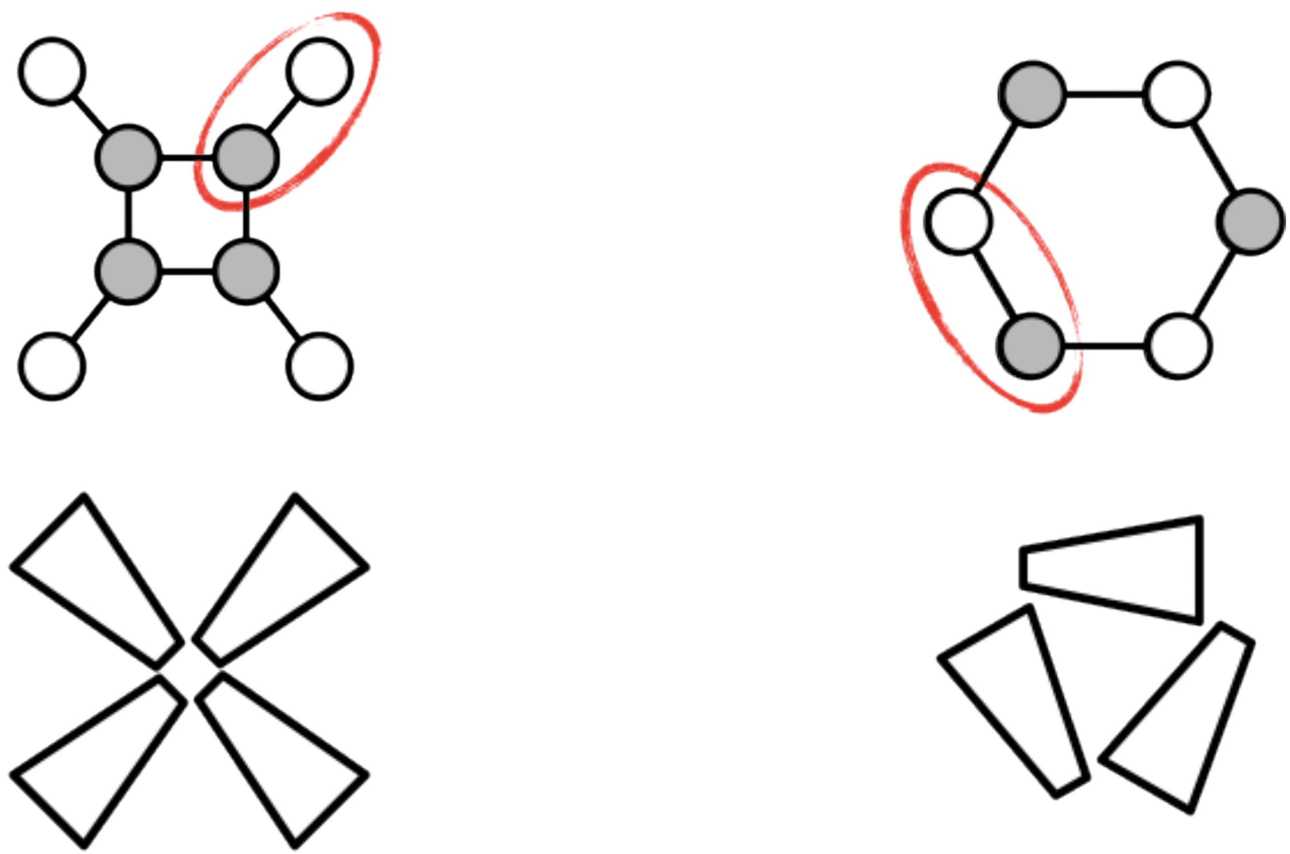




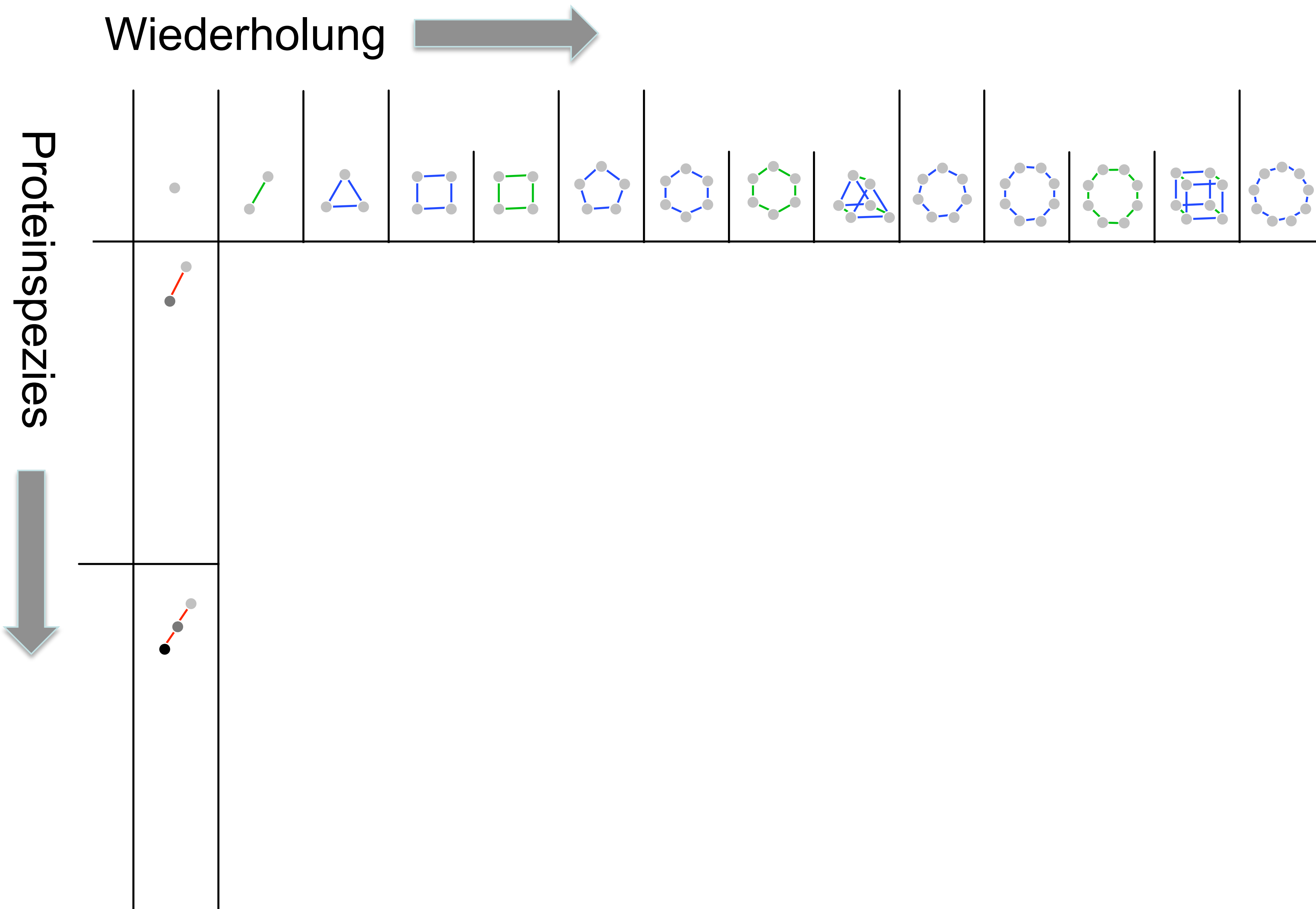
A-A B-C

$$(2,2) \quad \begin{pmatrix} 1 & 1 \\ 1 & 0 \end{pmatrix}$$

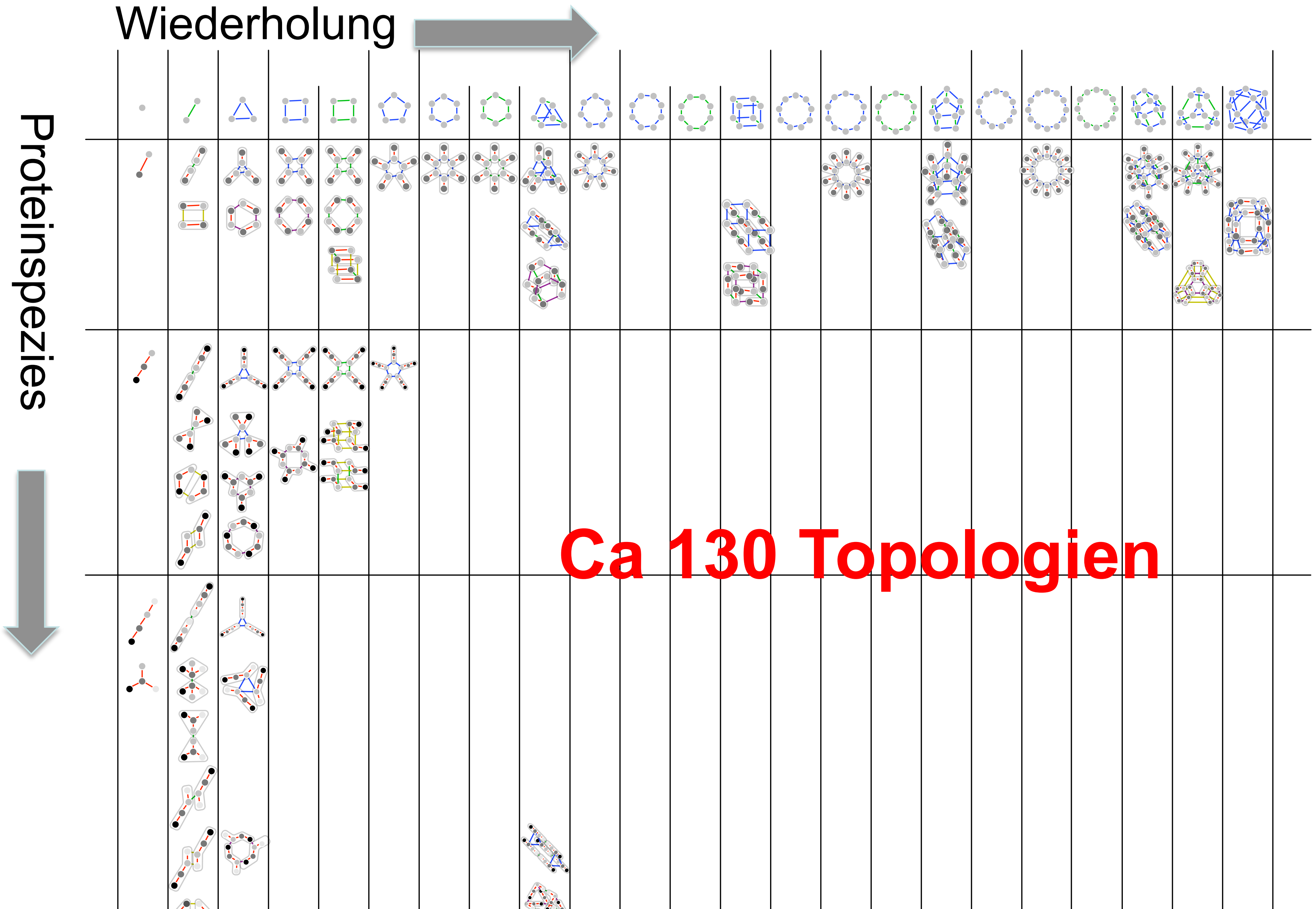
Equal numbers of self-assembly building blocks…



“Periodensystem” der Proteinkomplexe



“Periodensystem” der Proteinkomplexe

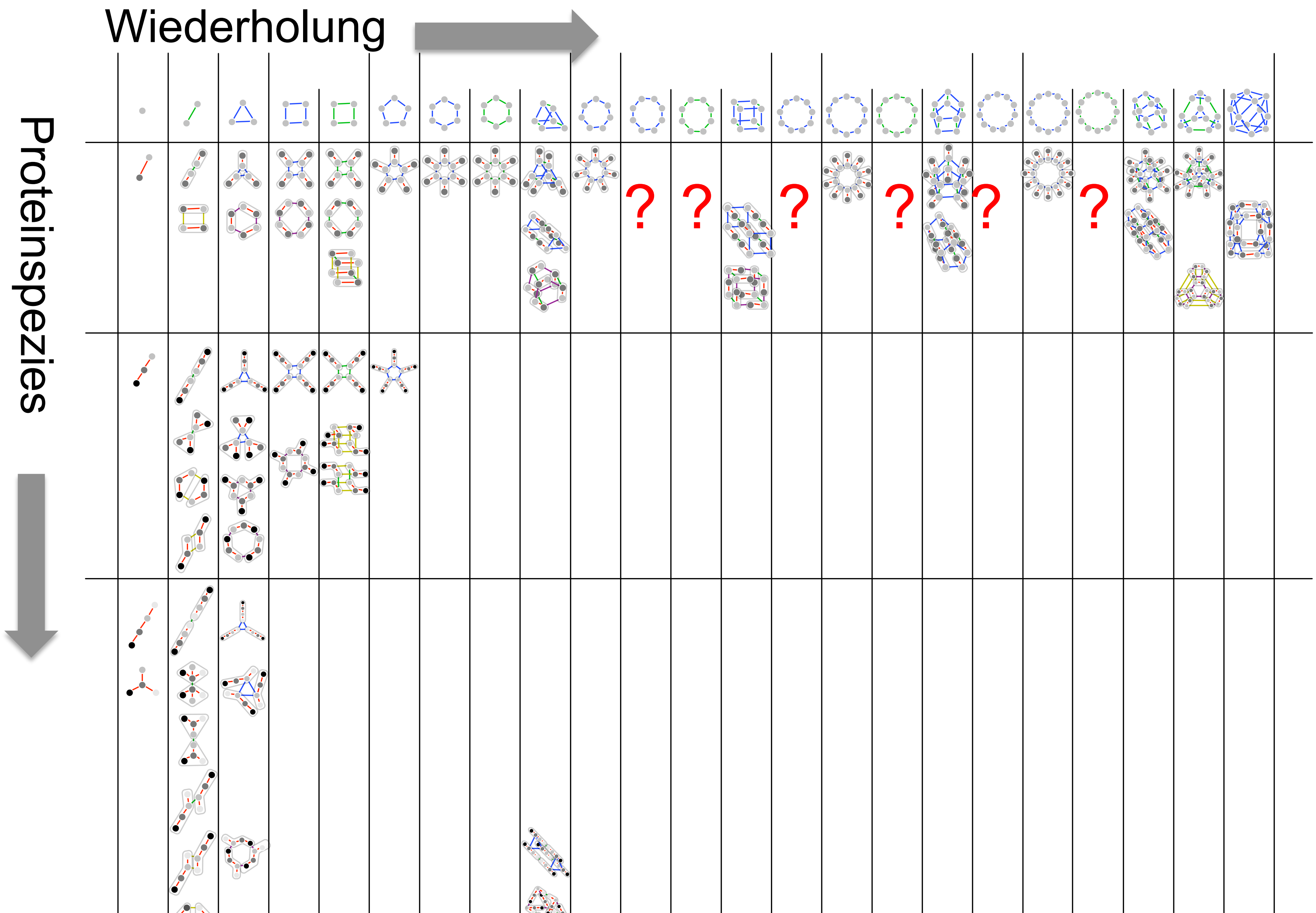


Periodensystem der Elemente

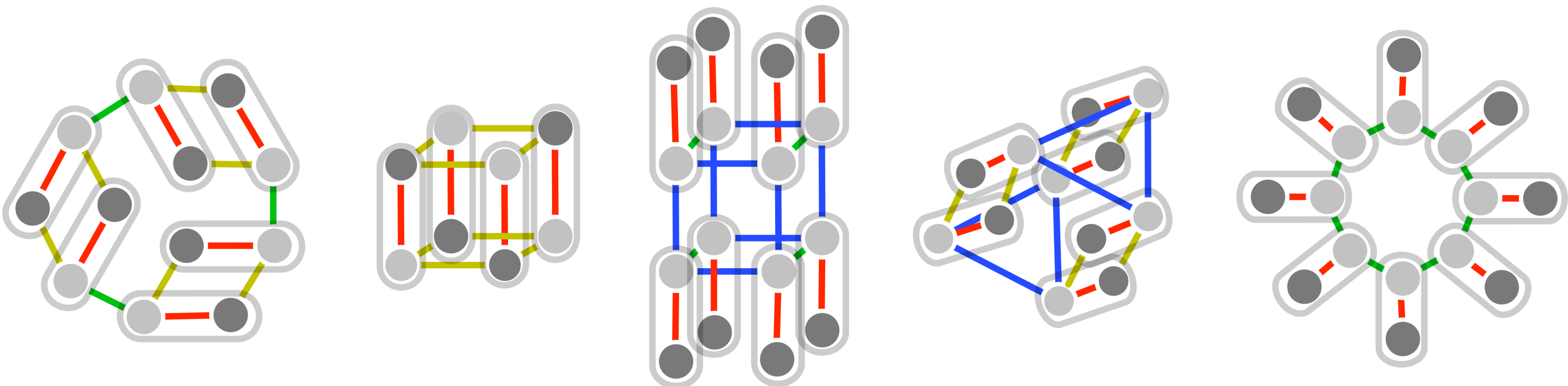
hydrogen 1 H 1.0079																		helium 2 He 4.0026
lithium 3 Li 6.941	beryllium 4 Be 9.0122												boron 5 B 10.811	carbon 6 C 12.011	nitrogen 7 N 14.007	oxygen 8 O 15.999	fluorine 9 F 18.998	neon 10 Ne 20.180
sodium 11 Na 22.990	magnesium 12 Mg 24.305												aluminium 13 Al 26.982	silicon 14 Si 28.086	phosphorus 15 P 30.974	sulfur 16 S 32.065	chlorine 17 Cl 35.453	argon 18 Ar 39.948
potassium 19 K 39.098	calcium 20 Ca 40.078		scandium 21 Sc 44.956	titanium 22 Ti 47.867	vanadium 23 V 50.942	chromium 24 Cr 51.996	manganese 25 Mn 54.938	iron 26 Fe 55.845	cobalt 27 Co 58.933	nickel 28 Ni 58.693	copper 29 Cu 63.546	zinc 30 Zn 65.39	gallium 31 Ga 69.723	germanium 32 Ge 72.61	arsenic 33 As 74.922	selenium 34 Se 78.96	bromine 35 Br 79.904	krypton 36 Kr 83.80
rubidium 37 Rb 85.468	strontium 38 Sr 87.62		yttrium 39 Y 88.906	zirconium 40 Zr 91.224	niobium 41 Nb 92.906	molybdenum 42 Mo 95.94	technetium 43 Tc [98]	ruthenium 44 Ru 101.07	rhodium 45 Rh 102.91	palladium 46 Pd 106.42	silver 47 Ag 107.87	cadmium 48 Cd 112.41	indium 49 In 114.82	tin 50 Sn 118.71	antimony 51 Sb 121.76	tellurium 52 Te 127.60	iodine 53 I 126.90	xenon 54 Xe 131.29
caesium 55 Cs 132.91	barium 56 Ba 137.33	57-70 *	lutetium 71 Lu 174.97	hafnium 72 Hf 178.49	tantalum 73 Ta 180.95	tungsten 74 W 183.84	rhenium 75 Re 186.21	osmium 76 Os 190.23	iridium 77 Ir 192.22	platinum 78 Pt 195.08	gold 79 Au 196.97	mercury 80 Hg 200.59	thallium 81 Tl 204.38	lead 82 Pb 207.2	bismuth 83 Bi 208.98	polonium 84 Po [209]	astatine 85 At [210]	radon 86 Rn [222]
francium 87 Fr [223]	radium 88 Ra [226]	89-102 * *	lawrencium 103 Lr [262]	rutherfordium 104 Rf [261]	dubnium 105 Db [262]	seaborgium 106 Sg [266]	bohrium 107 Bh [264]	hassium 108 Hs [269]	meitnerium 109 Mt [268]	ununnilium 110 Uun [271]	unununium 111 Uuu [272]	ununbium 112 Uub [277]		ununquadium 114 Uuq [289]				

*Lanthanide series	lanthanum 57 La 138.91	cerium 58 Ce 140.12	praseodymium 59 Pr 140.91	neodymium 60 Nd 144.24	promethium 61 Pm [145]	samarium 62 Sm 150.36	europium 63 Eu 151.96	gadolinium 64 Gd 157.25	terbium 65 Tb 158.93	dysprosium 66 Dy 162.50	holmium 67 Ho 164.93	erbium 68 Er 167.26	thulium 69 Tm 168.93	ytterbium 70 Yb 173.04
* *Actinide series	actinium 89 Ac [227]	thorium 90 Th 232.04	protactinium 91 Pa 231.04	uranium 92 U 238.03	neptunium 93 Np [237]	plutonium 94 Pu [244]	americium 95 Am [243]	curium 96 Cm [247]	berkelium 97 Bk [247]	californium 98 Cf [251]	einsteinium 99 Es [252]	fermium 100 Fm [257]	mendelevium 101 Md [258]	nobelium 102 No [259]

“Periodensystem” der Proteinkomplexe

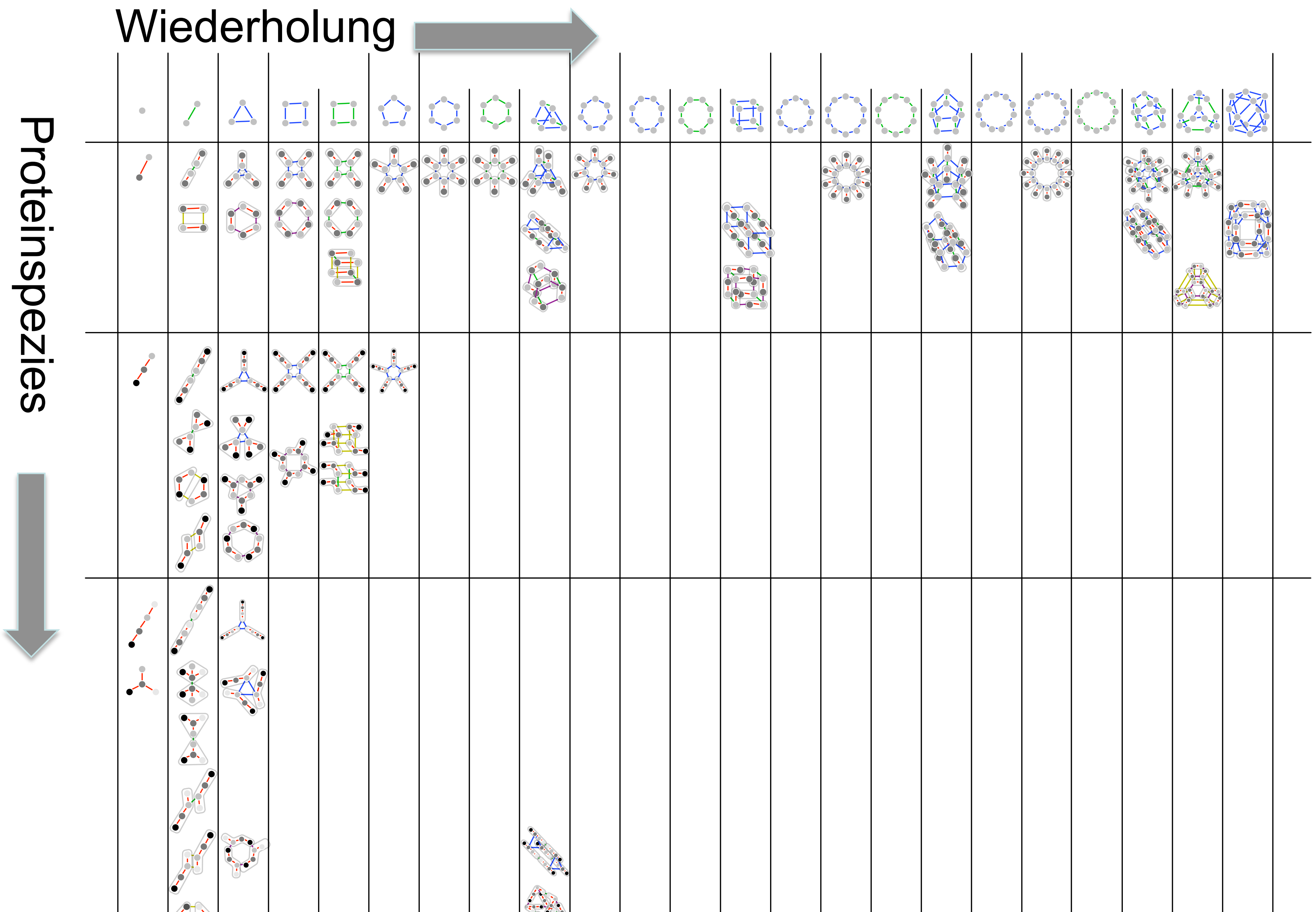


Top 5 noch nicht bekannte Topologien

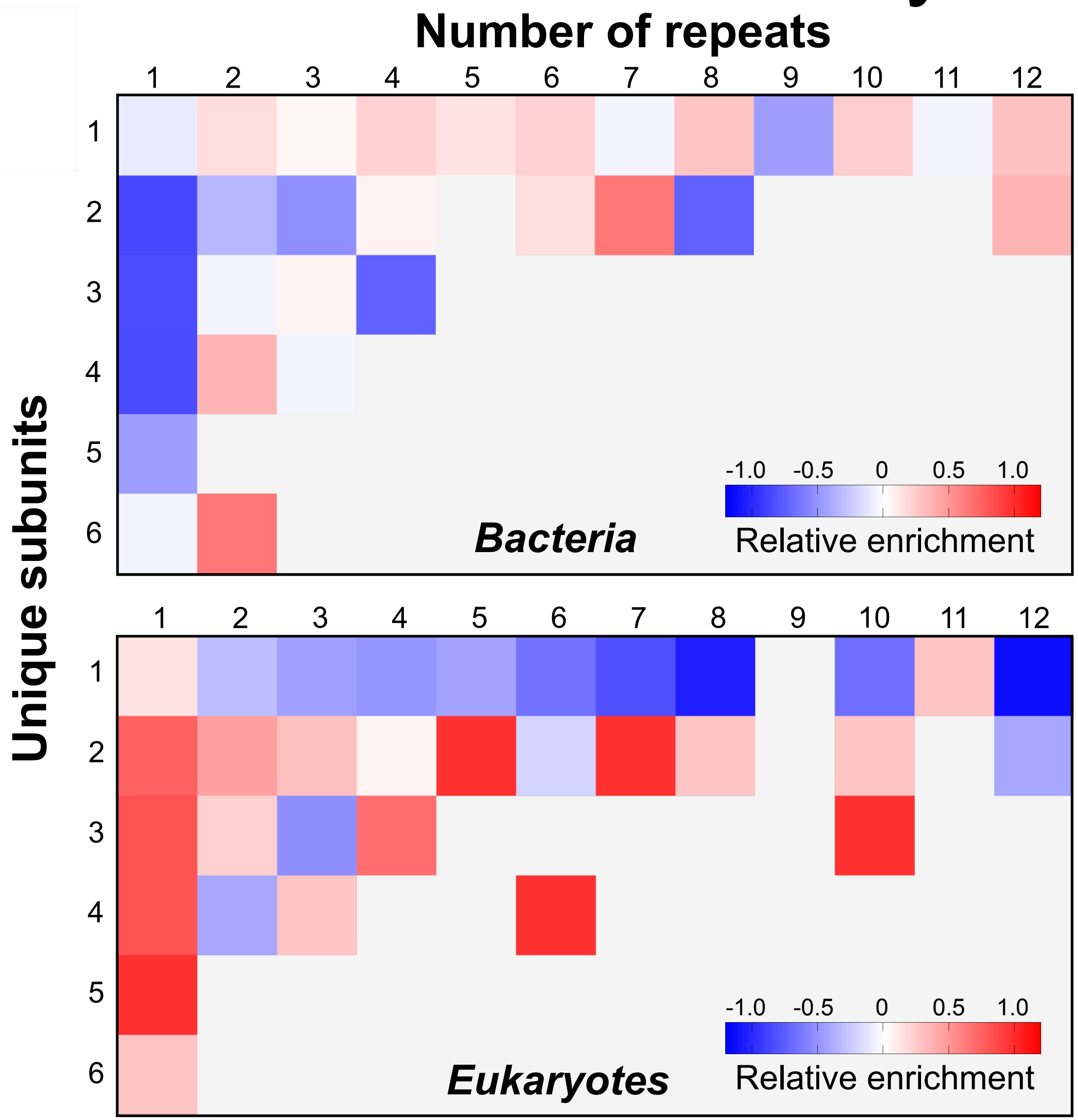


2 Proteinspezies, 8-16 Einheiten insgesamt

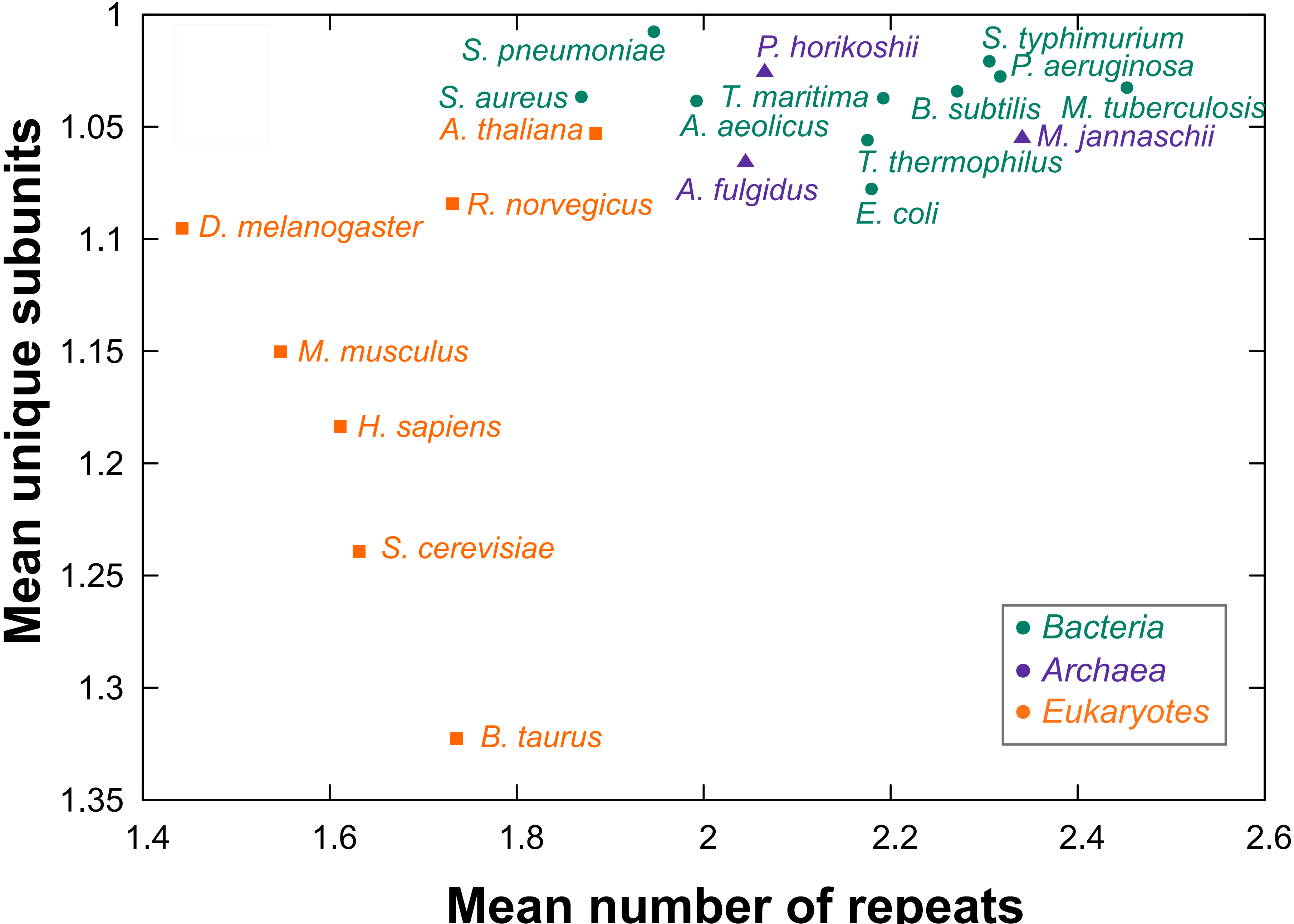
“Periodensystem” der Proteinkomplexe



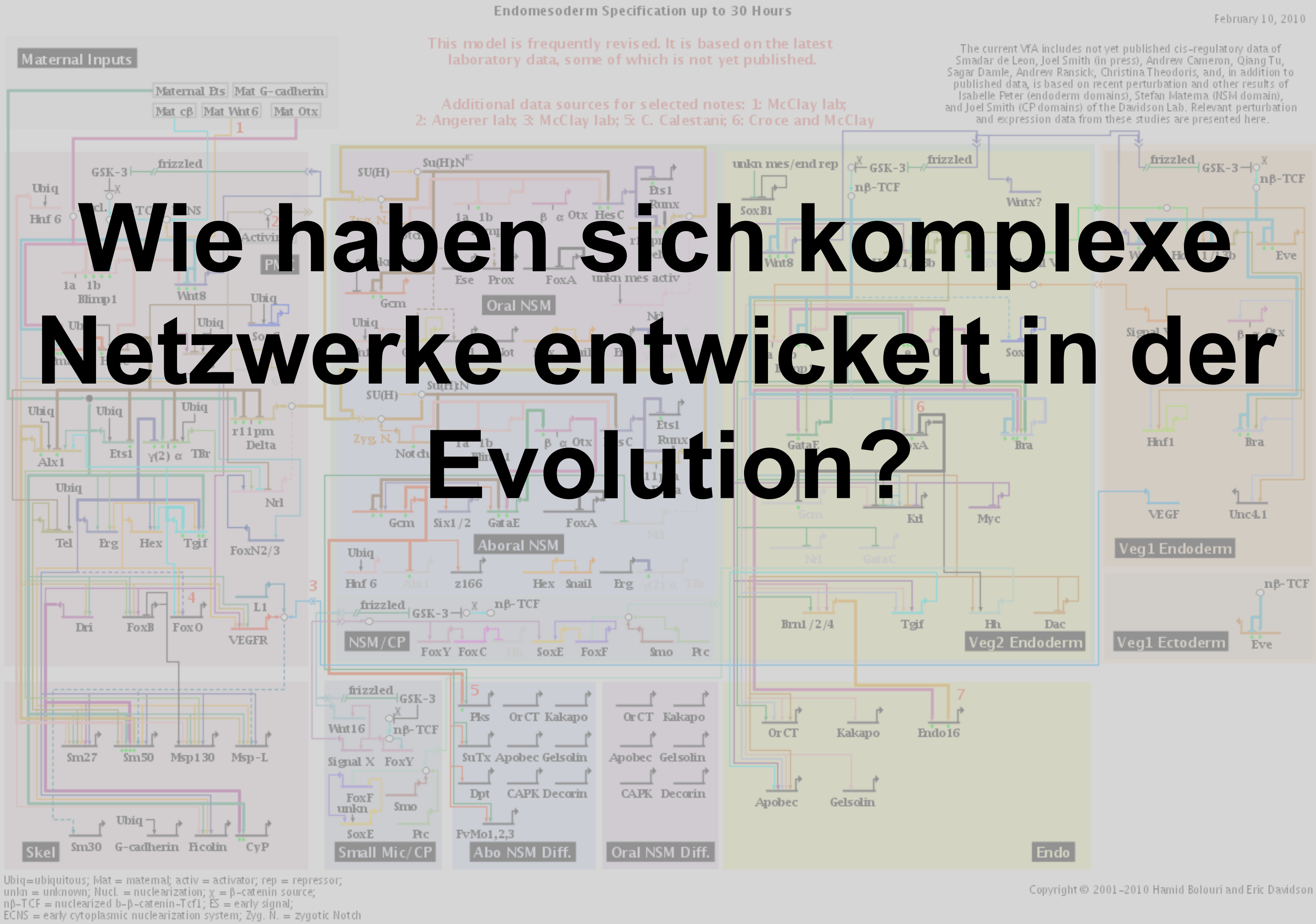
Unterschiedliche Topologien: Bakterien vs Eukaryonten



Unterschiedliche Topologien je nach Genom

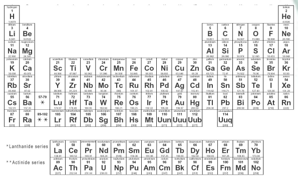


Wie haben sich komplexe Netzwerke entwickelt in der Evolution?



Fragen

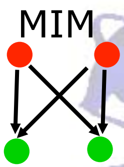
- Wie entwickelt sich ein regulatorisches Netzwerk?
- Wie entwickeln sich Proteinkomplexe?
- Evolution im “Periodensystem” der Proteinkomplexe



Repetition bei Prokaryoten vs Eukaryoten

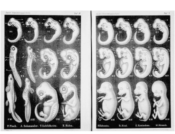
Fragen

- Wie entwickelt sich ein regulatorisches Netzwerk?



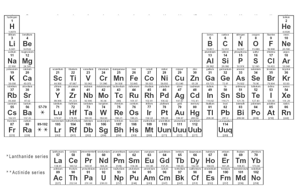
Genduplikation als Motor

- Wie entwickeln sich Proteinkomplexe?



Evolution = Assemblierungsweg

- Evolution im “Periodensystem” der Proteinkomplexe



Repetition bei Prokaryoten

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