

Omicron and B.1.1.640

Update 05-Dec-2021

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cov.lanl.gov

- 1) Data set and reference spike sequence.
- 2) Dynamics: Botswana and South Africa.
- 3) Evidence suggesting outlier B.1.1.529-related viruses may be recombinants.
- 4) dN/dS ratios in different regions of the SARS-CoV-2 genome and Spike, focus on Omicron.

Omicron: B.1.1.529

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Pango lineage designation changes in these sequences since 11/23/2021: B.1.1 → B.1.1.263 → B.1.1.529

B.1.1.529: 549 sequences with this designation in GISAID

Botswana, earliest 11/11/2021

South Africa, 11/09/2021

Nations with sequences in GISAID, many noted in GISAID to be travelers or targeted sampling:

- Botswana	23	- Belgium	6	- Canada	12
- Ghana	33	- Czech Republic	1	- USA	26
- Reunion	2	- France	6	- Mexico	1
- South Africa	227	- UK	84	- Australia	14
- Nigeria	3	- Germany	15	- Brazil	3
- Hong Kong	9	- Italy	4		
- India	3	- Ireland	1		
- Japan	2	- Norway	3		
- Israel	4	- Netherlands	17		
- Malaysia	1	- Portugal	13		
- Singapore	2	- Scotland	9		
- South Korea	3	- Spain	7		
- Maldives	1	- Switzerland	7		
- Sri Lanka	1	- Sweden	1		
		- Austria	11		
		- Denmark	2		

Mutation list of the most common form of Spike among Omicron sequences



Note: This reference sequence was derived from a small set of sequences available 11/23/2021 from Botswana, South Africa and Hong Kong. As more sequences from dozens of countries became available, and spikes with this set of mutations have remained the most commonly sampled form of Spike in the lineage B.1.1.529 in GISAID.

LANL's codon aligned curated reference sequences in fasta files, that include B.1.1.529 can be found at GISAID:

GISAID -> EpiCoV -> Downloads -> LANL Alignments

NTD

A67V, **H69-**, **V70-**, T95I, **G142D**, **V143-**, **Y144-**, **Y145-**, **N211-**, L212I, **+214EPE**,

RBD

G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A,

Q493R, G496S, Q498R, N501Y, Y505H

Furin cleavage enhancing

T547K, D614G, **H655Y**, **N679K**, **P681H**, N764K, D796Y, N856K, **Q954H**, **N969K**, **L981F**

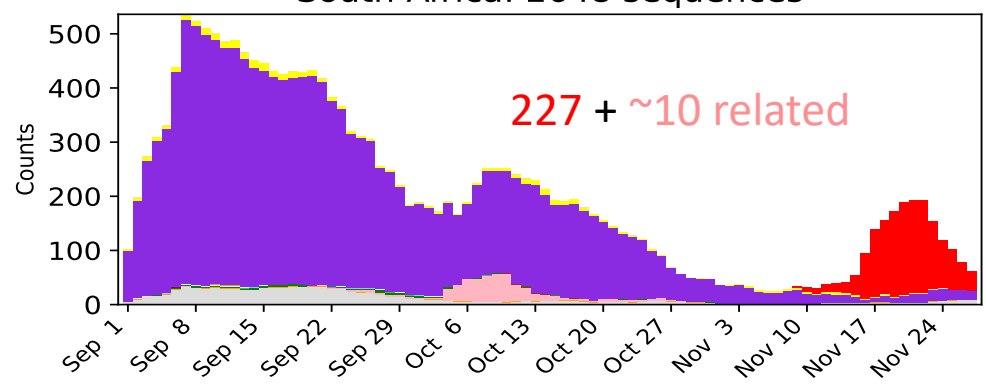
Heptad Repeat 1



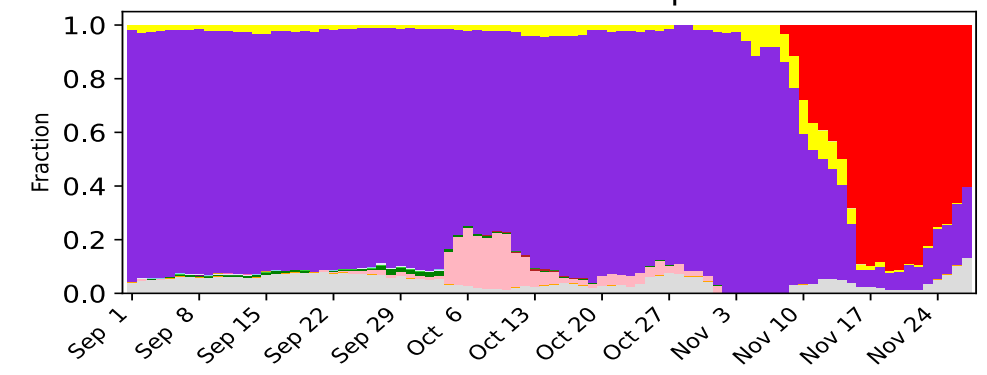
- █ Omicron
- █ B.1.640
- █ B.1.1.318
- █ C.1.2
- █ Delta
- █ Delta_AY.4.2
- █ Delta_AY.35
- █ Delta_AY.47
- █ Delta_AY.98.1
- █ Delta_AY.33
- █ Delta_AY.26
- █ Delta_AY.25
- █ Gamma
- █ Mu
- █ Lambda
- █ Beta
- █ Alpha
- █ other

Omicron: B.1.1.529 South Africa

South-Africa: 2648 sequences



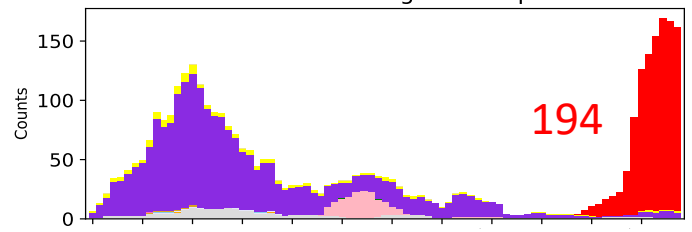
South-Africa: 2648 sequences



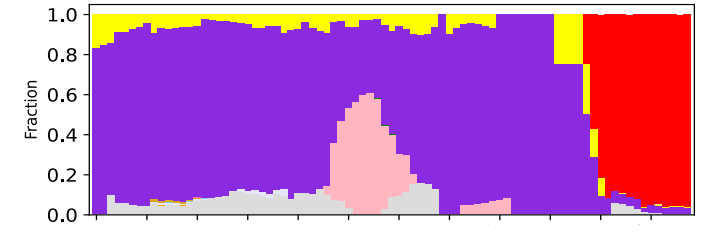
Western Cape 14



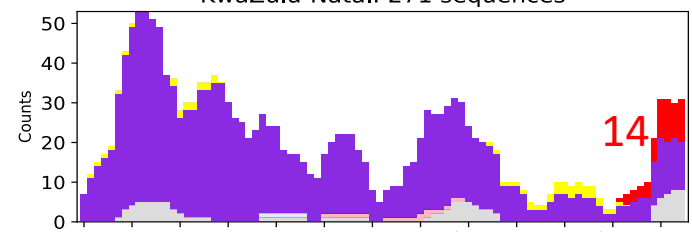
South-Africa.Gauteng: 570 sequences



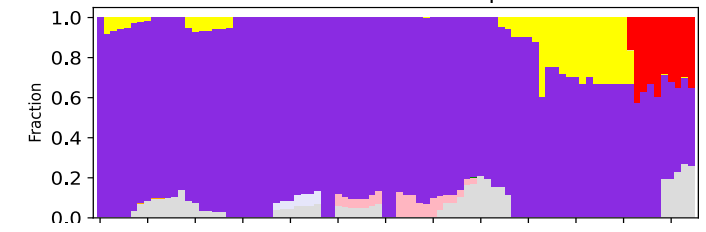
South-Africa.Gauteng: 570 sequences



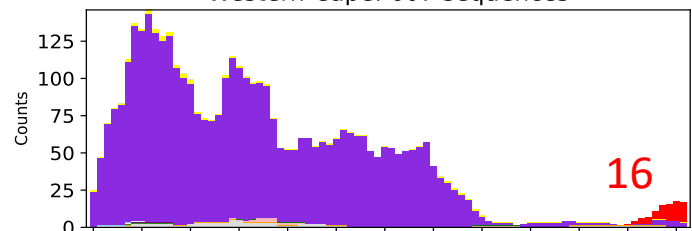
KwaZulu-Natal: 271 sequences



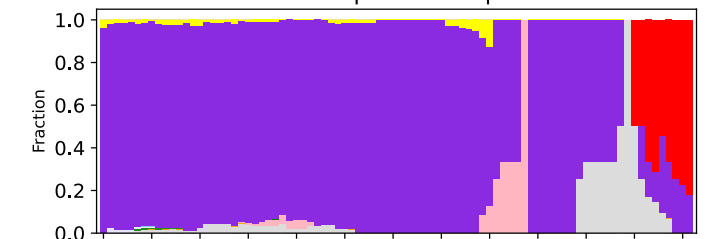
KwaZulu-Natal: 271 sequences



Western-Cape: 607 sequences



Western-Cape: 607 sequences



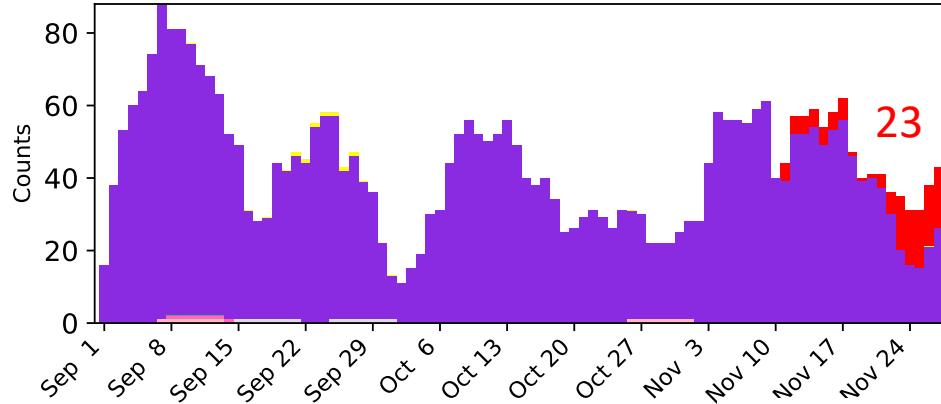
Omicron: B.1.1.529: Botswana

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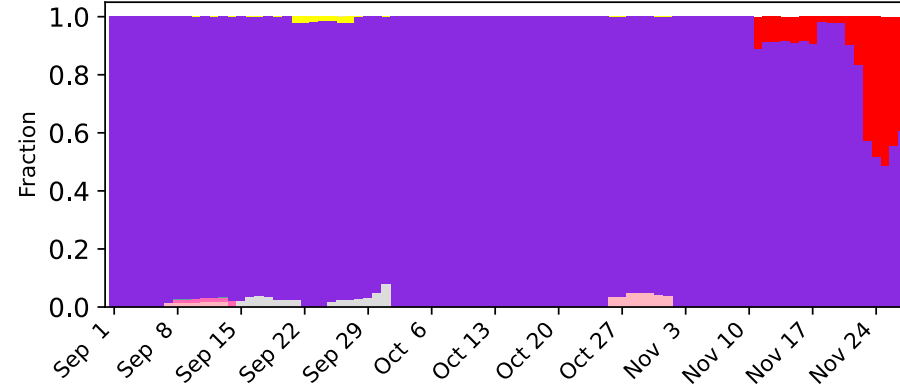


- Omicron
- B.1.640
- B.1.1.318
- C.1.2
- Delta
- Delta_AY.4.2
- Delta_AY.35
- Delta_AY.47
- Delta_AY.98.1
- Delta_AY.33
- Delta_AY.26
- Delta_AY.25
- Gamma
- Mu
- Lambda
- Beta
- Alpha
- other

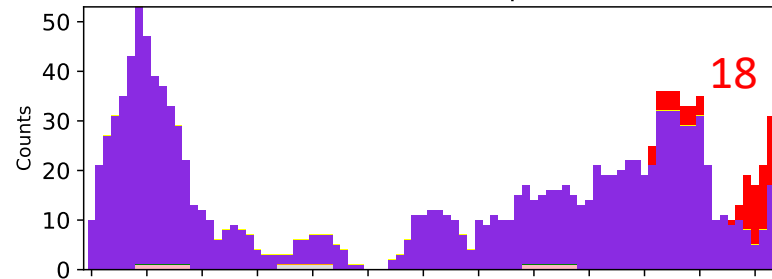
Botswana: 571 sequences



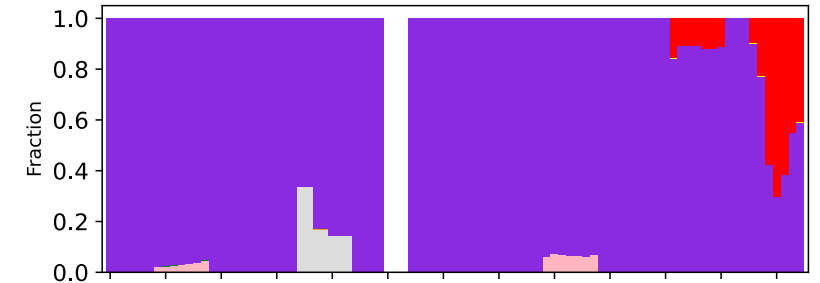
Botswana: 571 sequences



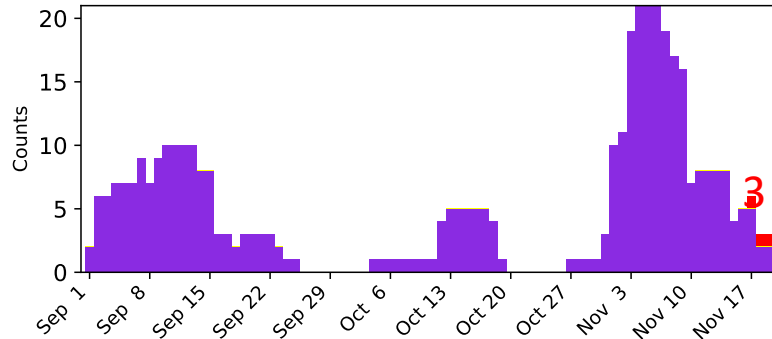
Gaborone: 219 sequences



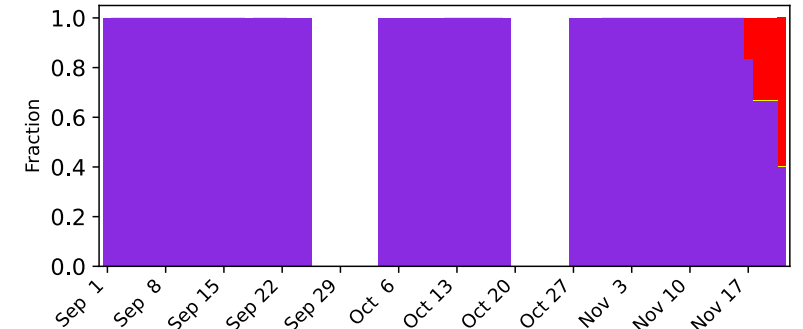
Gaborone: 219 sequences



Palapye: 61 sequences



Palapye: 61 sequences



Omicron is highly mutated compared to other variants identified to date (see spread sheet under Spike variants).



Classification Group	Date of addition to website listing, newest entries highlighted in yellow	WHO designation, * means it is WHO listed for further monitoring as of Nov. 26, 2021	Pango lineage where the form of Spike is most commonly found, see columns L and M for complete list. Grey lettering with an underscore indicates an ancestral amino acid. Colors as in column E.	Most common Spike backbones of variant form. NTD supersite, RBD, positive charge near the furin cleavage site or H655Y. Liu et al. bioRxiv 2021, 10.1101/2021.08.12.456173 & Alba et al. bioRxiv 2021, 10.1101/2021.08.05.455290
WHO VOC*	Aug. 9, 2021	Alpha α	Alpha (B.1.1.7 + Q.* Pango sublineages)	H69-,V70-,Y144-, N501Y ,A570D,D614G, P681H ,T716I,S982A,D1118H
	Aug. 9, 2021	Beta β	B.1.351	D80A,D215G, L242-,A243-,L244-,K417N,E484K,N501Y ,D614G,A701V
	Aug. 9, 2021	Gamma γ	P.1	L18F,T20N ,P26S,D138Y,R190S, K417T,E484K,N501Y ,D614G, H655Y ,T1027I,V1176F
	Aug. 9, 2021	Delta δ	Delta (B.1.617.2 + AY.* Pango sublineages)	T19R ,T95I, G142D,E156-,F157-,R158G,L452R,T478K ,D614G, P681R ,D950N
	Nov. 26, 2021	Omicron ο	B.1.1.529 (Previously called B.1.1)	A67V,H69-,V70-,T95I,G142D,V143-,Y144-,Y145-,N211-,L212I,+214EPE,G339D,S371L,S373P,S375F,K417N,N440K,G446S,S477N,T478K,E484A,Q493R,G496S,Q498R,N501Y,Y505H ,T547K,D614G, H655Y,N679K,P681H ,N764K,D796Y,N856K,Q954H,N969K,L981F
WHO VOI*	Aug. 9, 2021	Lambda Λ	C.37	G75V,T76I,R246N,S247-,Y248-,L249-,T250-,P251-,G252-,D253-, L452Q,F490S ,D614G,T859N
	Aug. 9, 2021	Mu μ	B.1.621	T95I, +143T,Y144S,Y145N,R346K,E484K,N501Y ,D614G, P681H ,D950N
*WHO Variant of Concern or interest				
Rare but highly complex Spike variants recently identified in Africa				
Recent rare complex variants	Sept. 11, 2021	*	C.1.2	P9L,C136F, Y144-,R190S,D215G,A243-,L244-,Y49H,E484K,N501Y ,D614G, H655Y,N679K ,T716I,T859N
	Nov.18, 2021	*	B.1.640 (Previously called B.1 or B.1.576)	P9L,E96Q, C136-,N137-,D138-,P139-,F140-,L141-,G142-,V143-,Y144-,R190S,I210T,R346S,N394S,Y449N,F490R,N501Y ,D614G, P681H ,T859N,D936H

Other variants of interest and concern over 2021:

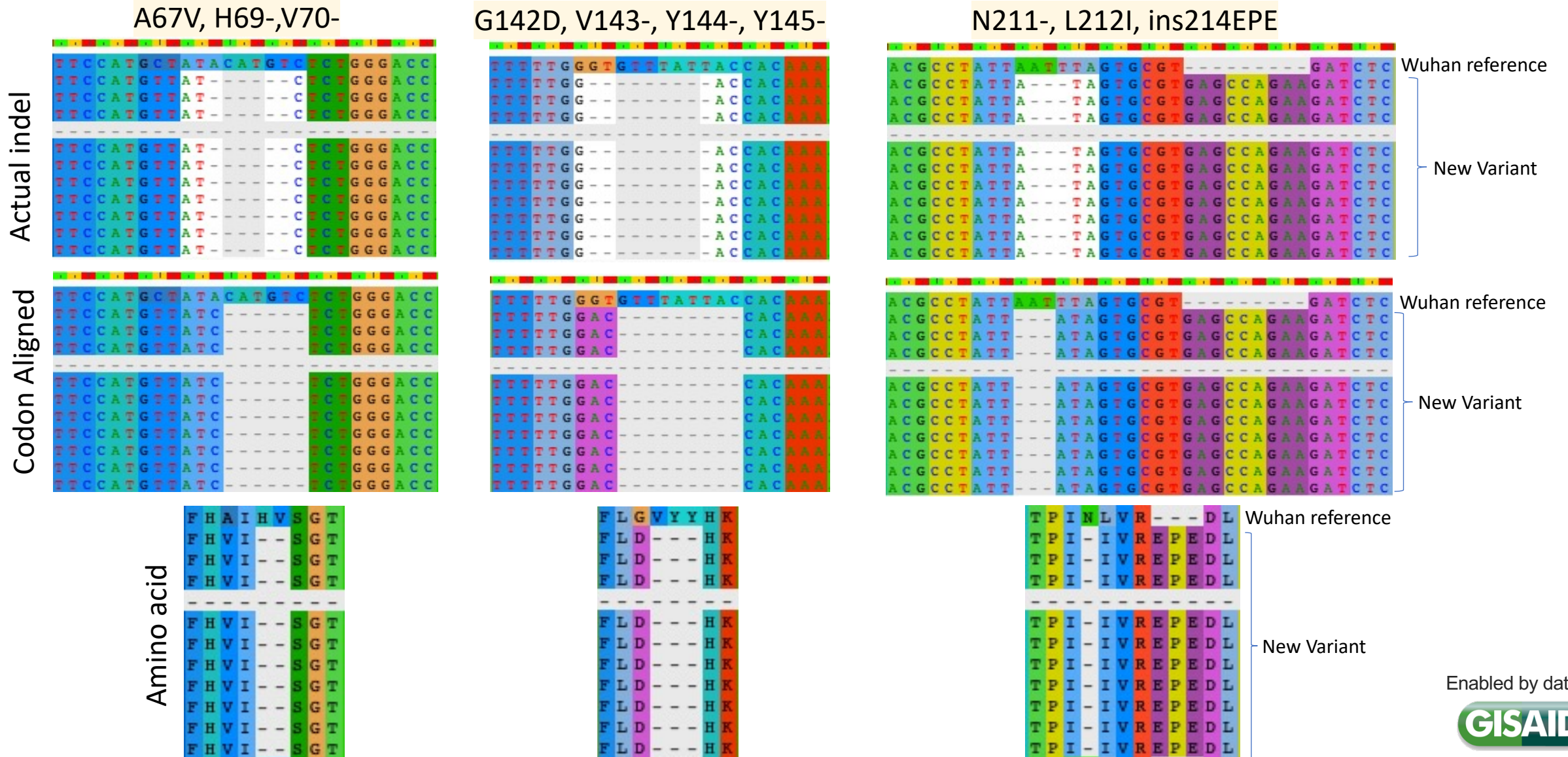
Earlier lineage expansion, but transient	Aug. 9, 2021	* Iota ι	B.1.526	L5F,T95I, D253G,E484K ,D614G,A701V
	Aug. 9, 2021	* Eta η	B.1.525	Q52R,A67V,H69-,V70-,Y144-, E484K ,D614G, Q677H ,F888L
	Aug. 9, 2021	Zeta ζ	P.2	E484K ,D614G,V1176F
	Aug. 9, 2021	Epsilon ε	B.1.429 (+B.1.427)	S13I,W152C,L452R ,D614G
	Aug. 9, 2021		B.1.1.519	T478K ,D614G, P681H ,T732A
	Aug. 9, 2021		B.1.637 (previously grouped in B.1.526)	D80G, Y144-,F157S,L452R ,D614G,T859N,D950H
	Aug. 9, 2021		C.36.3	S12F,H69-,V70-, W152R,R346S,L452R ,D614G, Q677H ,A899S
	Aug. 9, 2021		B.1.1.318 (B.1.1.318 + AZ.* Pango sublineages)	T95I, Y144-,E484K ,D614G, P681H ,D796H
	Nov.18, 2021	*	AZ.5 (Formerly a B.1.1.318 Pango sublineage)	D80Y,T95I, Y144-,W258L,E484K ,D614G, P681H ,D796H
	Aug. 9, 2021		B.1.619	I210T, N440K,E484K ,D614G,D936N,S939F,T1027I
	Aug. 9, 2021		B.1.620	P26S,H69-,V70-,V126A, Y144-,L242-,A243-,L244-,H245Y,S477N,E484K ,D614G, P681H ,T1027I,D1118H
	Sept. 11, 2021		B.1	T19R, E484K ,D614G,D950N
	Aug. 9, 2021	* Kappa κ	B.1.617.1	T95I, G142D,E154K,L452R,E484Q ,D614G, P681R ,Q1071H
	Aug. 9, 2021		A.23.1	F157L,V367F ,Q613H,ancestral D614-,P681R
	Aug. 9, 2021		A.27	L18F,L452R,N501Y , ancestral D614-,A653V,H655Y ,D796Y,G1219V
	Aug. 9, 2021		B.1.177.82	A222V, A262S ,P272L,D614G
	Aug. 9, 2021		B.1.234	G142S ,E180V,D614G Q677H
	Aug. 9, 2021		B.1.1.284	M153T ,G184S,D614G, Q677H
	Aug. 9, 2021		B.1.466.2	N439K ,D614G, P681R
	Aug. 9, 2021		R.1	W152L,E484K ,D614G,G769V
	Aug. 9, 2021		B.1.258.17	H69-,V70-, L189F,N439K ,D614G,V772I
	Aug. 9, 2021		B.1.575	S494P ,D614G, P681H ,T716I
	Aug. 9, 2021		B.1.214.2	+214TDR,Q414K,N450K ,D614G,T716I
	Aug. 9, 2021		B.1.1.523	E156-,F157-,R158-,F306L,E484K,S494P ,D614G,E780A,D839V,T1027I
	Aug. 9, 2021		P.4	G142V ,N164K,Q173K, L452R ,D614G,S704L,I720V,V1176F

New B.1.1.529 variant from Botswana/South Africa, Insertions and Deletions



B.1.1.:

A67V, H69-, V70-, T95I, G142D, V143-, Y144-, Y145-, N211-, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F

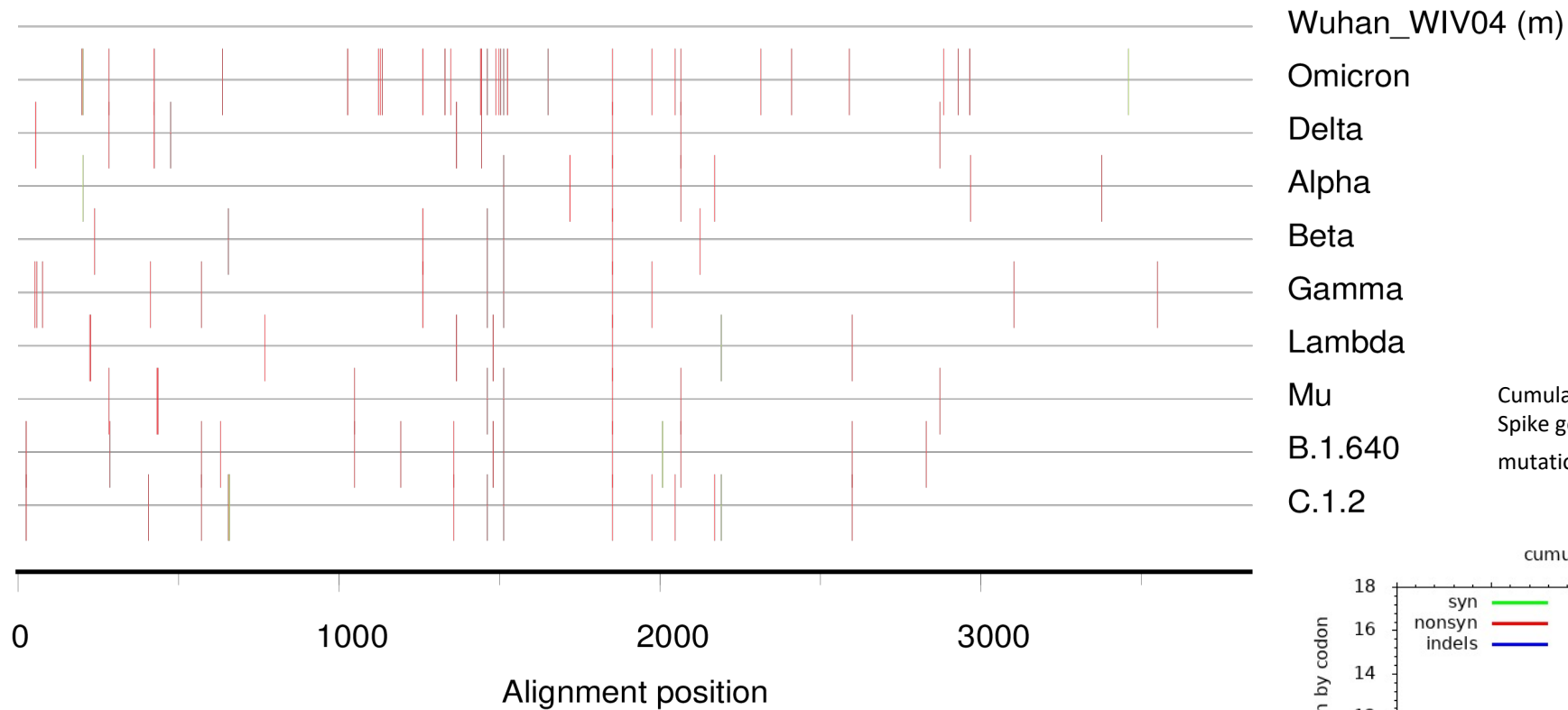




A view of synonymous and nonsynonymous substitutions in Spike and a simple dN/dS comparing VOI/VOC sequences to the ancestral virus.

dN/dS

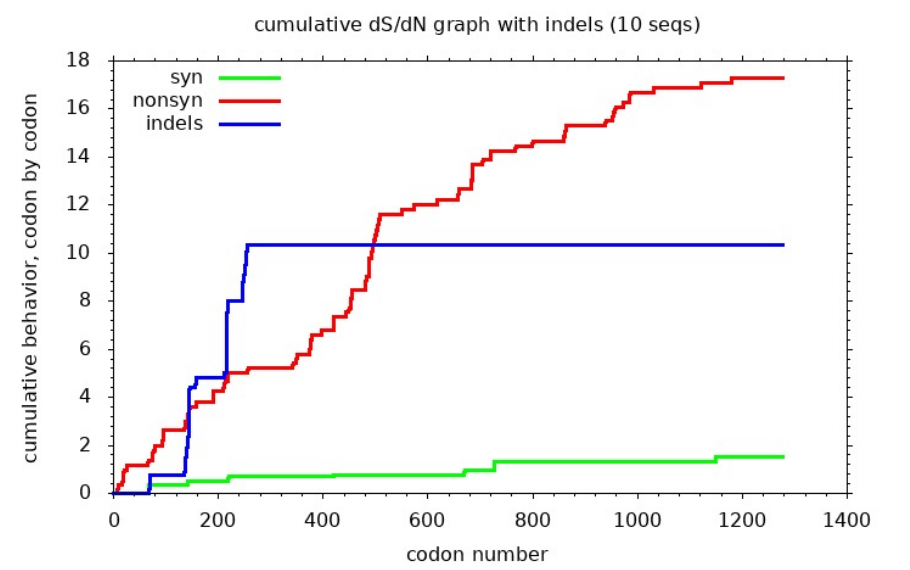
Silent and Non-silent Mutations compared to the Wuhan reference sequence



Omicron: dN/dS = 2.95
 Observed:
 Silent: 3/842 possible
 Nonsilent: 31/2961 possible

Cumulative silent and non-silent mutations in codons across the Spike gene show regions in Spike were nonsynonymous mutations cluster (steep red line) or are rare (flat sections).

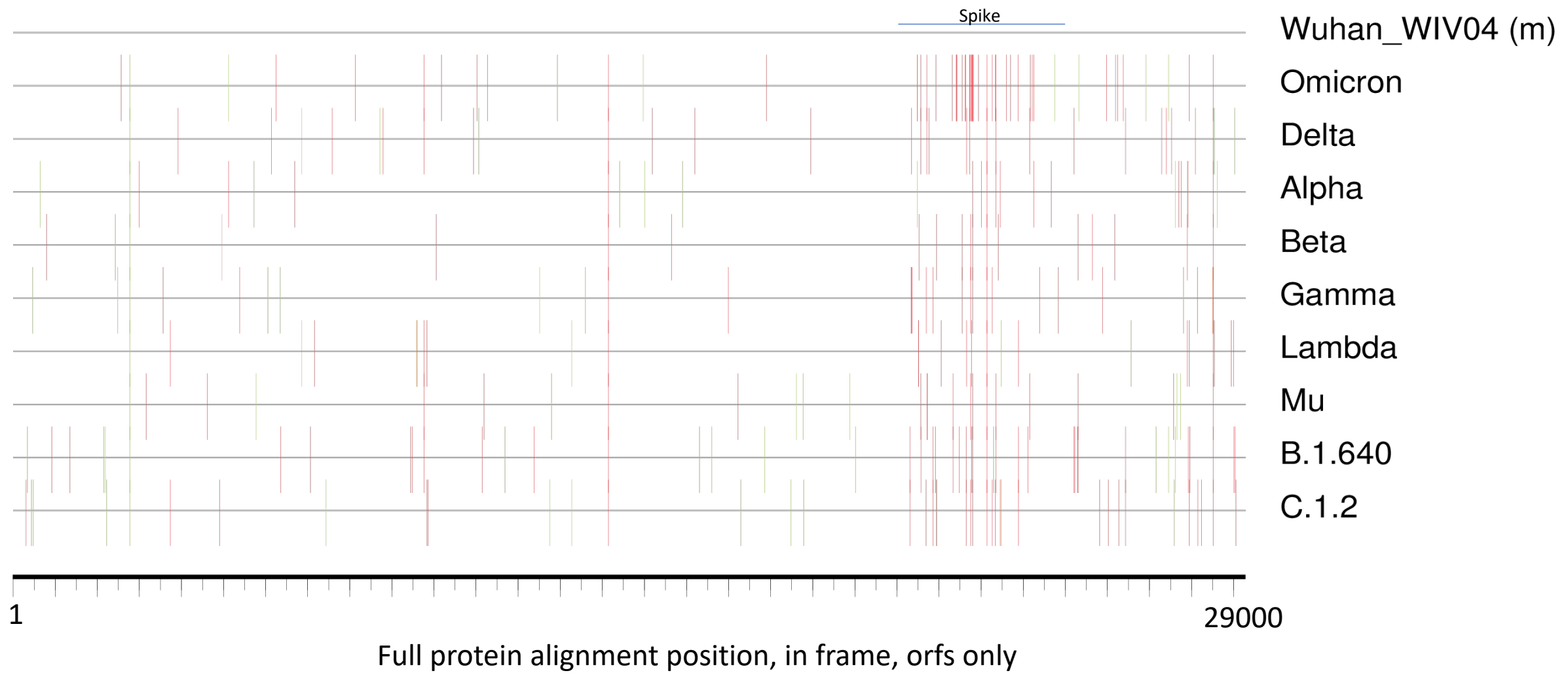
Average dN/dS for each reference strain to Wuhan is 2.4





Non-synonymous mutations tend to cluster in Spike relative to the other sections of the proteome.
Omicron isn't particularly highly mutated relative to other variants outside of Spike.

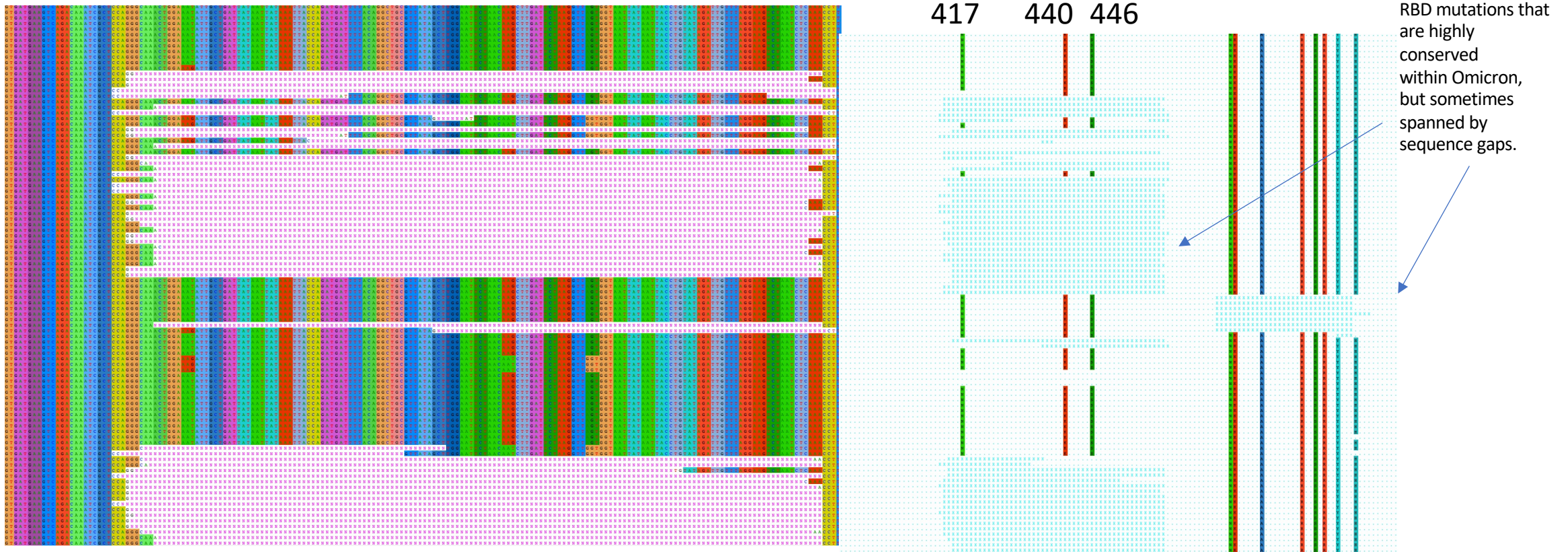
Silent and Non-silent Mutations compared to the Wuhan reference sequence



Two things to be mindful of for determining reference strains: currently there are still lots of gappy sequences, so an Omicron consensus sequence derived treating N's as ancestral will undercount mutation frequencies in the lineage.



Sequence gaps in Spike at the DNA level (left, pink N's) and protein level (right, blue x's)

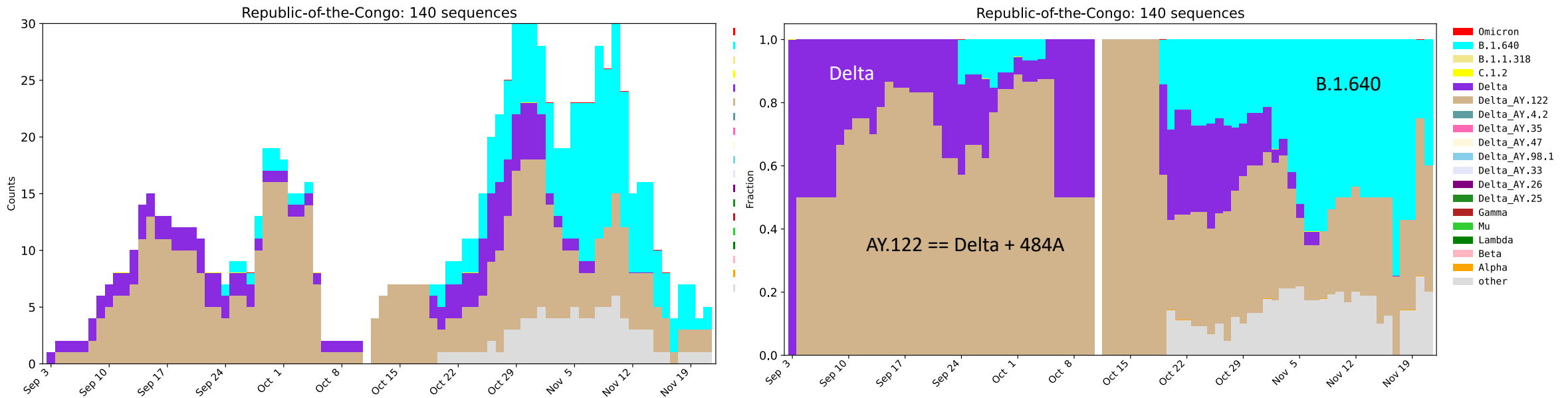


Also there is an insertion in Omicron at Spike 214.

Vertical stripes are amino acid changes in Omicron relative to the Wuhan sequence

B.1.640 is also of interest.

It is not increasing as quickly as Omicron, and not as highly mutated, but still has multiple Spike mutations. It can be found 124 times, and is commonly sampled the Republic of the Congo. It has been sampled in France 65 times, and also sampled in Italy, Reunion, Belgium, Spain, the UK, and in the USA.



In the Republic of the Congo, Delta + 484A is increasingly sampled regionally within the Delta sublineage, then both are being replaced by B.1.640



The discovery of Omicron and the analysis presented here relied upon the work of many, acknowledged here are contributors of some of the first key sequences in GISAID:

B.1.1.529 GISAID:

Botswana Harvard HIV Reference Laboratory: Sikhulile Moyo, Wonderful T. Choga, Dorcas Maruapula, Keoratile Ntshambiwa, Sefetogi Ramaologa, Thongbotho Mphoyakgosi, Boitumelo Zuze, Botshelo Radibe, Legodile Kooepile, Ontlametse T. Bareng, Pamela Smith-Lawrence, Kgomotso Moruisi, Roger Shapiro, Shahin Lockman, Joseph Makhema, Mphaphi B. Mbulawa, Mosepele Mosepele, Simani Gaseitsiwe

South Africa:

LANCET LABORATORY National Institute for Communicable Diseases of the National Health Laboratory Service: Amoako DG, Everatt J, Scheepers C, Glass A, Viana R, Mohale T, Ntuli N, Mahlangu B, Mnguni A, Ismail A, Bhiman JN

Division of Medical Virology, National Health Laboratory Service (NHLS), Tygerberg Hospital / Stellenbosch University:

Jean Maritz, Nadine Cronje, Petra Raimond, Tongai Maponga, Shannon Wilson, Kamela Mahlakwane, Tania Stander, Gert van Zyl, Wolfgang Preiser

CERI, Centre for Epidemic Response and Innovation, Stellenbosch University and KRISP, KZN Research Innovation and Sequencing Platform, UKZN

Amy Strydom, Adriano Mendes, Micheala Davids, Sim Mayaphi and Marietjie Venter, NGS-SA (Scheepers C, Hsiao M, von Gottberg A, Bhiman J, Lessells R, Bester P, Engelbrecht S, Preiser W, Mdlalose N, Mlisana K, Goedhals D, Everatt J, Amoaka D, Makatini Z, Hardie D, Maponga T, Iranzadeh A, Williamson C, Venter M, Oluwakemi M, Nyaga M) Giandhari J, Pillay S, Naidoo Y, Ramphal U, Ramphal Y, Arisha Maharaj, Moir M, San JE, Tshiabuila D, Tegally H, Wilkinson E, de Oliveira T

With thanks also to the many others whose work enabled the resolution of this variant new and its early trajectory

B.1.640 GISAID:

Republic of the Congo: Fondation Congolaise pour la Recherche Médicale (FCRM): Mfoutou Mapanguy Claujens Chastel; Batchi-Bouyou Armel Landry; Dr. Jean Claude Djontu; Dr. Abel Lissom; Prof. Dr. Thirumalaisamy P. Velavan; Prof. Francine Ntoumi

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