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## Highly pathogenic avian influenza and its complex patterns of reassortment

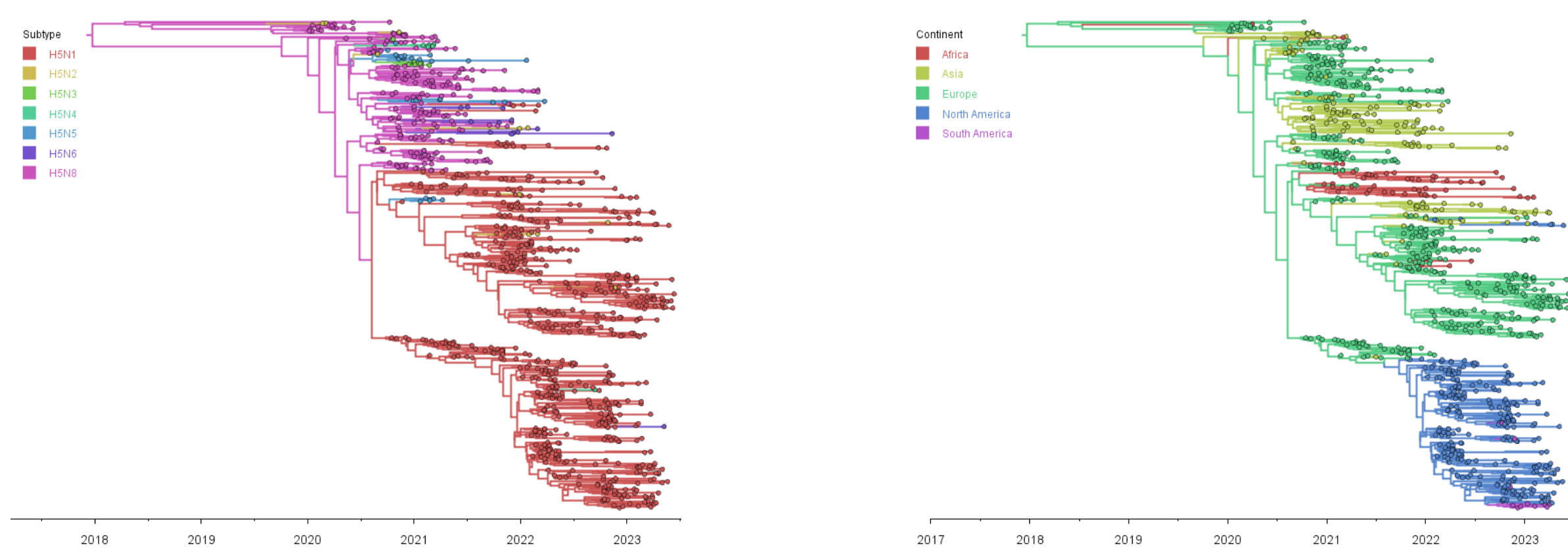
Samantha Lycett<sup>1</sup>, Will Harvey<sup>1</sup>, Lu Lu<sup>1</sup>, Anne Pohlmann<sup>2</sup>, Martin Beer<sup>2</sup>, Thijs Kuiken<sup>3</sup>, Rute Pinto<sup>1</sup>, Darrell Kapczynski<sup>4</sup>, Daniel Perez<sup>5</sup>, Paul Digard<sup>1</sup>  
<sup>1</sup>Roslin Institute, University of Edinburgh, UK; <sup>2</sup>Friedrich-Loeffler-Institute Federal Research Institute for Animal Health, Greifswald, Germany,  
<sup>3</sup>Erasmus Medical Center, Rotterdam, The Netherlands; <sup>4</sup>USDA-ARS Athens Georgia, USA; <sup>5</sup>University of Georgia, Athens, USA

### Avian Influenza and Disease X

- Reservoir of influenza subtypes and diversity in wild bird populations
- Recent highly pathogenic H5 global outbreaks, clade 2.3.4.4b in wild birds, poultry and mammal spillovers
- For 2014/2015, 2016/2017 and 2020/2021 outbreaks the main subtype in Europe was H5N8
- However for 2021/2022 and 2022/2023 seasons, the virus acquired a different neuraminidase making subtype H5N1
- H5NX viruses have components originating from the reservoir through reassortment

### H5NX 2020-2023 Global Sequence Data

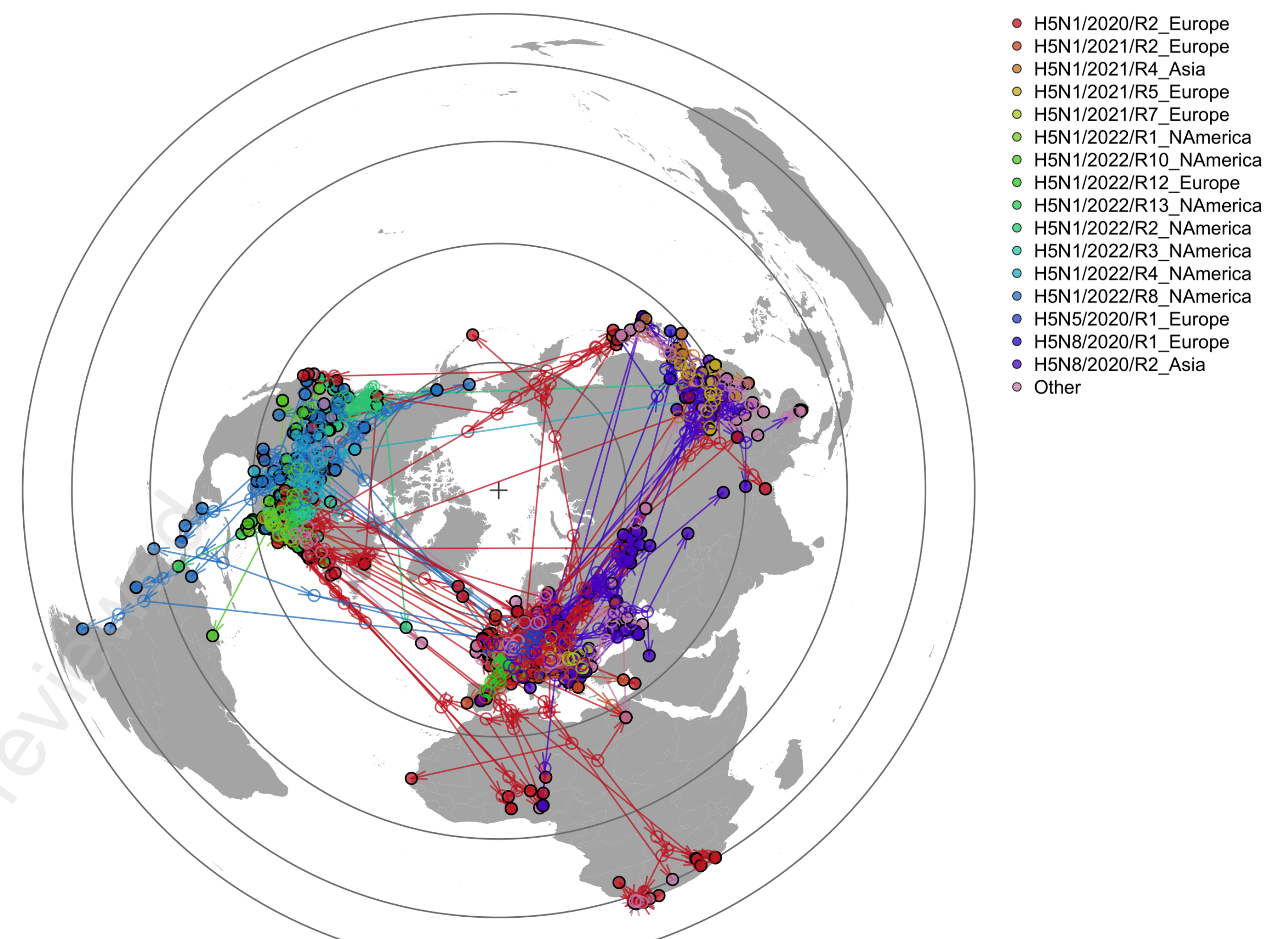
- 5000+ H5NX 2.3.3.4b whole genomes from 2020-2023 including H5N8, H5N1



HA subsample time-scaled phylogeny with discrete traits by subtype and continent, and reassortment code

### Aims and Questions:

- What new H5NX HPAI reassortants ?
- Where are the H5NX HPAI reassortants being generated ?
- Do they have different spreading patterns and host ranges ?



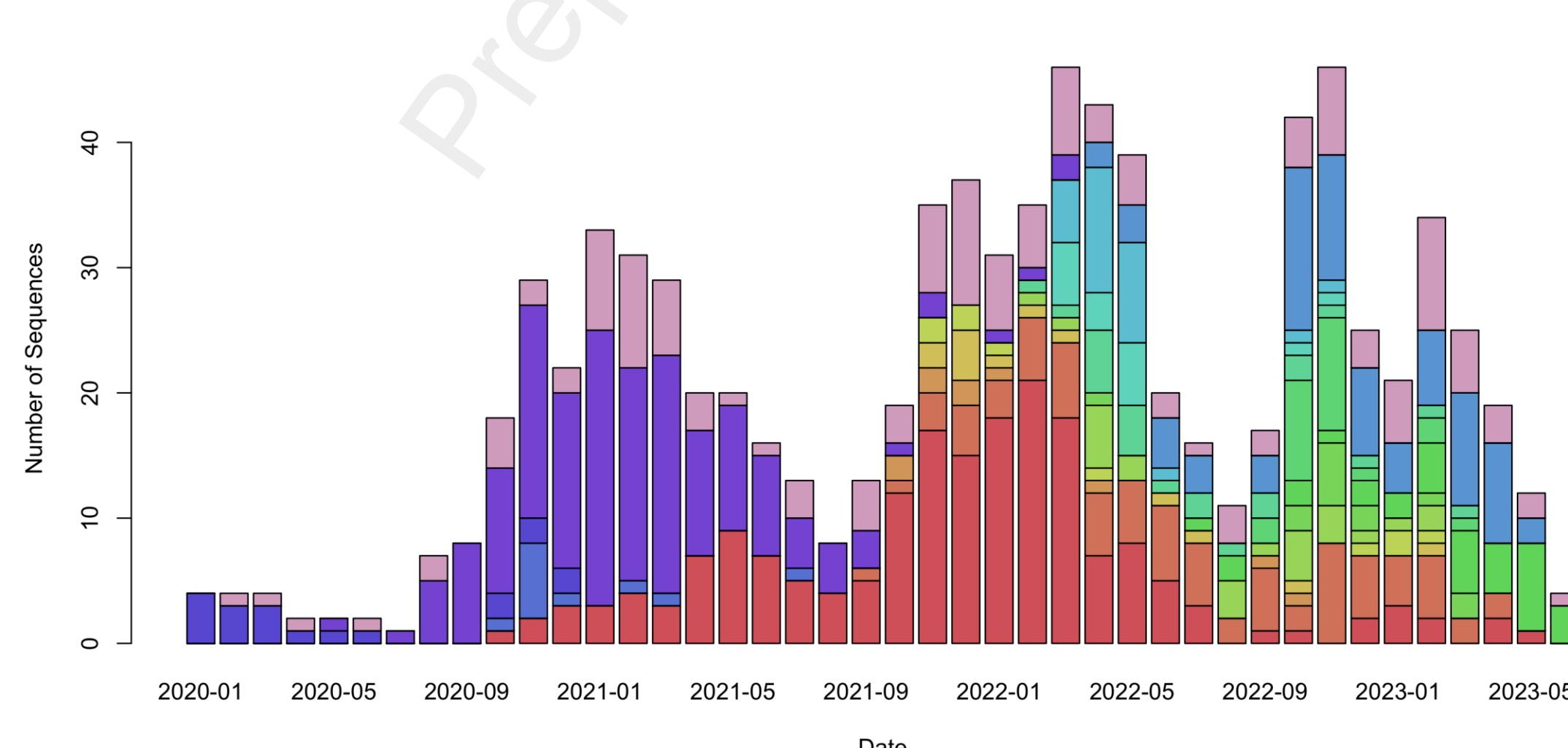
Spatial phylogeography of 2020-2023 Reassortants; From North Pole, coloured by reassortment code

### H5NX 2020-2023 Reassortants in Detail

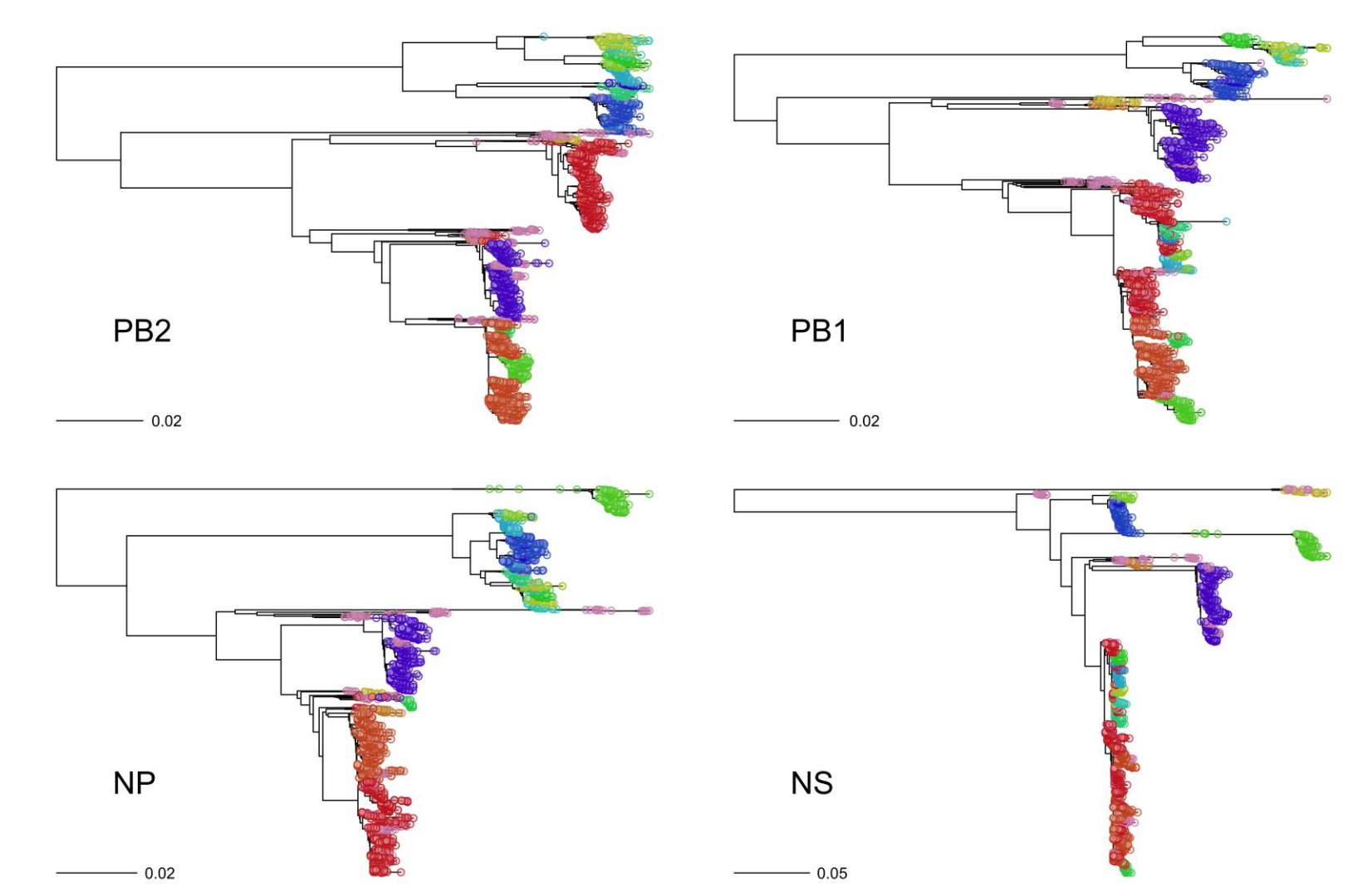
- Each segment split into clusters of 1-2% genetic distance and given segment code
- 8 Segment codes combined to Reassortment code to describe diversity

Reassortment code	PB2	PB1	PA	HA	NP	NA	MP	NS
H5N1/2020/R2_Europe	1	1	1	1	1	1	1	1
H5N1/2021/R2_Europe	2	2	2	2	2	2	2	2
H5N1/2021/R4_Asia	3	3	3	3	3	3	3	3
H5N1/2021/R5_Europe	4	4	4	4	4	4	4	4
H5N1/2021/R7_Europe	5	5	5	5	5	5	5	5
H5N1/2022/R1_NAmerica	6	6	6	6	6	6	6	6
H5N1/2022/R10_NAmerica	7	7	7	7	7	7	7	7
H5N1/2022/R12_Europe	8	8	8	8	8	8	8	8
H5N1/2022/R13_NAmerica	9	9	9	9	9	9	9	9
H5N1/2022/R2_NAmerica	10	10	10	10	10	10	10	10
H5N1/2022/R3_NAmerica	11	11	11	11	11	11	11	11
H5N1/2022/R4_NAmerica	12	12	12	12	12	12	12	12
H5N1/2022/R8_NAmerica	13	13	13	13	13	13	13	13
H5N5/2020/R1_Europe	14	14	14	14	14	14	14	14
H5N8/2020/R1_Europe	15	15	15	15	15	15	15	15
H5N8/2020/R2_Asia	16	16	16	16	16	16	16	16

Clusters per segment and Reassortment code



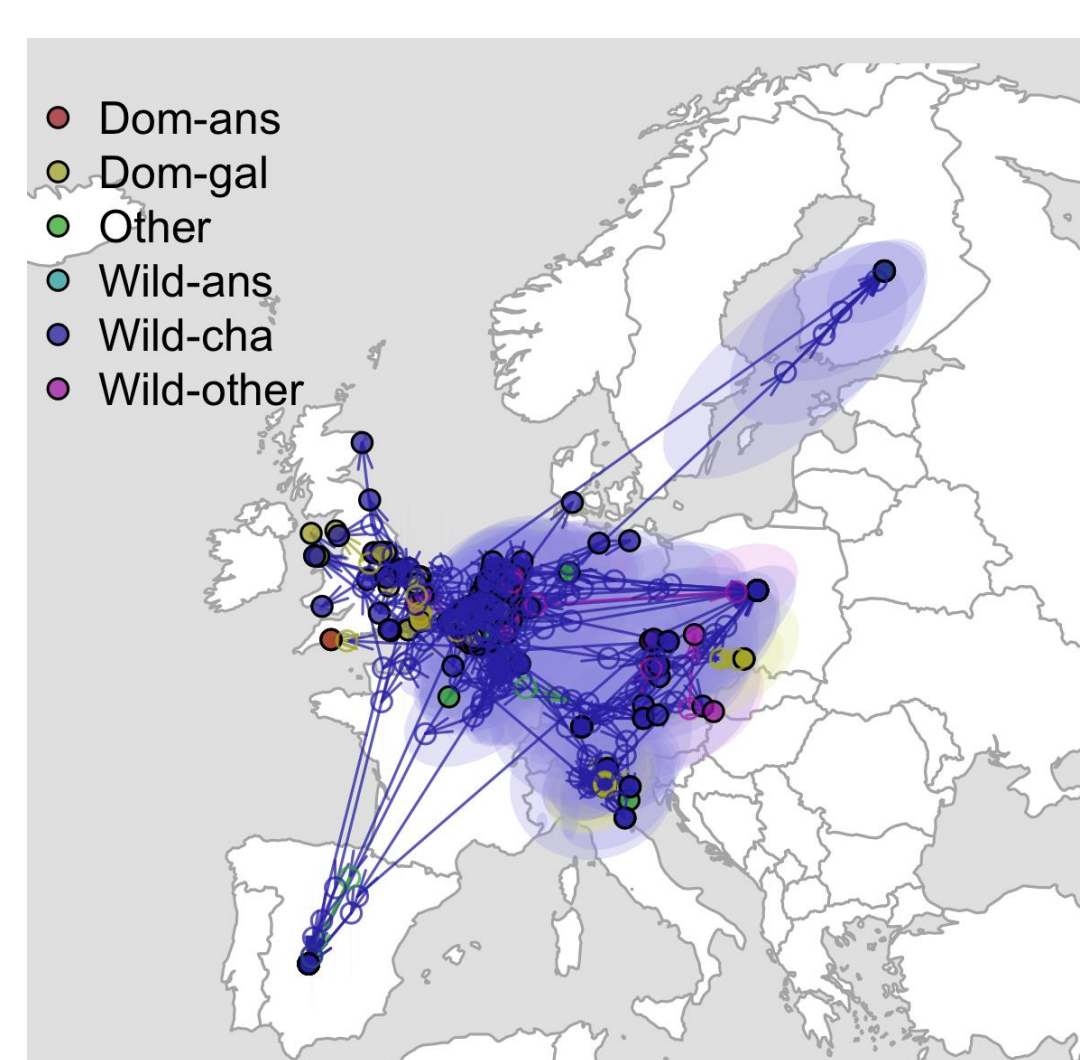
Subsampled sequences over time with Reassortment code



Phylogenies of individual segments showing clusters

### Reassortants and Host Species

- Reassortants sampled from mix of wild birds and poultry, and some mammals
- Spill overs into Mammals from wild Anseriformes and Charadriiformes (gulls) estimated from phylogenies
- One reassortant is spreading fast in European Charadriiformes, it has exchanged PB2, PA, NP and NS
- These reassortants are mammalian infective, but not yet very mammalian transmissible

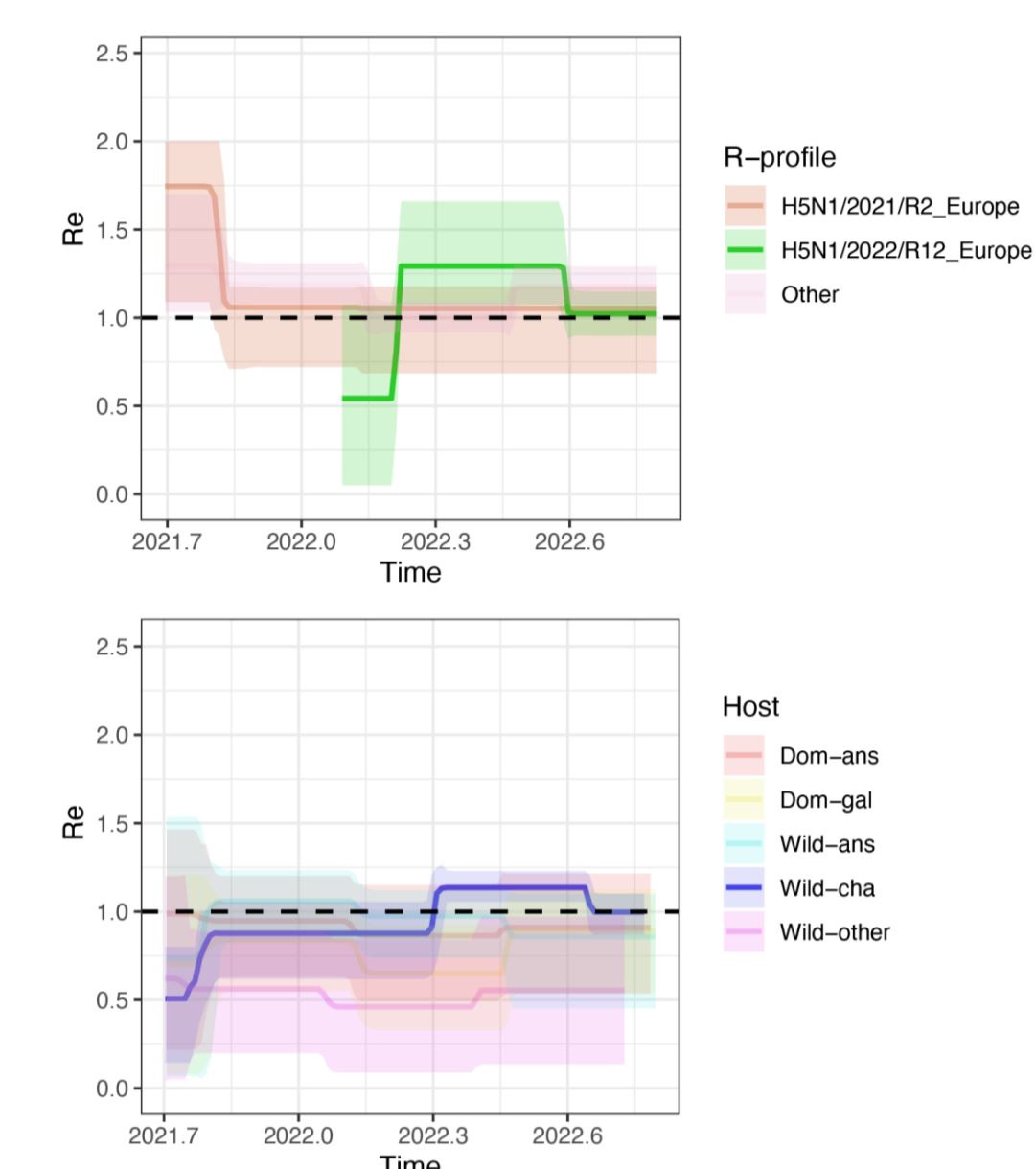


Phylogeography of 2022/R12\_Europe reassortant

### Predicting Risk from phylogenies

- Local Branching Index provided a relative lineage growth measure with different bird species in the tree
- Multitype birth-death model (BDMM) estimated effective reproductive numbers (Re) in structured populations of host and reassortant types
- Phylodynamic measures detected the early emergence of the 2022/R12\_Europe reassortant, leading to significant outbreaks in wild Charadriiformes.

Effective reproductive numbers (Re)



### Implications

- H5N1 strain has reassorted with previously co-circulating low pathogenic viruses.
- New reassortants with exchanged polymerases and other internal protein coding segments have emerged, and are fitter in certain avian populations.
- We predict the reassortants will continue to spread in the autumn in Europe, and expect further reassortments in the Americas.