Bio-communication and Natural Genome Editing

A new concept for the emergence of biological information

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Life = Material Reality = Physics + Chemistry

- Life emerges out of atoms and molecules
- Life = physics + chemistry (E.Schrödinger)
- Life can be depicted by mathematical equations

Life = physics + chemistry + information

- DNA is a information storage medium
- DNA consists of atoms and molecules
- Information is a molecular feature (M. Eigen)

Mathematical Theories of Language
involved in Biochemistry

- systems theory,
- information theory,
- biolinguistics,
- bioinformatics,
- synthetic biology,
- mathematical biology

Falsified:
Mathematical theories of natural languages

- Ludwig Wittgensteins pragmatic turn:
  - natural languages depend on social groups
  - „the meaning is its use“ (depends on context, not syntax)

- Kurt Gödels incompleteness theorem
  - The construction of a contradiction-free axiomatic system is impossible
    (as suggested by Hilbert, Russel, Whitehead)

Falsified: main assumptions in molecular biology

- one gene - one Protein
- non-coding DNA is JUNK
- DNA - RNA - Proteins - anything else
- Mutations (replication errors) drive genetic variation

Results: Empirical Knowledge about Natural Codes

- **No natural code codes itself**
- There must be **agents** which use such codes.
- Code user follow **syntactic, semantic, pragmatic rules.**
- Rule-following is inherently a kind of **social** interaction

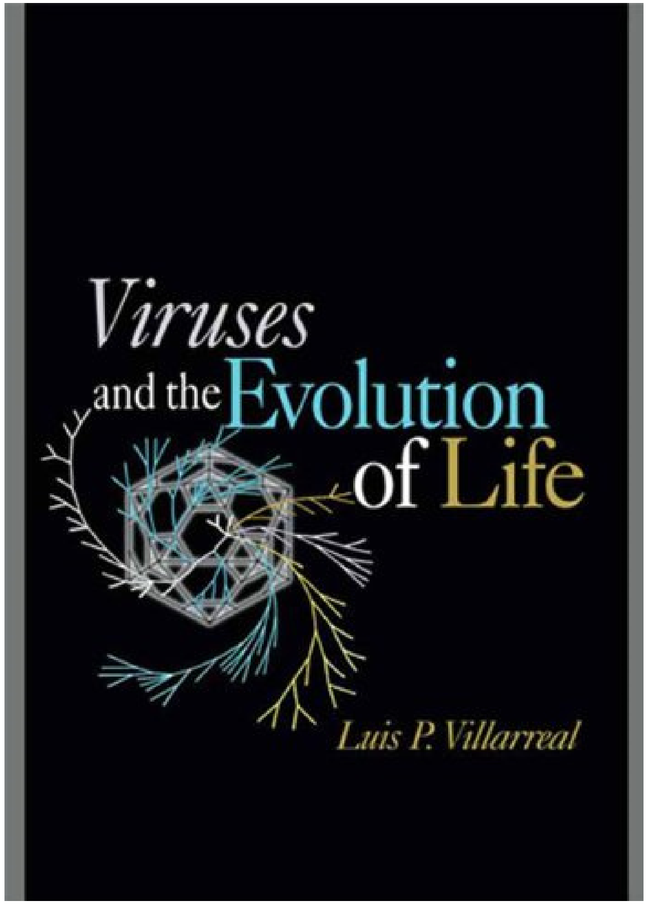
Essential Agents in Cellular Life

If the genetic code is really a natural code there must be **agents** that

- **generate** code sequences *de novo*
- **identify** sequence-specific target sites
- **integrate** in pre-existing genetic content arrangements without destruction of former content
- **recombine** according adaptational needs
- **mark** sequence sites to epigentically vary meaning

What are these agents?

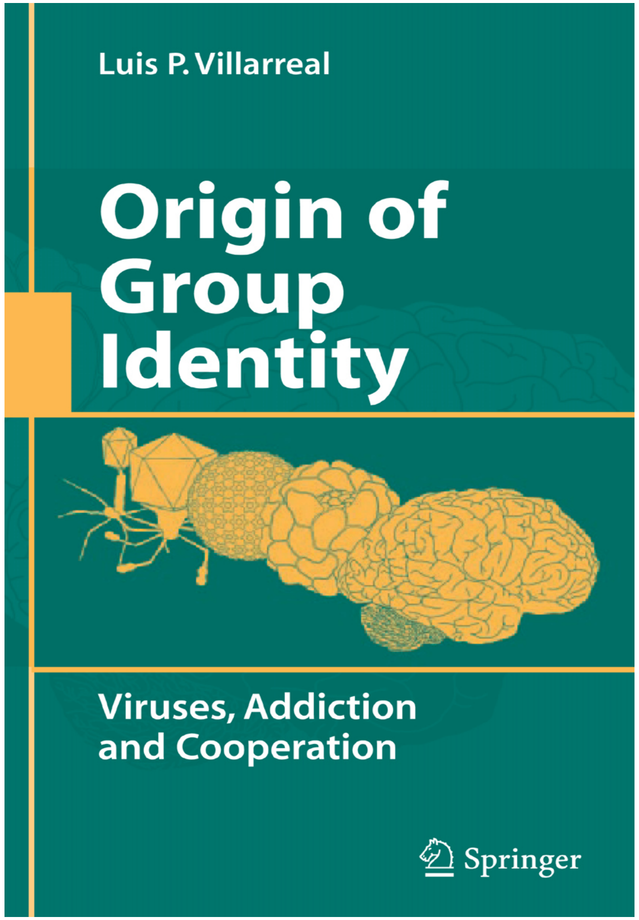
Essential Agents in Cellular Life



Viruses and the Evolution of Life

Luis P. Villarreal

2005



Luis P. Villarreal

Origin of Group Identity

Viruses, Addiction and Cooperation

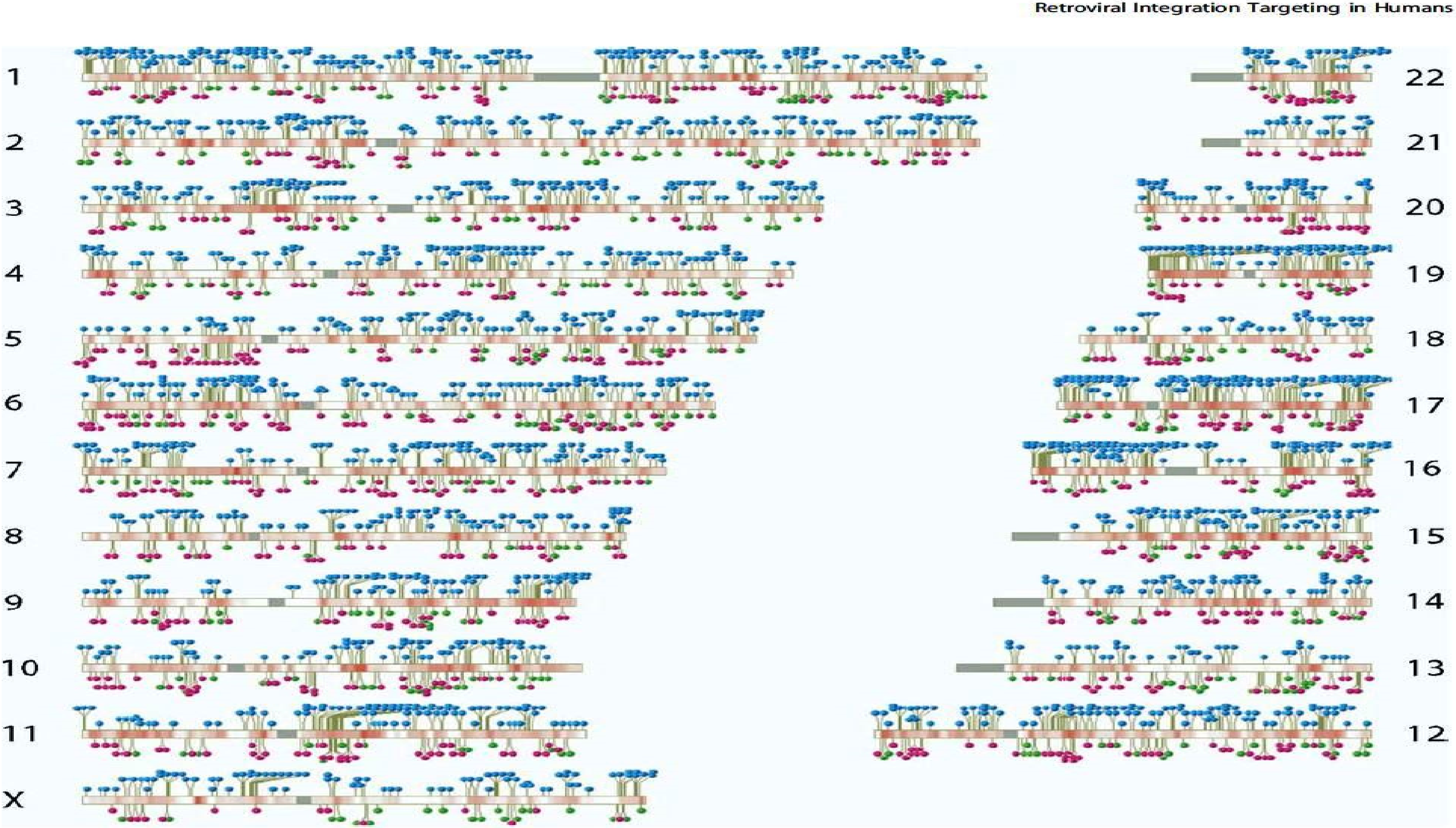
Springer

2009

Essential Agents in Cellular Life

Examples of viruses/viral parts that **insert** into and **recombine** host genetic content

- Viruses are the most abundant biological agents on this planet (10 times)
- Only viruses assemble double stranded or single stranded RNA or DNA (+ and –)
- Omnipresent phages in prokaryotes
- The eukaryotic nucleus has a variety of large dsDNA virus features
- Persistent viral parts in mitochondria and other organelles
- Endogenous retroviruses (active and/or defective)
- Intronic regions that are spliced out during exon assembly



Mitchell RS, Beitzel BF, Schroder ARW, Shinn P, Chen H, et al. (2004) Retroviral DNA integration: ASLV, HIV, and MLV show distinct target site preferences. PLoS Biol 2(8): e234.

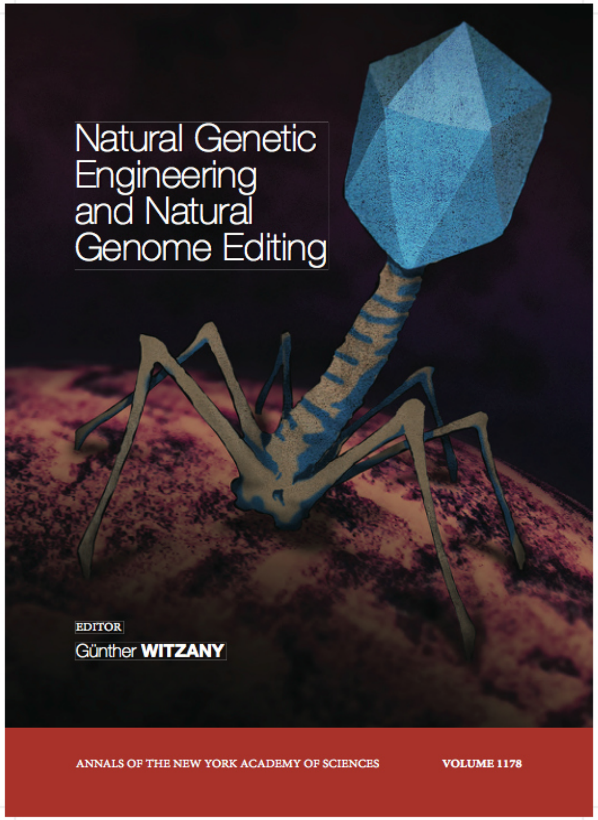
Some persistent viruses/virus-derived parts

- DNA-Viruses
- DNA-transposons
- RNA-Viruses
- non-retroviral RNA viruses
- endogenous retroviruses
- LTRs-retrotransposons
- non-LTRs (SINEs, LINEs, ALUs)
- group II introns
- group I introns
- non-coding RNAs

Viral derived parts are active in

- Transcription
- Post-transcriptional RNA-Editing + RNA Splicing
- Translation
- DNA replication
- Chromatin organisation
- Epigenetic modifications
- DNA recombination

Biocommunication and Natural Genome Editing



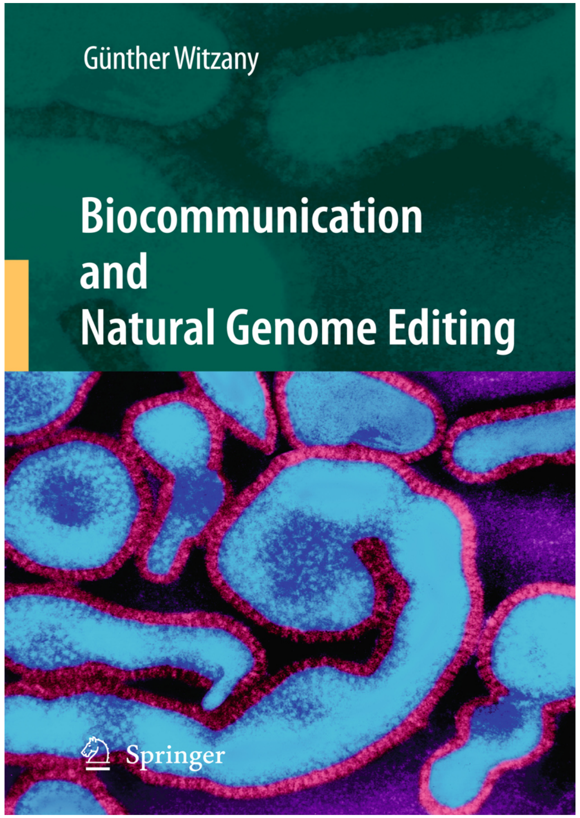
Natural Genetic Engineering and Natural Genome Editing

EDITOR
Günther **WITZANY**

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES VOLUME 1178

2009

Annals of the New York Academy of Sciences

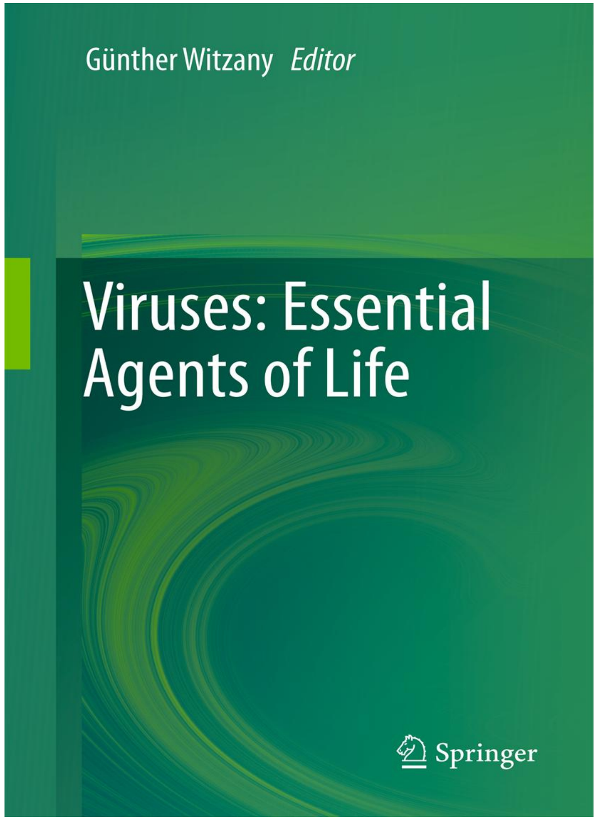


Günther Witzany

Biocommunication
and
Natural Genome Editing

Springer

2010



Günther Witzany *Editor*

Viruses: Essential Agents of Life

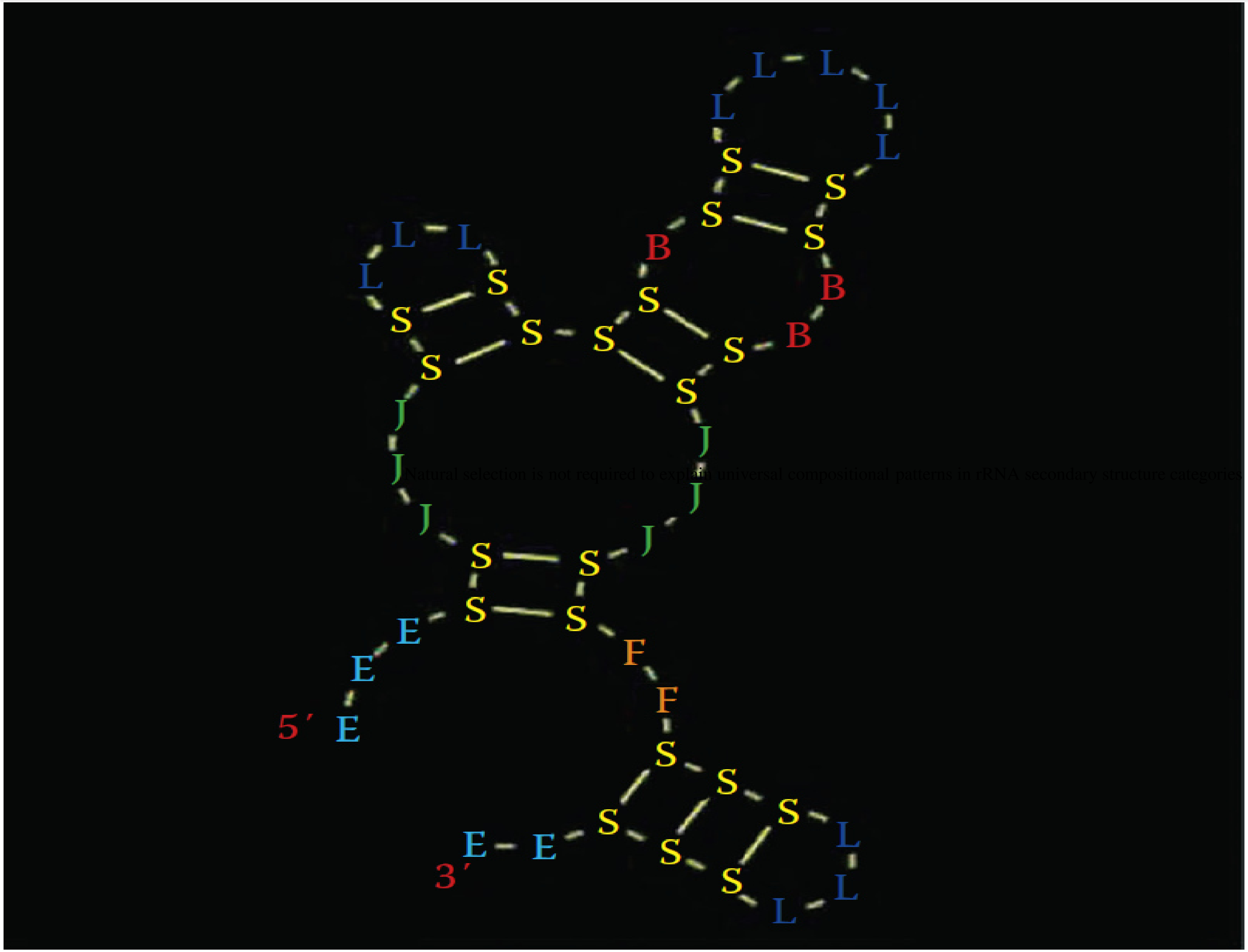
Springer

2012

Non-Coding RNAs: Viral derived Moduls

- 1,5 % of the human genome code for proteins
- 98,5% represent non-coding RNAs
- C.Elegans and Home Sapiens share app. 20,000 genes

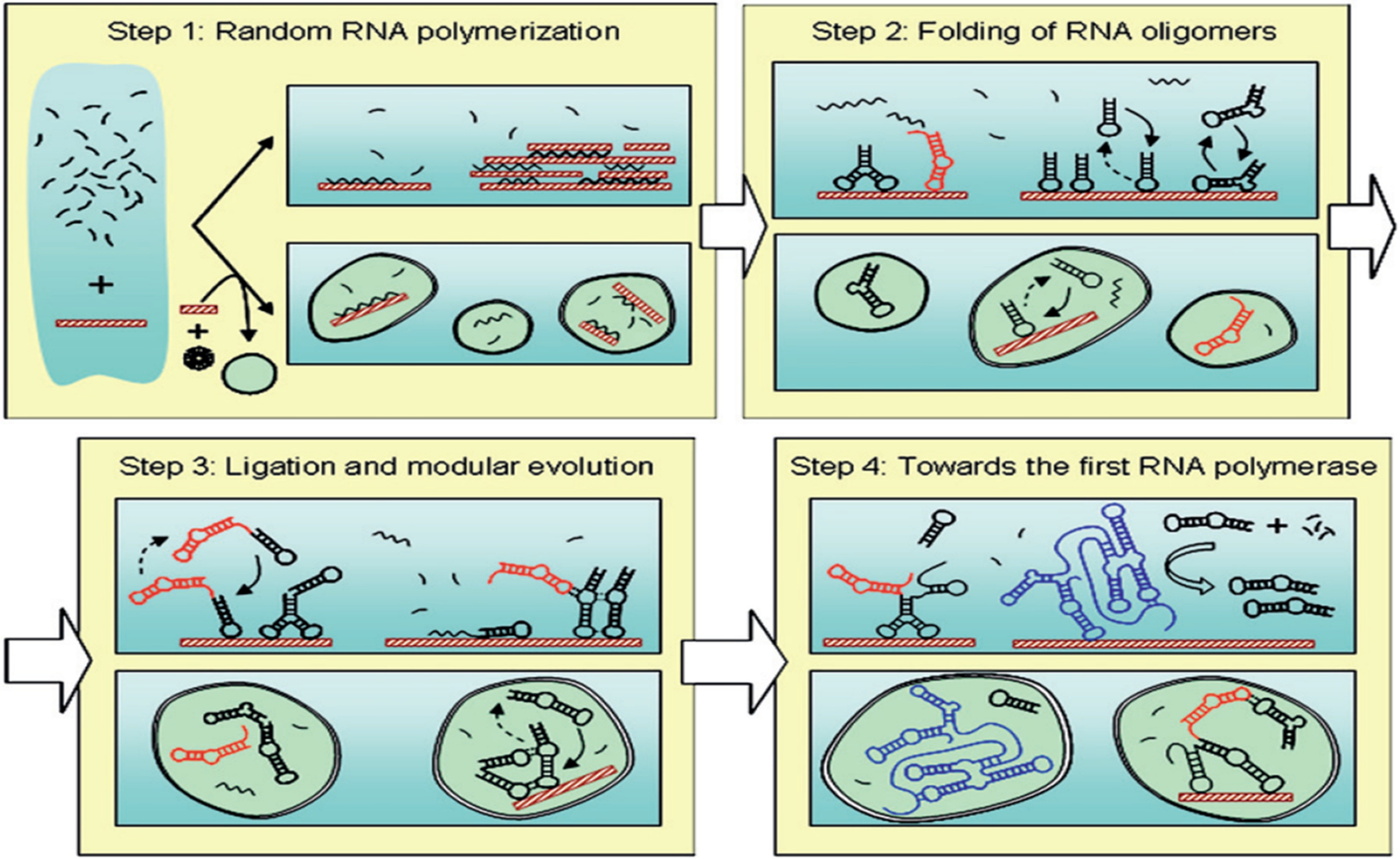
  The difference is regulation of these genes
- ncRNAs are co-opted adaptations of former genetic colonizers that now act as regulatory elements



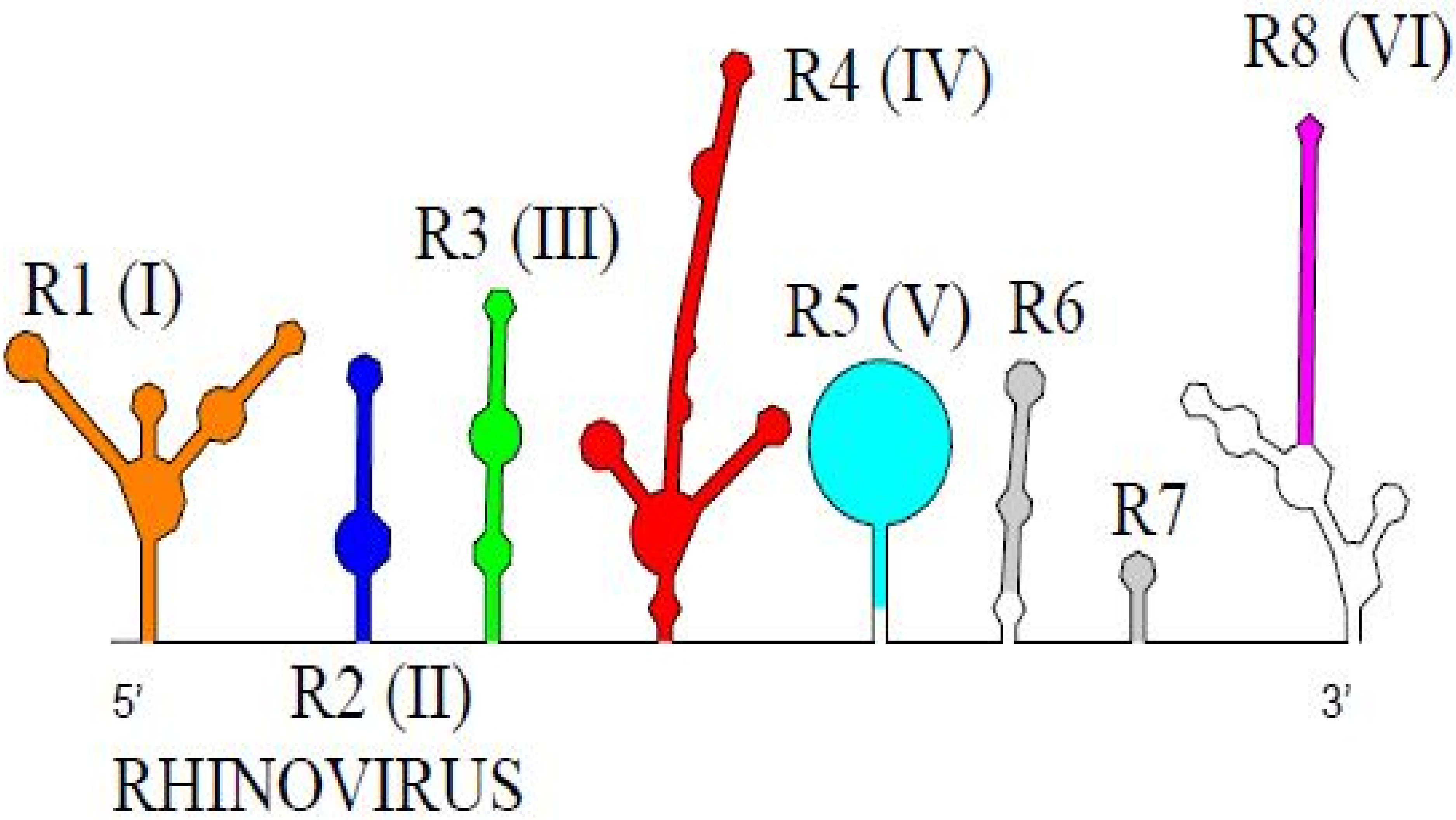
Grammar rules of RNAs:
basepairung and non-base-pairing
Nucleotides

- 🟨 Stem
- 🟦 Loop
- 🟥 Bulge
- 🟩 Junction
- 🟦 End
- 🟧 Flexible
- 🟪 Total

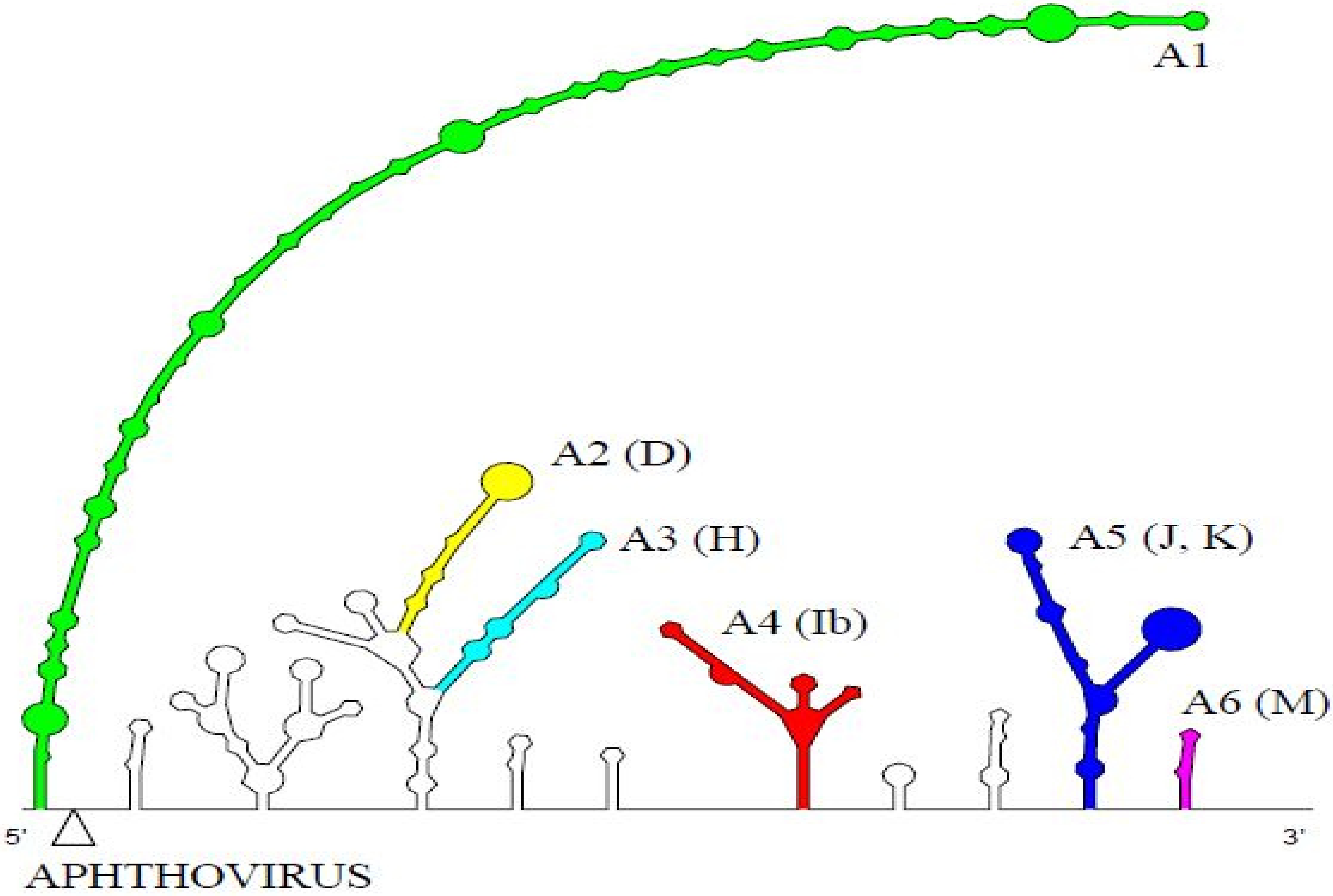
Smit S, Yarus M, Knight R Natural selection is not required to explain universal compositional patterns in rRNA secondary structure categories. RNA. 2006 Jan;12(1):1-14.

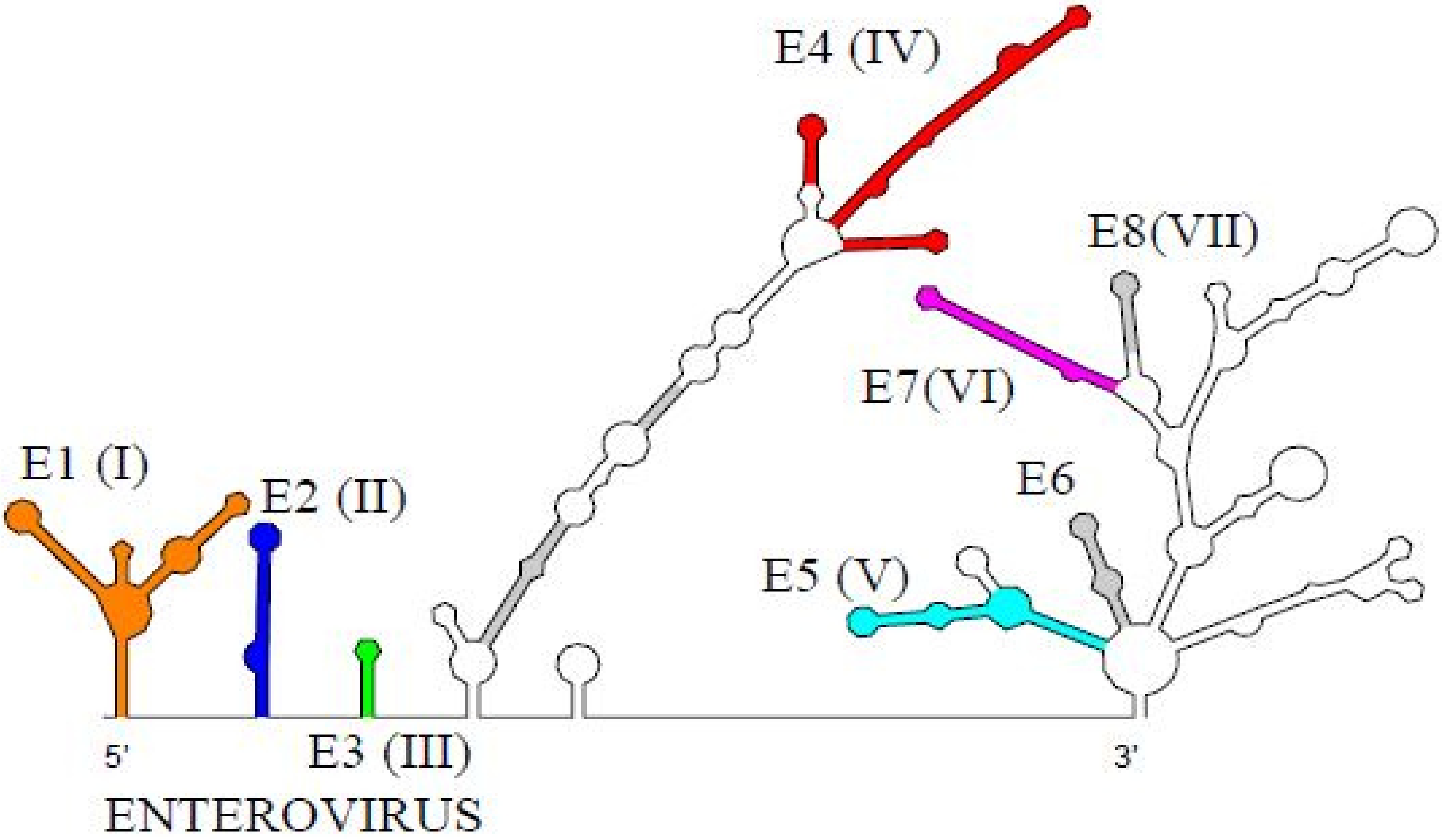


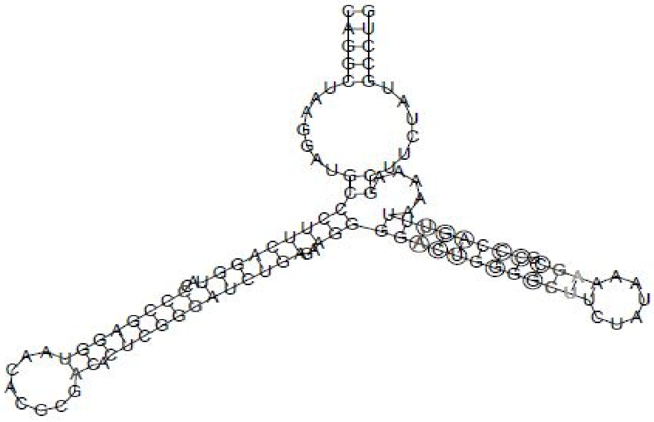
Briones C, Stich M, Manrubia SC (2009) The dawn of the RNA world: toward functional complexity through ligation of random RNA oligomers. RNA 15:743–749



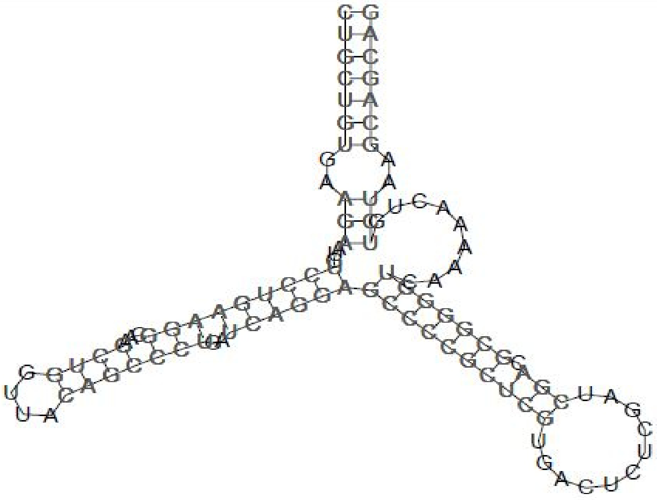
Witwer C1, Rauscher S, Hofacker IL, Stadler PF Conserved RNA secondary structures in Picornaviridae genomes. Nucleic Acids Res. 2001 Dec 15;29(24):5079-89s


A1
A2 (D)
A3 (H)
A4 (Ib)
A5 (J, K)
A6 (M)
5'
3'
APHTHOVIRUS

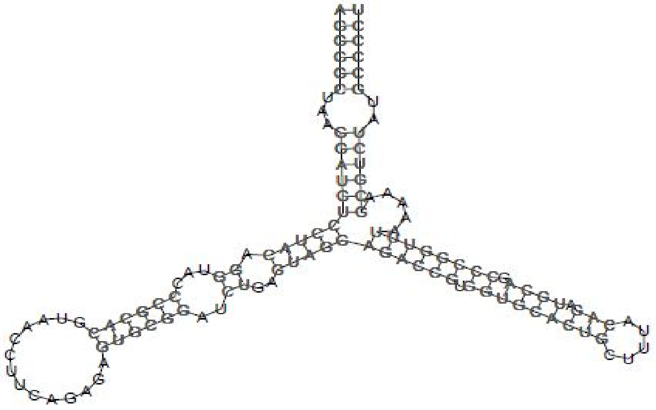

E4 (IV)
E8(VII)
E7(VI)
E1 (I)
E2 (II)
E6
E5 (V)
5'
E3 (III)
3'
ENTEROVIRUS



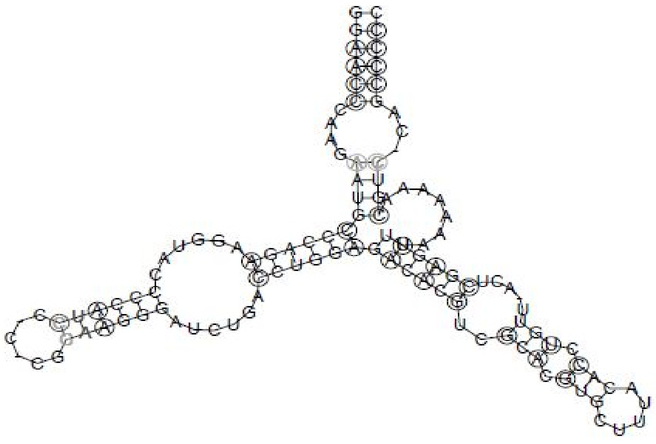
FMDV (Aphthovirus)



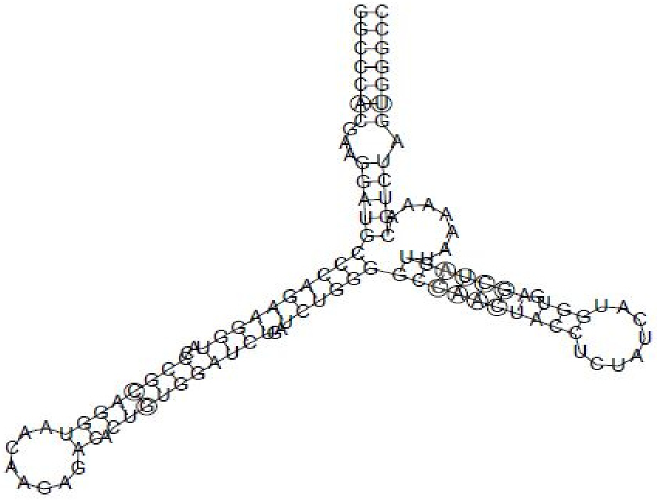
ERV-1 (Aphthovirus)



ERV-2 (Erbovirus)

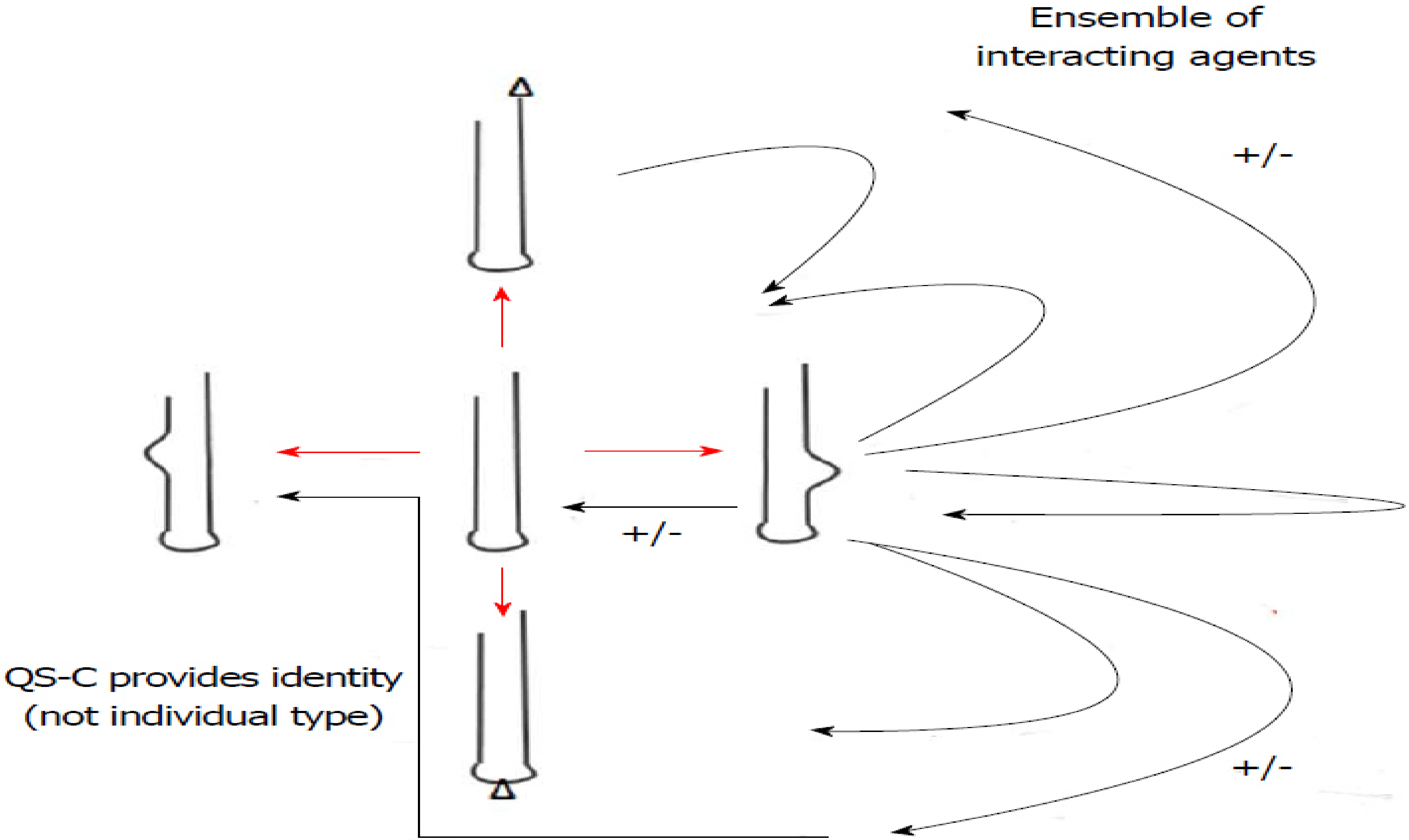


Cardiovirus



Parechovirus

Hepatovirus



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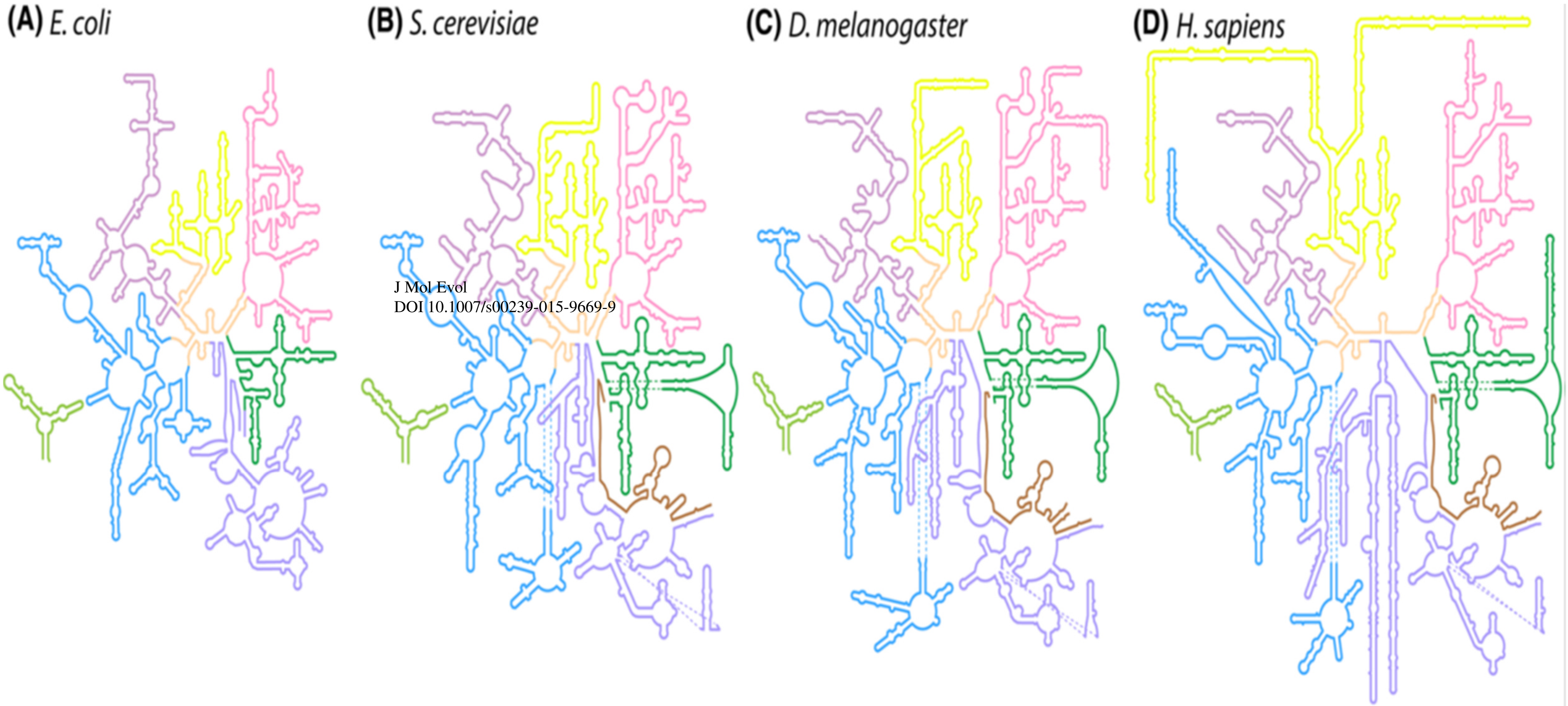
RNA stem loops: Group Building



Jessica C. Bowman • Nicholas V. Hud • Loren Dean Williams. The Ribosome Challenge to the RNA World. J Mol Evol DOI 10.1007/s00239-015-9669-9

Life = Physics + Chemistry + Communication

- Genetic Information is not randomly derived
- RNA Agents generate, identify, integrate, recombine and mark nucleic acid sequences
- Natural genome editing is the result of consortial interactions of viral and subviral agents with cellular host
- Natural genome editing agents follow syntactic, semantic and pragmatic rules (optimizes energy cost)

RNA Sociology

non-mechanistic explanation of

Consortial interactions

- ✓ From single RNA stem loops to group (identity) building
- ✓ Emergence of biological identity
  (self/non-self identification competence)
- ✓ Context dependent interactions

De novo generation of

- ✓ Nucleic acid sequences
- ✓ Coherent integration into pre-existing ones
- ✓ Innovation by variations in RNA stem loops
- ✓ Genetic identity

Thank you very much
for your attention!