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Factors Identification for Mitochondrial DNA Substitution Models

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Introduction

Key Questions

Which factors are significant in determining:

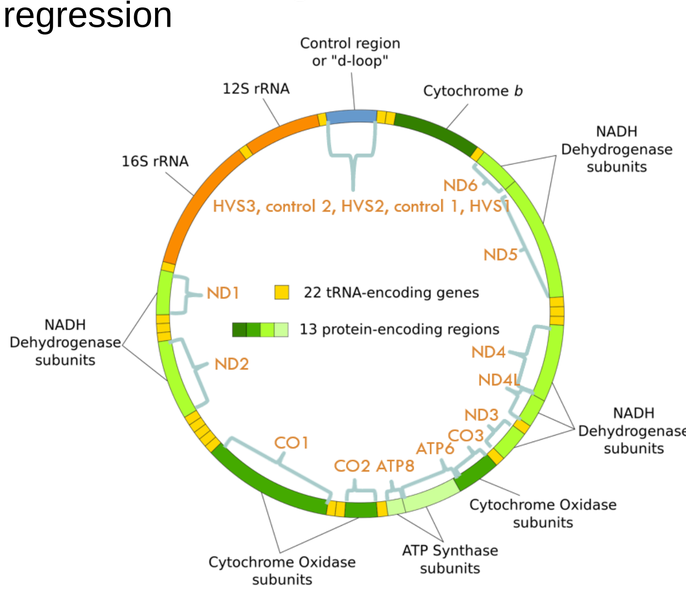
1. The substitution rate?
2. The substitution type?
   - Transition vs. transversion
   - Synonymous vs. non-synonymous

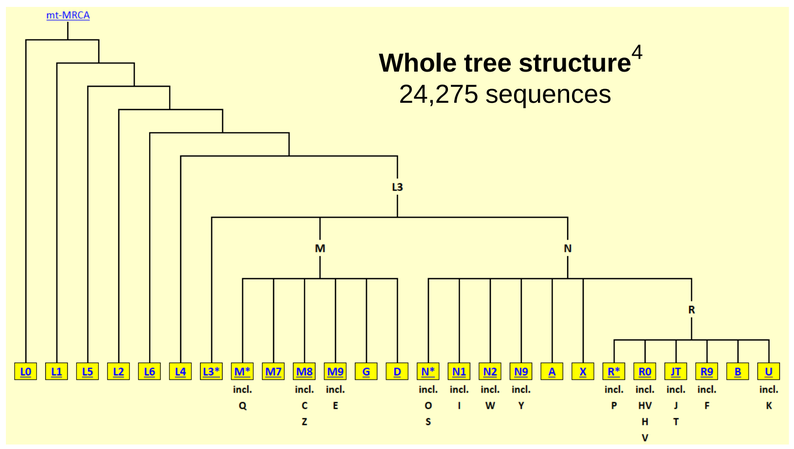
Relevant candidates:

Region/sub region, site, time, nucleotide, neighbor nucleotides, codon, codon position, amino acid, |synonymous amino acid group|, clade, CpG dinucleotides

Assumption:

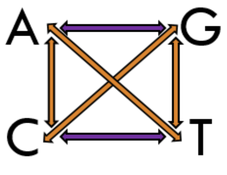
If all relevant factors are known then the substitution rate can be modeled via a Poisson regression, and the substitution type via a logistic regression





L4 Subtree

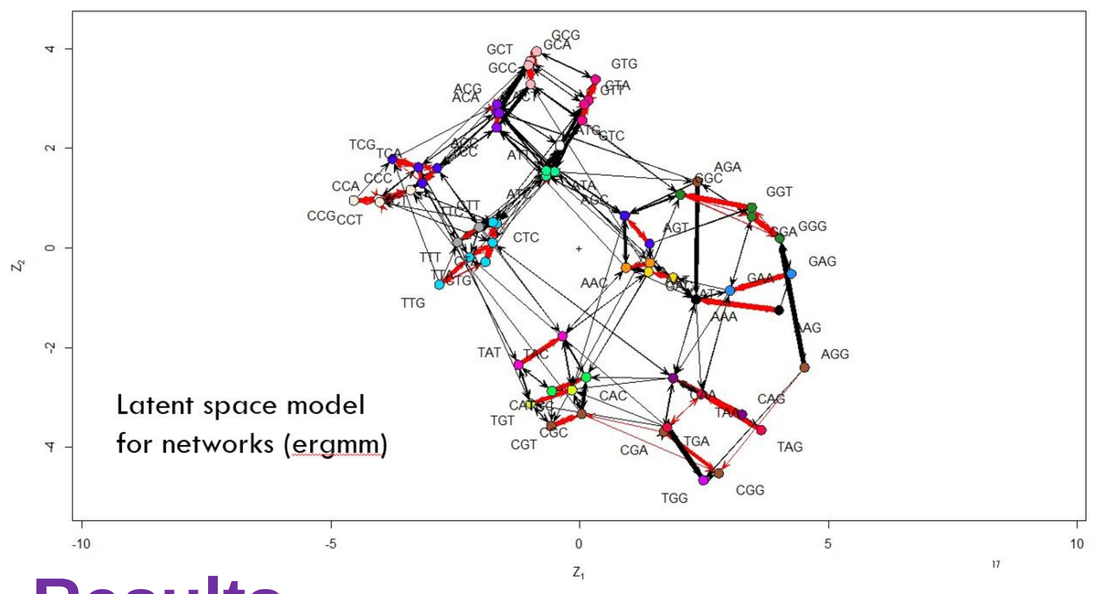
General Statistics



	A	G	C	T
A		5270	639	150
G	4830		79	51
C	299	62		5986
T	97	58	6760	

		# of events	mean	std	median	0.75 quantile	max (100% quantile)
coding region	transitions	14633	0.9473037	3.102829	0	1	103
	transversions	619	0.04007251	0.3348809	0	0	19
	total	15252	0.9873762	3.153734	0	1	103
control region	transitions	8213	7.319964	36.54745	0	3	1035
	transversions	816	0.7272727	10.30587	0	0	315
	total	9029	8.047237	38.10185	0	4	1036

Synonymous vs. non-synonymous mutations



Results

Sub-regions tests

a. Test the distribution of the bases using a two-sample χ^2-test
b. Test the number of substitutions at each site using Kruskal-Wallis
c. Negative binomial fit for the number of substitutions in both sub-regions compared together vs. apart (GLR)
d. Negative binomial regression for the number of substitutions with the sub-region as an explaining variable
e. Compare the distribution of codons using a two-sample χ^2-test (only relevant for codon locations)

	rRNA12S	rRNA16S	Different
rRNA12S	X		b,c,d
rRNA16S		X	b,c,d
Different	b,c,d	b,c,d	X

	Control 1	Control 2	HVS1	HVS2	HVS3
Control 1	X	d	c	b,d	a,b
Control 2	d	X	b,c,d	b,c,d	a,b
HVS1	c	b,c,d	X	b,d	a,b,c,d
HVS2	b,d	b,c,d	b,d	X	a,c,d
HVS3	a,b	a,b	a,b,c,d	a,c,d	X

	ND1	ND2	ND3	ND4	ND5	ND4L	ND6	CO1	CO2	CO3	ATP8	ATP6	CYB
ND1	X						a,e				b,d	b,d	
ND2		X					e	a			b,d	b,d	
ND3			X				a				b,d	b,d	
ND4				X			e	a			b,d	b,c,d	b,c,d
ND5					X		a,e	a			b,d	b,d	
ND4L						X					b,d	b,c,d	b,c
ND6	a,e	e	a	e	a,e		X	a,e	a	a,e	b,d	b,d,e	a,e
CO1		a		a	a		a,e	X			a,b,d	b,c,d	b,c,d
CO2							a		X		a,b,d	b,d	b,d
CO3							a,e			X	a,b,d	b,d	
ATP8	b,d	b,d	b,d	b,d	b,d	b,d	b,d	a,b,d	a,b,d	a,b,d	X		
ATP6	b,d	b,d	b,d	b,c,d	b,d	b,c,d	b,d,e	b,c,d	b,d	b,d		X	b,d
CYB				b,c,d		b,c	a,e	b,c,d	b,d			b,d	X

Conclusions

- We have yet to find a direct Poisson regression model for the number of substitutions per site, suggesting that there are missing relevant factors
- Adding relevant factors results in a higher theta parameter for the Negative Binomial regression (as well as higher likelihood)
- It is beneficiary (GLR wise) to separate the substitution model according to the codon position

Bibliography

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