
Contents

I	Introduction	1
1.1	Why study RNA virus evolution?	1
1.1.1	Ways to study viral evolution	2
1.1.2	The scope of this book	4
1.2	RNA viruses and evolutionary biology	5
1.2.1	The RNA virus world	6
1.3	The basics of viral biology	8
1.3.1	A cursory history of virology	8
1.3.2	Virology 101	9
1.3.3	Exploring the virosphere	13
2	The origins of RNA viruses	15
2.1	Introduction	15
2.1.1	The perils of deep viral phylogeny	15
2.2	Theories for the origin of RNA viruses	16
2.2.1	The regressive origin theory	17
2.2.2	RNA viruses as escaped genes	18
2.2.3	RNA viruses and the RNA world	20
2.2.4	Eigen's paradox	22
2.2.5	The taxonomic distribution of RNA viruses	24
2.2.6	Conserved protein structures	25
2.3	Deep phylogenetic relationships among RNA viruses	28
2.3.1	The 'higher-order' relationships of RNA viruses	29
2.3.2	Phylogenies based on genome organization	34
2.3.3	Phylogenies based on protein structure	34
2.4	RNA viruses and the evolution of the genetic code	35
3	The mechanisms of RNA virus evolution	37
3.1	The evolutionary dynamics of RNA viruses	37
3.1.1	Mutation rates in RNA viruses and their determinants	37
3.1.2	A comparison of substitution rates in viruses	39
3.1.3	Differences in viral generation time	42

3.1.4	Slowly evolving RNA viruses?	43
3.1.5	Rapidly evolving ssDNA viruses	44
3.1.6	What sets the rate of RNA virus evolution?	45
3.1.7	Trade-offs and the evolution of mutation rates	46
3.1.8	Mutation rates and mutational loads	47
3.1.9	Are RNA viruses trapped by high mutation rates?	48
3.2	Recombination and reassortment in RNA virus evolution	48
3.2.1	Recombination frequency in RNA viruses	50
3.2.2	Detecting recombination in RNA viruses	51
3.2.3	What determines the rate of recombination in RNA viruses?	52
3.2.4	Recombination and deleterious mutation	53
3.3	Natural selection, genetic drift, and the genetics of adaptation	55
3.3.1	Effective population sizes in viral evolution	56
3.3.2	Transmission bottlenecks	58
3.3.3	The dynamics of allele fixation: estimating selection coefficients	59
3.3.4	The importance of hitch-hiking	62
3.3.5	Patterns of synonymous and nonsynonymous evolution	63
3.3.6	Natural selection and transmission mode	63
3.3.7	Escape from intrinsic immunity	65
3.3.8	Strictly neutral evolution in RNA viruses?	66
3.3.9	Determinants of codon bias (and nucleotide composition) in RNA viruses	68
3.4	Deleterious mutation and RNA virus evolution	70
3.4.1	Deleterious mutation and intra-host genetic diversity	73
3.4.2	The importance of defective interfering particles and complementation	74
3.4.3	Complementation may be commonplace in RNA viruses	75
3.5	Epistasis in RNA virus evolution	77
3.5.1	Epistasis and robustness	78
3.5.2	The importance of RNA secondary structure	80
3.5.3	Convergence and pleiotropy	82
3.6	The importance of intra-host viral diversity	83
4	The RNA virus quasispecies	87
4.1	What is a quasispecies?	87
4.2	The great quasispecies debate	90
4.2.1	What's in a name: quasispecies or polymorphism?	91
4.2.2	Is quasispecies theory different from 'classical' population genetics?	92
4.2.3	Does genetic drift destroy the quasispecies?	92
4.2.4	The evidence from 'digital organisms'	93
4.2.5	Experimental tests of quasispecies theory	93
4.2.6	Comparative analyses of RNA virus quasispecies	96

4.2.7 Recombination and the quasispecies	99
4.2.8 'Memory' in viral quasispecies	99
4.3 Error thresholds, extinction thresholds, and error catastrophes	100
4.4 Concluding remarks	103
5 Comparative genomics and the macroevolution of RNA viruses	104
5.1 The evolution of genome architecture in RNA viruses	104
5.1.1 The evolution of genome size	104
5.1.2 The exceptions: coronaviruses and roniviruses	107
5.1.3 The evolution of genome organization: an overview	109
5.1.4 The evolution of genome segmentation	111
5.1.5 The evolution of genome orientation and dsRNA viruses	113
5.1.6 The evolution of overlapping reading frames	114
5.2 The processes of genome evolution	116
5.2.1 Gene duplication in RNA virus evolution	117
5.2.2 LGT among viruses and hosts	118
5.2.3 Modular evolution	119
5.3 Patterns and processes of macroevolution in RNA viruses	120
5.3.1 Speciation in RNA viruses	121
5.3.2 A birth-death model of viral evolution	124
5.3.3 The birth and death of endogenous retroviruses	128
6 The molecular epidemiology, phylogeography, and emergence of RNA viruses	131
6.1 Phylodynamics: linking viral evolution at the phylogenetic and epidemiological scales	131
6.1.1 Coalescent approaches to viral epidemiology	133
6.2 Cross-species transmission, co-divergence, and emergence	135
6.2.1 The RNA/DNA divide again	135
6.2.2 Inferring co-divergence	137
6.2.3 The evolution of persistence in RNA viruses	138
6.2.4 Host phylogeny and viral emergence	139
6.3 The evolutionary genetics of viral emergence	142
6.3.1 Adaptation and emergence	142
6.3.2 'Off-the-shelf' emergence	144
6.3.3 The fitness landscapes of emergence	146
6.3.4 Recombination, reassortment, and viral emergence	147
6.4 The phylogeography of human viruses	148
6.4.1 Viruses differ in phylogeographic pattern	149
6.5 Major transitions in human ecology and viral evolution	153
6.5.1 The transitions	154
6.5.2 Immunodeficiency and disease emergence	155

7 Case studies in RNA virus evolution and emergence	156
7.1 The evolutionary biology of influenza virus	156
7.1.1 The diversity of influenza virus	156
7.1.2 The evolution of avian influenza virus	158
7.1.3 Antigenic drift and shift	161
7.1.4 Antigenic cartography and the punctuated evolution of HA	162
7.1.5 Genome-wide evolutionary processes	165
7.2 The emergence and evolution of HIV	167
7.2.1 A brief history of HIV/AIDS	167
7.2.2 The genetic diversity of HIV	169
7.2.3 What and why are subtypes?	172
7.2.4 The origins and spread of HIV	173
7.2.5 The intra- and inter-host evolutionary dynamics of HIV	176
7.2.6 The great obsession moves to HIV	177
7.2.7 Epidemiological scale dynamics	178
7.3 The evolution of dengue virus	180
7.3.1 The origins of DENV	182
7.3.2 DENV biodiversity	184
7.3.3 Lineage birth-death in DENV	186
7.3.4 DENV fitness	187
7.3.5 Comparing dengue and yellow fever	188
7.3.6 Why no yellow fever in Asia?	190
7.4 The phylogeography and evolution of rabies virus	191
7.4.1 The world of lyssaviruses	192
7.4.2 The spatiotemporal dynamics of RABV	195
8 Epilogue	198
References	201
Index	249