This file contains Supplementary Discussion and Supplementary Figure S1

Supplementary Discussion

Leghorn chickens and highly pathogenic avian influenza. Highly pathogenic avian influenza was first described scientifically in Leghorn chickens in Italy in 1878[15,46], just a few years after newspaper reports of putative HPAI in chickens, ducks, and other domestic species during the epizootic of 1872 (ref 13). Leghorn chickens from northern Italy were at the centre of European HPAI outbreaks from the 1870s onwards, and evidently carried LPAI viruses as well[16], a pattern that re-occurred there in 1999-2006 (ref 16). So-called 'Poultry Mania', the intense interest in poultry breeding and exhibiting from the 1850s to the 1870s, involved trade in Leghorn chickens between the U.S., Britain, and Italy[47]. Given increasingly intensive farming practices from the 1870s onward, as Leghorn breeds gained popularity as prolific egg layers[16], the trans-Atlantic movement of LPAI-infected domestic poultry (or fowl) represents a plausible means of dispersal of avian influenza virus and establishment of the hemispheric clades evident in the trees (Fig. 2).

The ecology of domestic and wild bird populations in relation to AIV. Many AIV strains that circulate in chickens and turkeys show high replicative fitness in ducks (both domestic and wild), often with an LPAI or even apathogenic phenotype[48-50]. For example, during an outbreak of H7N7 HPAI in chickens in Australia in 1976, ducks on a neighbouring farm were found to harbour a closely related virus even though they showed no signs of disease[51]. (See Fig. S1d for the detailed H7 phylogeny and notice the two sequences from 1976 at the base of the Australian clade; also note the spillover of this domestic avian lineage into to a wild bird host in 1985). Domestic ducks harbour a huge amount of AIV genetic diversity, and viruses that can infect domestic ducks can also infect wild ducks[50]. They belong to the same species as wild mallards (the most frequently sampled wild waterfowl host of AIV); they intermingle with wild ducks on farms, in rice paddies, and in markets worldwide every day; and they are extremely numerous (likely more numerous than their wild counterparts)

Indeed, much of the knowledge of AIV genetic diversity in wild birds comes from mallards and closely related dabbling ducks in North America. For North America, the long-term average total wild duck population is ~33 million, of which ~7.5 million are mallards[52]. In comparison, the total domestic duck population worldwide is about 1 billion[53]. And the total domestic chicken population worldwide is about 15 billion[53]. Thus, domestic birds likely vastly outnumber the wild waterfowl hosts that are conventionally viewed as the primordial hosts of influenza A virus. And even in 2013 domestic birds are not ecologically isolated from wild species in most parts of the world.

There are yearly bottlenecks in influenza prevalence in wild ducks during the spring migration then an increase in prevalence in the autumn: in North America, prevalence falls to ~1% during the spring migration and rises to ~30% prior to and during the autumn migration, likely due to the large numbers of immunologically naïve young birds of that breeding season[54]. Hence, the long-term circulation of the virus in domestic avian hosts (e.g. see Fig. S1d and note the decades-spanning clade of H7 viruses among domestic birds in Australia and New Zealand, where H7 viruses are not known to circulate in wild birds[55]), with periodic amplification during large outbreaks, could be expected on basic ecological grounds to strongly influence the genetic diversity of AIV in wild avian populations (via domestic to wild AIV gene flow).

The seasonal prevalence patterns in wild ducks and the elevated risk of infection for juvenile, immunologically naïve birds in the breeding season also suggest an explanation for the much older genetic diversity in *HA* and *NA* (prior immunity in the older birds, which would favour the preservation of multiple *HA* and *NA* serotypes).

The origins of equine H3N8 *HA* and *NA*. Given the consistent pattern across the equine H3N8 internal genes (all nested within Western Hemisphere avian strains; Fig. 2), we think the most parsimonious scenario is that a single avian virus was the source of all these internal genes, no earlier than ~1954 based on the dating estimates of *NP*. That the other internal genes show earlier TMRCAs with avian strains is expected due to unsampled diversity[56] and the displacement in recent decades of some older South American AIV lineages by newer Eurasian variants (e.g. in *PB1*; Fig. S1b).

The equine H3N8 *HA* and *NA* exhibit phylogenetic patterns distinct from the internal protein-encoding segments, suggesting one or both of the major antigenic segments may have been circulating in equines for decades prior to 1963 and might be relicts of an equine IVA genome related to the putative H3N8 pandemic virus of 1889-92 (ref 57). The TMRCA of H3 in horses, birds, and humans was estimated at just prior to the 1889 pandemic; and the U content of the equine H3-encoding segment in 1963 was already 'mammalian' (i.e. above the avian range) (Extended Data Fig. 4). The U content of N8 was at the low extreme observed among Western Hemisphere avian N8, so it seems possible either that the equine N8 *NA* was a recent acquisition from Western Hemisphere birds (along with the internal genes) or that it had a deeper equine ancestry along the stem branch leading to the equine clade and had Eastern Hemisphere origins (but had circulated in horses long enough to attain U content higher than Eastern AIV strains by 1963).

Thus, the 1963 panzootic virus may have originated through the combination, shortly before 1963, of an existing equine *HA* with the internal genes and perhaps the *NA* of a South American avian strain. However, given that no H3 genes from AIV strains have been sampled from South America at any time point, to our knowledge, it seems conceivable that a divergent avian lineage with a U content above the range of the current sample was the source of its *HA*, so an entirely avian origin shortly before 1963 is difficult to exclude.

Relatively recent dispersals of AIV internal genes from the Eastern Hemisphere to the Western Hemisphere. Fig. S1 shows the *PB1*, *PA*, *NP*, and *NS* lineage A clades that have replaced (or nearly replaced) the earlier 'West-1' variants in the Western Hemisphere. These 'West-2' and 'West-3' clades descend from close relatives of the H7 'fowl plague' viruses from European and Asian domestic birds. For example, most Eastern Hemisphere AIV *NP* genetic diversity, as well as the West-2 lineage, evolved from ancestors closely related to the A/chicken/Brescia and A/chicken/Rostock HPAI viruses isolated in the 1930s. The West-2 lineage and A/chicken/Brescia share a most recent common ancestor at ~1923. The West-2 *NP* clade, which emerged in the West between ~1940 and ~1945, accounts for fully 97% of Western Hemisphere *NP* genes sampled in 2009-2013. And the *NP* gene from an influenza outbreak in domestic ducks in Manitoba in 1952 (ref 58) (or one almost identical to it) evidently gave rise to all the West-2 *NP* diversity (and therefore ~97% of the total) currently circulating in North American birds, both wild and domestic.

Similarly, 100% of AIV *PB1* sampled in the Western Hemisphere since 2009 is from the West-2 clade. This lineage descended quite recently from Eurasian AIV and is very closely related to the LPAI strain A/chicken/Germany/N/1949, sharing an MRCA with it not long before 1949. The West-2 lineage is nested among European AIV sequences from LPAI and HPAI viruses of domestic ducks and chickens (including A/chicken/Germany/N/1949), and emerged in the Western Hemisphere sometime between ~1940 and ~1955. Since the entire Eastern Hemisphere *PB1* lineage as well as the West-2 lineage descended from an early 20th century virus closely related to the 'fowl plague' HPAI viruses sampled in the 1920s and 1930s, it follows that *PB1* has undergone a worldwide sweep, within about one century, with all current *PB1* genetic diversity tracing back to this fowl plague-like ancestor at ~1910. Interestingly, this remarkably successful Eurasian avian *PB1* lineage was also the source of the newly-emerged *PB1* genes in both the 1957 H2N2 human pandemic virus and the 1968 H3N2 pandemic virus: the 1957 human *PB1* is the sister group to the West-2 avian *PB1* and the 1968

human *PB1* is the sister group to the West-3 avian *PB1* (Fig. S1b), suggesting a propensity of this *PB1* lineage for cross-species transmission into humans as well as successful spread among avian hosts.

Likewise, between the 1920s and 1940s an Eastern Hemisphere *NS* A variant emerged in the Western Hemisphere ('West-2'; Figs. 1h & S1h, Extended Data Table 2). Since that time it has nearly replaced the prior *NS* A variant—it accounted for 98.9% of *NS* A genes sampled in 2009-2013. Interestingly, it has not replaced the Western Hemisphere *NS* B lineage, which still accounts for about 30% of all *NS* genes sampled in the last 5 years.

Is the high uracil content in equine H7N7 sequences a laboratory artefact or the wild-type genotype? We investigated the possibility that the extremely high U content in the genes of all available equine H7N7 influenza viruses is an artefact, for example due to passaging these viruses in mammalian cells in the laboratory.

The metadata from the GenBank accessions of A/equine/Prague/2/1956 (sequenced by the NIAID Influenza Genome Sequencing Consortium and directly submitted to GenBank in 2011) indicates that it is from a low-passage strain, apparently having experienced just two egg passages and no mammalian (MDCK) passages. Notably, its U content is essentially identical across all genes to that of other strains derived from the same isolate, some of which might have experienced more extensive passaging but for which there is no available information on passage history: A/equine/Prague/1/1956 and A/equine/Prague/1956, also from the NIAID Influenza Genome Sequencing Consortium and directly submitted to GenBank in 2011 and 2012, respectively. The remaining previously published complete genome of an equine H7N7 virus (prior to the reassortment event(s) which saw most of the H7N7 genome replaced by H3N8 segments) is A/equine/Lexington/1/1966. It was sequenced by the NIAID Influenza Genome Sequencing Consortium and was directly submitted to GenBank in 2009. In no case is there any record of these viruses (or any other equine H7N7 virus) being passaged in mammalian cells.

Aside from these sequences, several additional H7 *HA* genes are available, primarily from a 1992 study by Gibson *et al.*[59]. These additional sequences come mostly from viruses isolated in the U.K. and Switzerland from the 1960s and 1970s and maintained at the National Institute of Biological Standards and Control in the UK. Passage history is not reported in this study. These viruses (along with A/equine/Prague/1956 and A/equine/Lexington/1/1966, which were also sequenced as part of the same study), isolated on different continents and sequenced several years ago, also exhibit exceptionally high U content, suggesting that the vagaries of different storage conditions and sequencing protocols in different laboratories are unlikely to influence U content results. Similarly, several additional N7 *NA* sequences from the 1970s are available, most sequenced by the NIAID Influenza Genome Sequencing Consortium over the last few years, with consistently high U contents.

For the current study we located and sequenced an additional equine H7N7 complete genome from 1964 with, to our knowledge, a very limited passage history and then only in chicken eggs: A/equine/Detroit/3/1964 was evidently passaged once in 1990 in chicken eggs and either 2 or 3 times prior to that, also in chicken eggs. Its U content is very high, like the previously sequenced viruses, indicating that these high U contents reflect the wild type and are not caused by passage in mammalian cells.

Finally, we took an evolutionary approach to this question. We reasoned that if the high U content found in each of these equine virus genomes had been independently acquired during passaging in mammal cells, these mutations would likely occur to a large degree at different sites in each genome. Considering which U residues are unique versus shared in the 1956 sequence and the 1966

sequences, we found an overwhelming pattern of shared variation (>95% and up to 98.9% of uracil sites, depending on the gene) strongly suggesting these occurred on the lineage leading to their common ancestor. Taken together, these lines of evidence seem to indicate that the high U content in equine H7N7 is a real reflection of the wild type.

Equine and avian H7N7. The basal position of the equine H7N7 lineage in relation to all AIV and the similar timing suggest the 1872-1873 panzootic may be connected to the sweep of internal genes that we infer; however the current data cannot exclude either the hypothesis that a putatively ancient equine H7N7 lineage was the source of these AIV genes or the alternative that a particularly successful AIV lineage jumped into horses at about the time it began sweeping through avian populations in the late 1800s. Regardless of the directionality of this host jump, it is noteworthy that the equine H7 HA is highly cleavable in avian cells[60] and is capable of producing a lethal infection in chickens with no additional mutations[61]. It also possesses 226Q and 228G residues predictive of the avian specificity for SAα2,3Gal sialic acid receptors, the major host range determinant in HA. In PB2, arguably the most important internal protein with respect to host range, all equine H7N7 viruses exhibit the 'avian' 627E residue.

REFERENCES

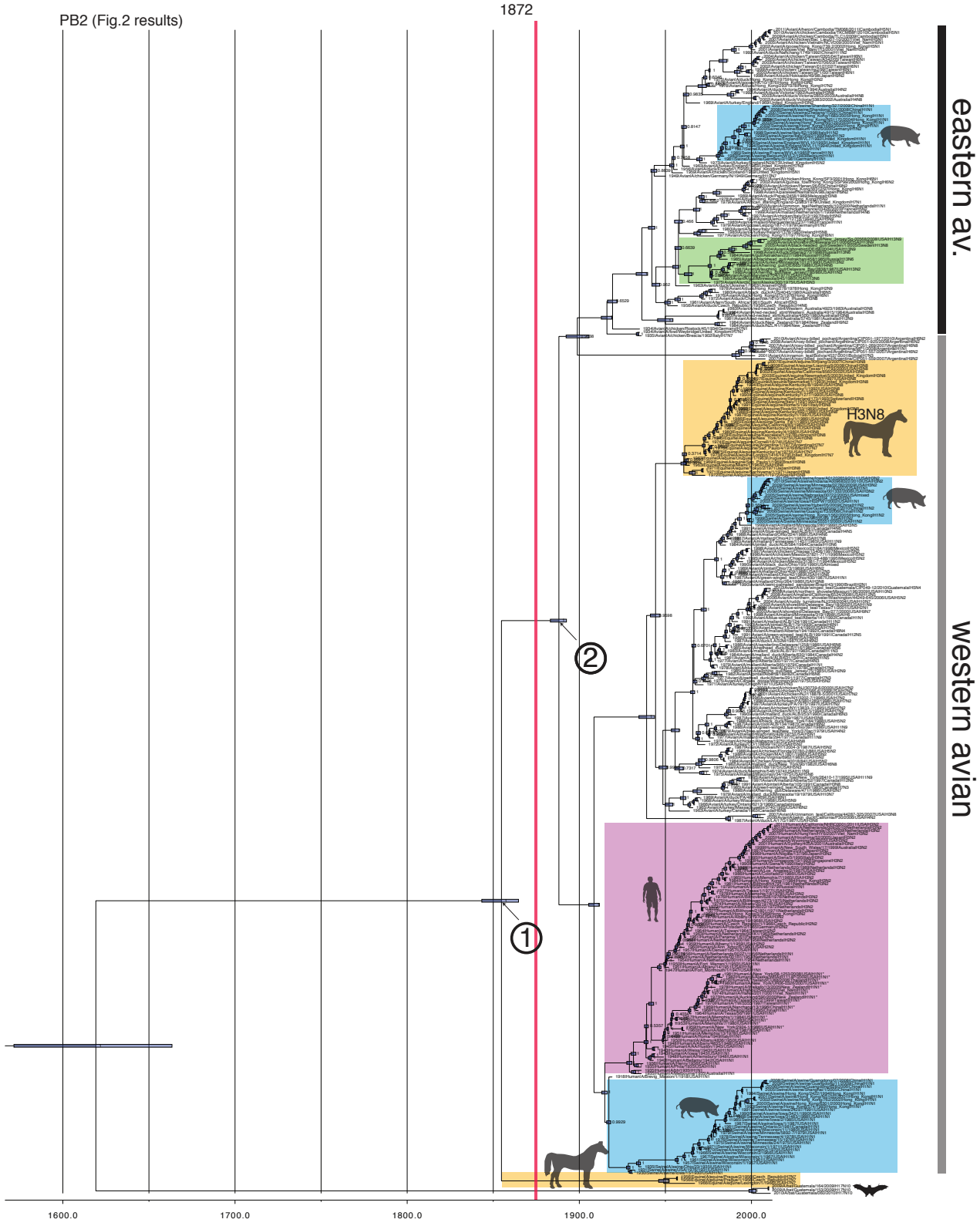
46. Lupiani, B. & Reddy, S. M. The history of avian influenza. *Comp. Immunol. Microbiol. Infect. Dis.* **32**, 311-323 (2009)
47. Pitkin, C. A. Size of white leghorns. *Poult. World* **5**, 407 (1877)
48. Homme, P. J. & Easterday, B. C. Avian influenza virus infections. IV. Response of pheasants, ducks, and geese to influenzaA/Turkey/Wisconsin/1966. *Avian Diseases* **14,** 285-290 (1970)
49. Beard, W. & Easterday, B. C. A/Turkey/Oregon/71, an avirulent influenza isolate with the hemagglutinin of fowl plague virus. *Avian Diseases* **17,** 173-181 (1973)
50. Slemons, R. D. & Easterday, B. C. Virus replication in the digestive tract of ducks exposed by aerosol to type-A influenza. *Avian Diseases* **22,** 367-377 (1978)
51. Westbury, H. A., Turner, A. J. & Kovesdy, L. The pathogenicity of three Australian fowl plague viruses for chickens, turkeys and ducks. *Vet. Microbiol.* **4,** 223-234 (1979)
52. http://www.flyways.us/status-of-waterfowl/population-estimates/2011-population-estimates
53. http://www.fao.org/docrep/004/ad452e/ad452e31.htm
54. Munster, V. J. *et al.* Spatial, temporal, and species variation in prevalence of influenza A viruses in wild migratory birds. *PLoS Pathog.* **3**, e61 (2007)
55. Sims, L. D. & Turner, A. J. Avian influenza in Australia. in *Avian Influenza* (ed. Swayne, D. E.) 239-250 (Blackwell Publishing, Iowa, 2008)
56. Smith, G. J. D. *et al.* Origins and evolutionary genomics of the 2009 swine-origin H1N1 influenza A epidemic. *Nature* **459**, 1122-1126 (2009)
57. Dowdle, W. R. Influenza A virus recycling revisited. *Bull. World Health Organ.* **77**, 820-828 (1999)
58. Walker, R. V. L. & Bannister, G. L. A filterable agent in ducks. *Can. J. Comparat. Med.* **17,** 248-250 (1953)
59. Gibson, C. A. *et al.* Sequence analysis of the equine H7 influenza virus haemagglutinin. *Virus Res.* **22,** 93-106 (1992)

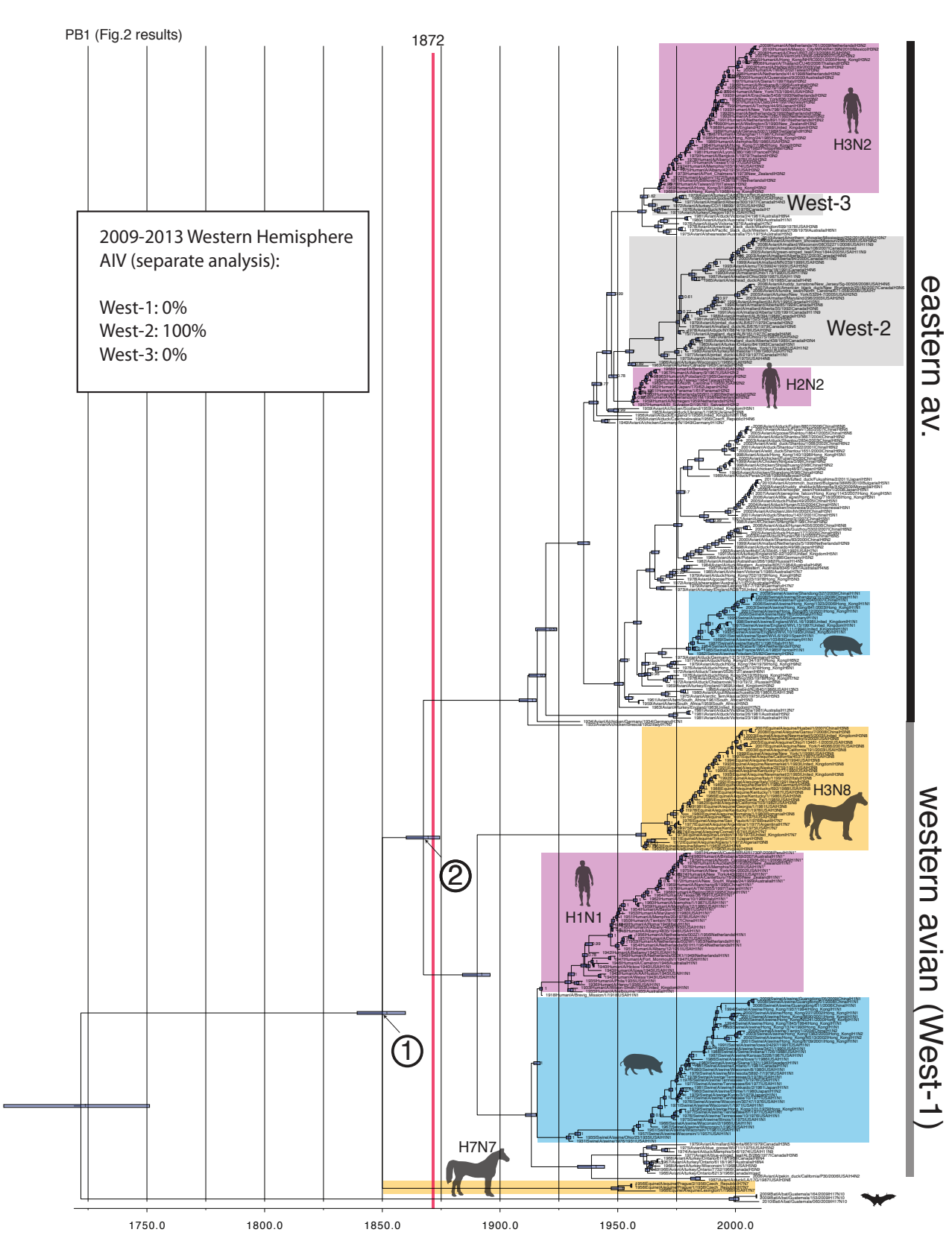
60. Treanor, J. J., Snyder, M. H, London, W. T. & Murphy, B. R. The B allele of the NS gene of avian influenza viruses, but not the A allele, attenuates a human influenza A virus for squirrel monkeys. *Virology* **171,** 1-9 (1989)

61. Kawaoka, Y. Equine H7N7 influenza A viruses are highly pathogenic in mice without adaptation: potential use as an animal model. *J. Virol.* **65,** 3891-3894 (1991)

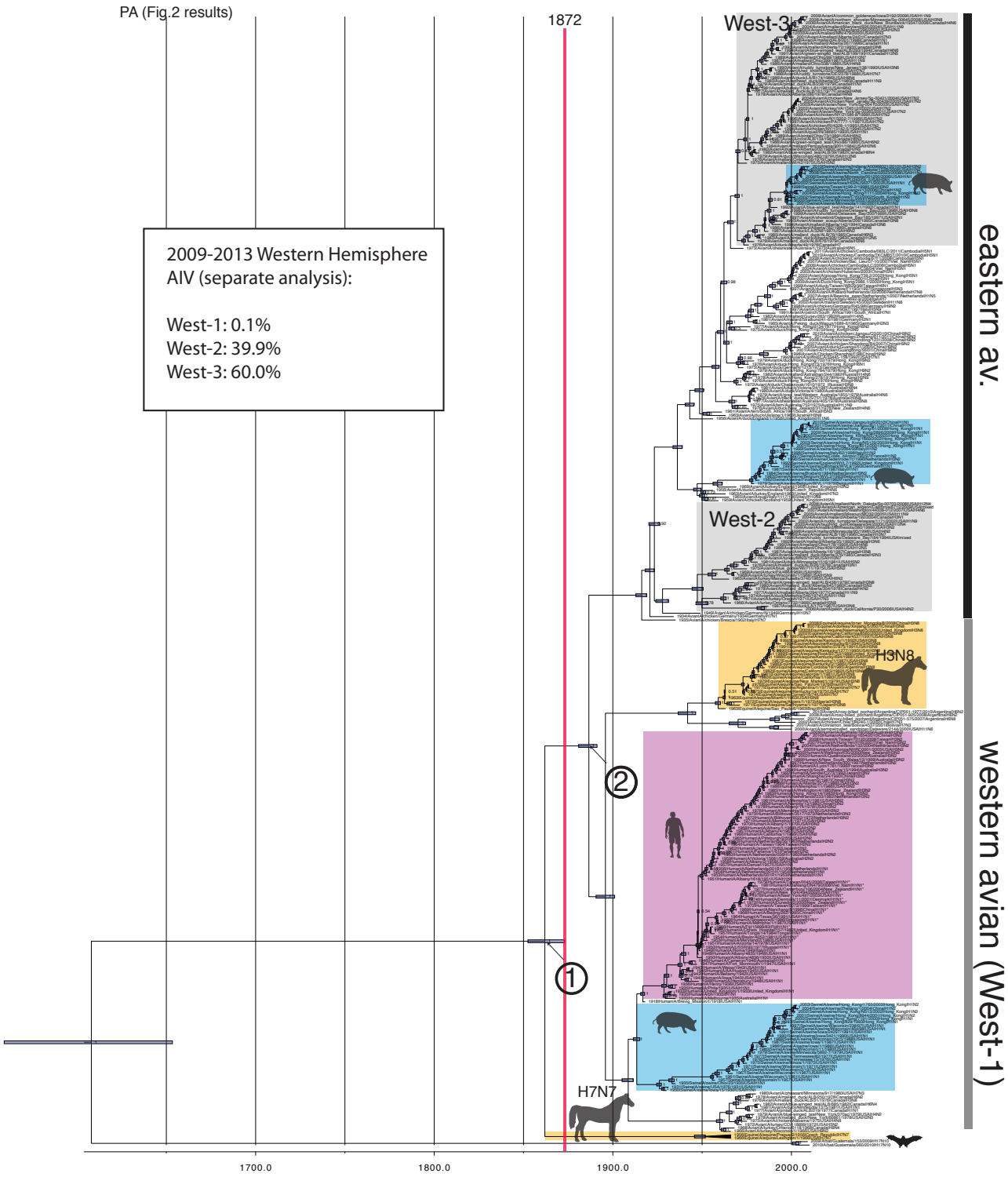
Figure S1
(please see figure legend below last panel)

a

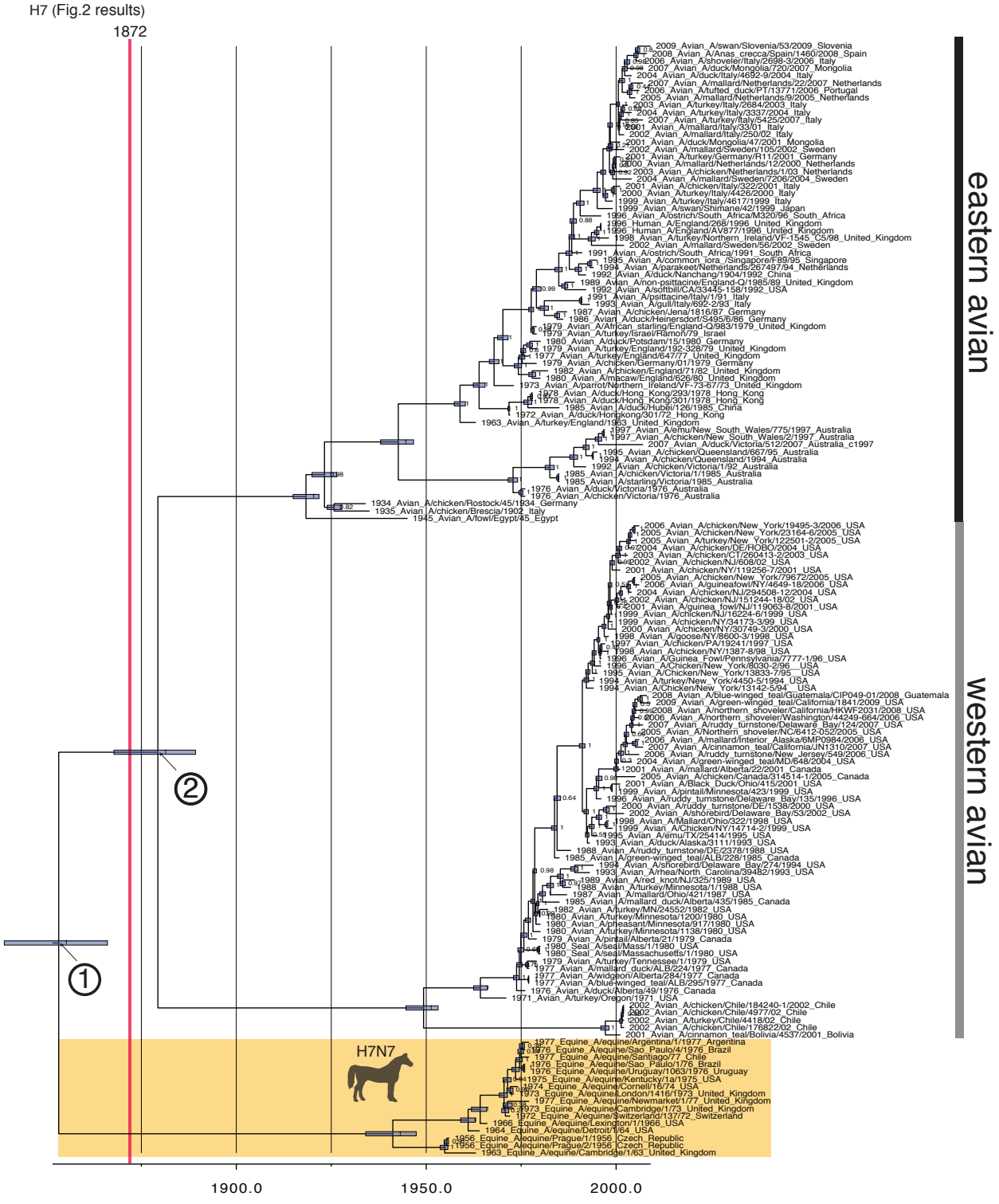


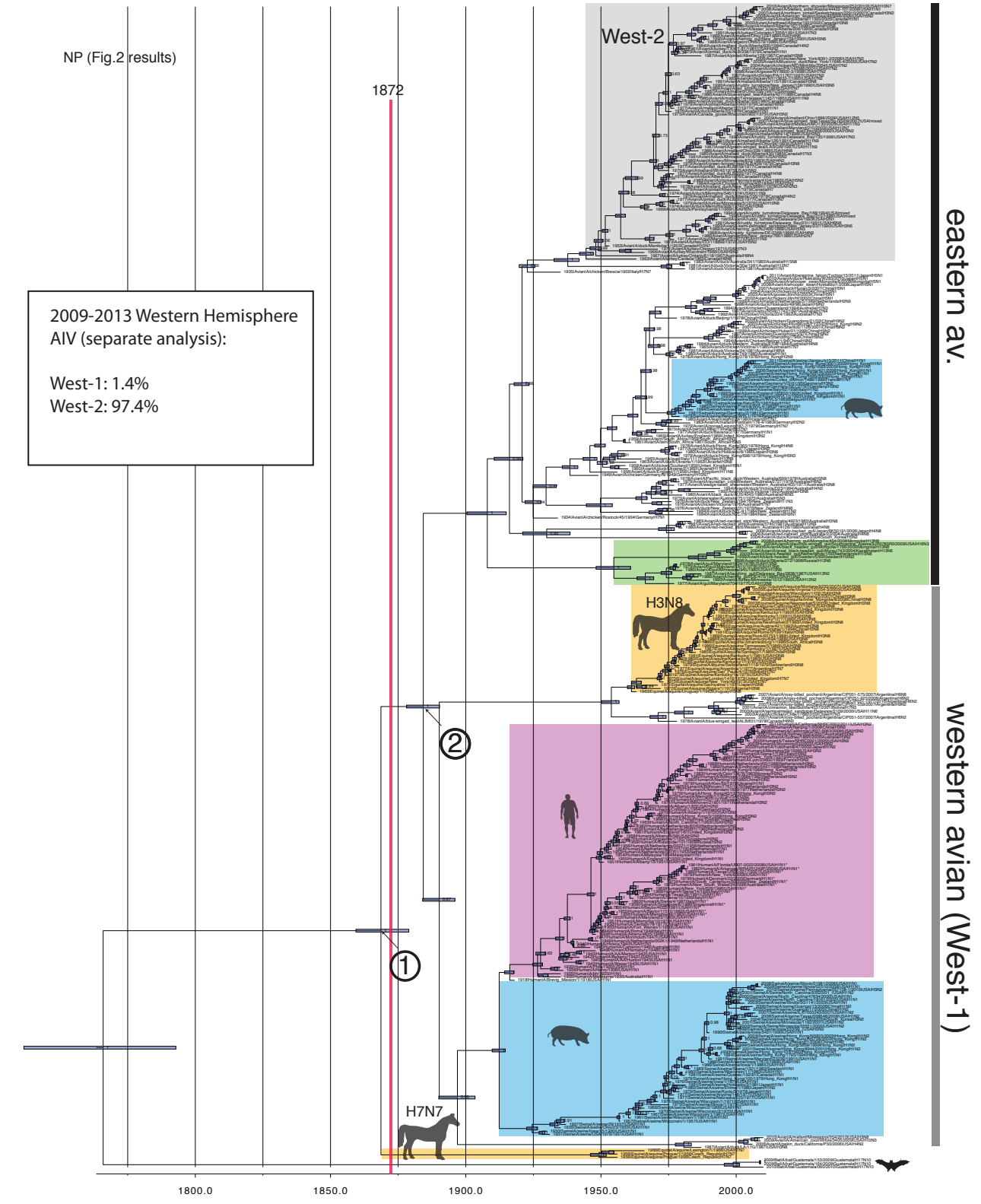

b
PB1 (Fig.2 results)
1872
2009-2013 Western Hemisphere AIV (separate analysis):
West-1: 0%
West-2: 100%
West-3: 0%
H3N2
West-3
West-2
H2N2
H3N8
H1N1
H7N7
①
②
eastern av.
western avian (West-1)
1750.0
1800.0
1850.0
1900.0
1950.0
2000.0

c

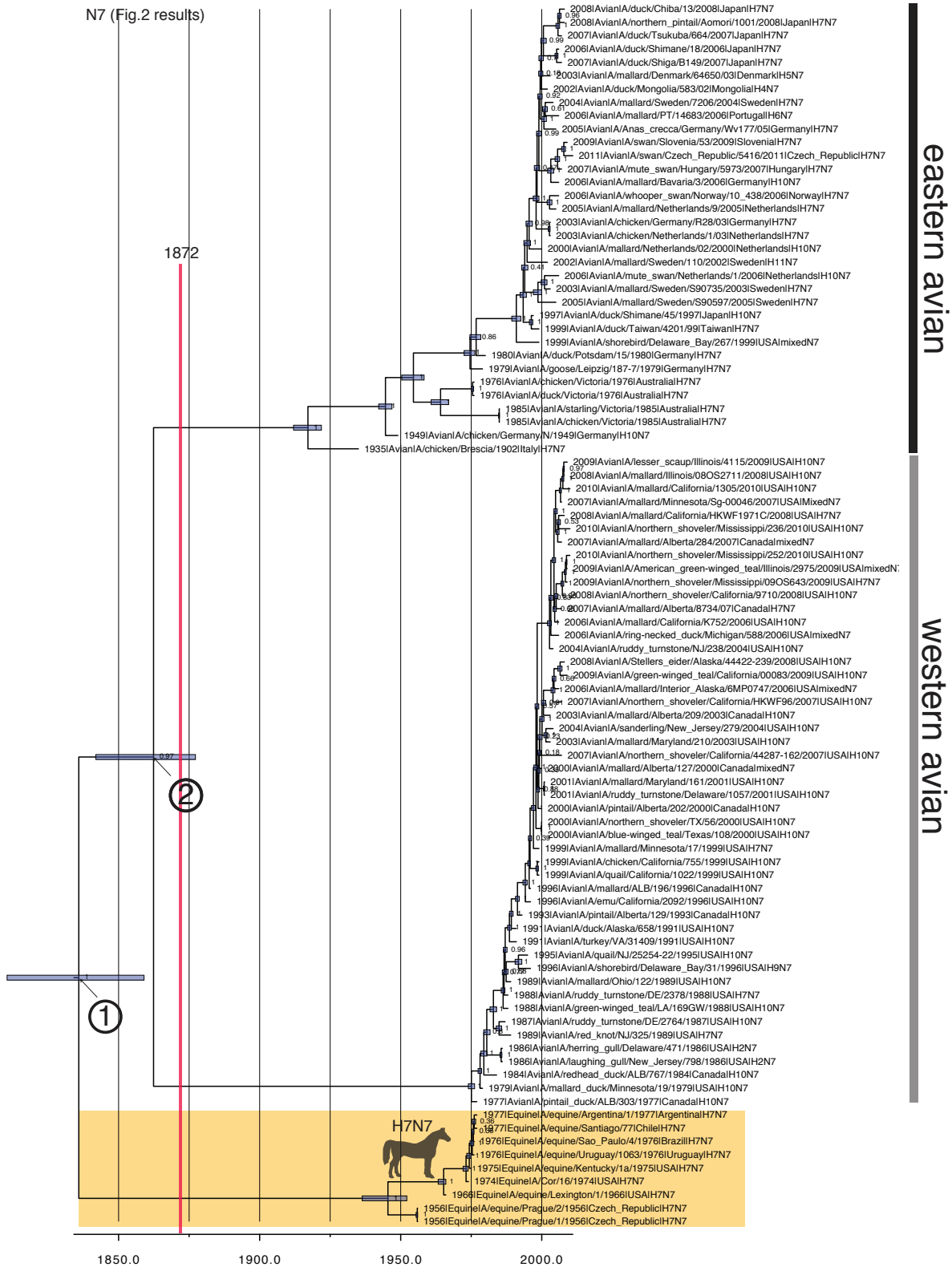

PA (Fig.2 results)
1872
West-3
West-2
H3N8
H7N7
2009-2013 Western Hemisphere AIV (separate analysis):
West-1: 0.1%
West-2: 39.9%
West-3: 60.0%
1700.0
1800.0
1900.0
2000.0
eastern av.
western avian (West-1)

d

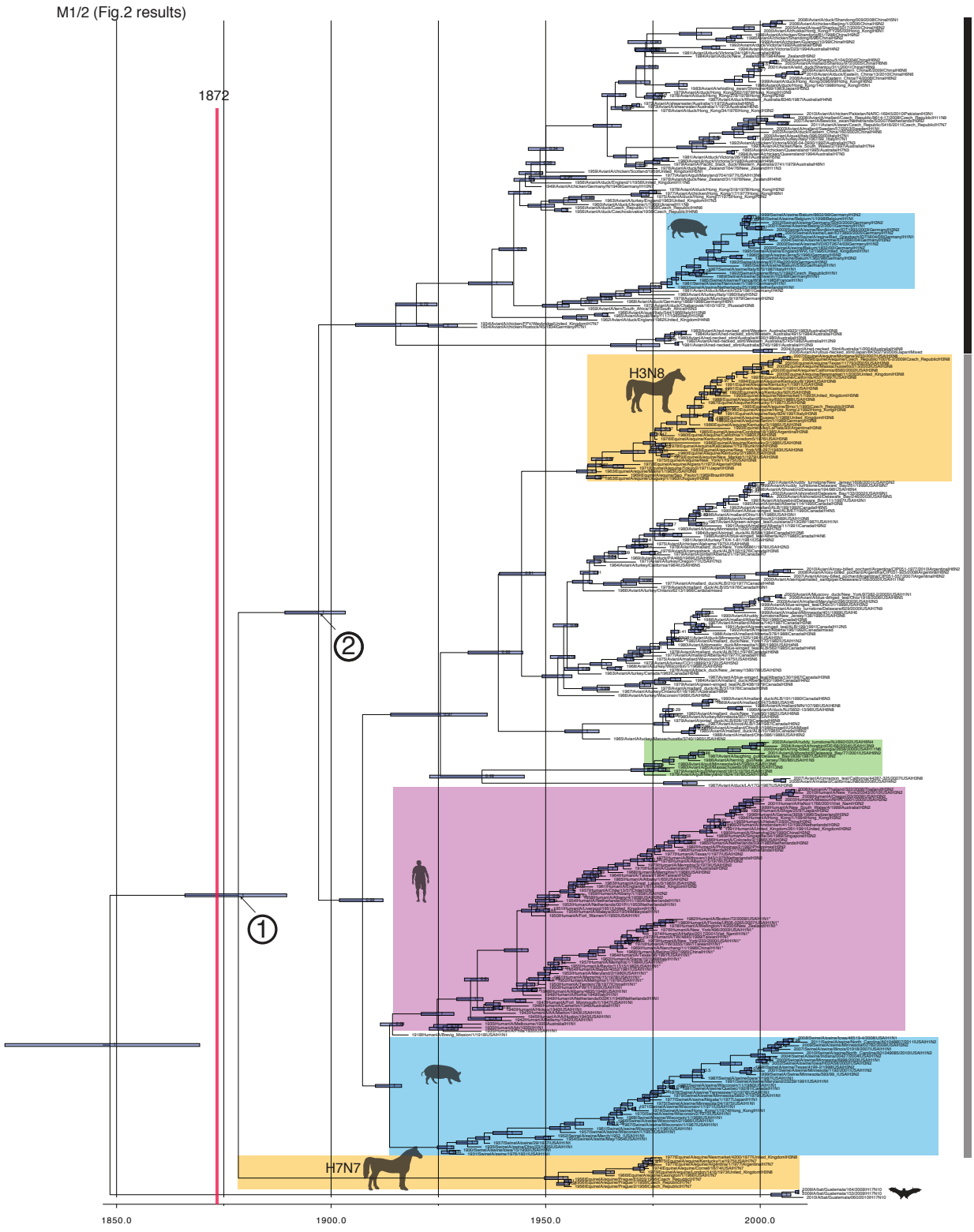

H7 (Fig.2 results)
1872
eastern avian
western avian
H7N7
①
②
1900.0
1950.0
2000.0


e
NP (Fig.2 results)
1872
2009-2013 Western Hemisphere AIV (separate analysis):
West-1: 1.4%
West-2: 97.4%
West-2
H3N8
H7N7
1
2
eastern av.
western avian (West-1)
1800.0
1850.0
1900.0
1950.0
2000.0

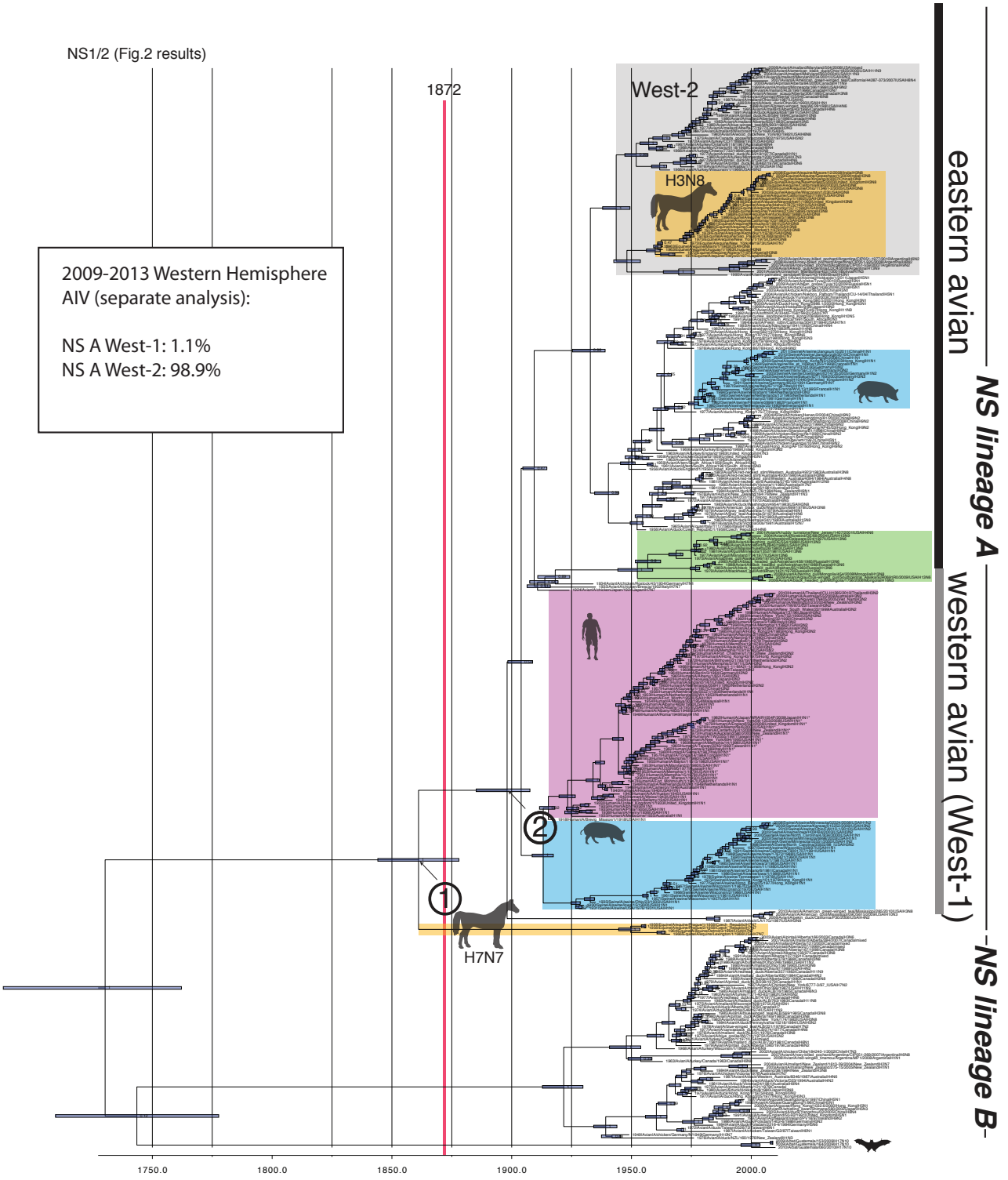
f


N7 (Fig.2 results)
1872
2008|Avian|A/duck/Chiba/13/2008|Japan|H7N7
2008|Avian|A/northern_pintail/Aomori/1001/2008|Japan|H7N7
2007|Avian|A/duck/Tsukuba/664/2007|Japan|H7N7
2006|Avian|A/duck/Shimane/18/2006|Japan|H7N7
2007|Avian|A/duck/Shiga/B149/2007|Japan|H7N7
2003|Avian|A/mallard/Denmark/64650/03|Denmark|H5N7
2002|Avian|A/duck/Mongolia/583/02|Mongolia|H4N7
2004|Avian|A/mallard/Sweden/7206/2004|Sweden|H7N7
2006|Avian|A/mallard/PT/14683/2006|Portugal|H6N7
2005|Avian|A/Anas_crecca/Germany/Wv177/05|Germany|H7N7
2009|Avian|A/swan/Slovenia/53/2009|Slovenia|H7N7
2011|Avian|A/swan/Czech_Republic/5416/2011|Czech_Republic|H7N7
2007|Avian|A/mute_swan/Hungary/5973/2007|Hungary|H7N7
2006|Avian|A/mallard/Bavaria/3/2006|Germany|H10N7
2006|Avian|A/whooper_swan/Norway/10_438/2006|Norway|H7N7
2005|Avian|A/mallard/Netherlands/9/2005|Netherlands|H7N7
2003|Avian|A/chicken/Germany/R28/03|Germany|H7N7
2003|Avian|A/chicken/Netherlands/1/03|Netherlands|H7N7
2000|Avian|A/mallard/Netherlands/02/2000|Netherlands|H10N7
2002|Avian|A/mallard/Sweden/110/2002|Sweden|H11N7
2006|Avian|A/mute_swan/Netherlands/1/2006|Netherlands|H10N7
2003|Avian|A/mallard/Sweden/S90735/2003|Sweden|H7N7
2005|Avian|A/mallard/Sweden/S90597/2005|Sweden|H7N7
1997|Avian|A/duck/Shimane/45/1997|Japan|H10N7
1999|Avian|A/duck/Taiwan/4201/99|Taiwan|H7N7
1999|Avian|A/shorebird/Delaware_Bay/267/1999|USA|mixed|N7
1980|Avian|A/duck/Potsdam/15/1980|Germany|H7N7
1979|Avian|A/goose/Leipzig/187-7/1979|Germany|H7N7
1976|Avian|A/chicken/Victoria/1976|Australia|H7N7
1976|Avian|A/duck/Victoria/1976|Australia|H7N7
1985|Avian|A/starling/Victoria/1985|Australia|H7N7
1985|Avian|A/chicken/Victoria/1985|Australia|H7N7
1949|Avian|A/chicken/Germany/N/1949|Germany|H10N7
1935|Avian|A/chicken/Brescia/1902|Italy|H7N7
2009|Avian|A/lesser_scaup/Illinois/4115/2009|USA|H10N7
2008|Avian|A/mallard/Illinois/08OS2711/2008|USA|H10N7
2010|Avian|A/mallard/California/1305/2010|USA|H10N7
2007|Avian|A/mallard/Minnesota/Sg-00046/2007|USA|mixed|N7
2008|Avian|A/mallard/California/HKWF1971C/2008|USA|H7N7
2010|Avian|A/northern_shoveler/Mississippi/236/2010|USA|H10N7
2007|Avian|A/mallard/Alberta/284/2007|Canada|mixed|N7
2010|Avian|A/northern_shoveler/Mississippi/252/2010|USA|H10N7
2009|Avian|A/American_green-winged_teal/Illinois/2975/2009|USA|mixed|N7
2009|Avian|A/northern_shoveler/Mississippi/09OS643/2009|USA|H7N7
2008|Avian|A/northern_shoveler/California/9710/2008|USA|H10N7
2007|Avian|A/mallard/Alberta/8734/07|Canada|H7N7
2006|Avian|A/mallard/California/K752/2006|USA|H10N7
2006|Avian|A/ring-necked_duck/Michigan/588/2006|USA|mixed|N7
2004|Avian|A/ruddy_turnstone/NJ/238/2004|USA|H10N7
2008|Avian|A/Stellers_eider/Alaska/44422-239/2008|USA|H10N7
2009|Avian|A/green-winged_teal/California/00083/2009|USA|H10N7
2006|Avian|A/mallard/Interior_Alaska/6MP0747/2006|USA|mixed|N7
2007|Avian|A/northern_shoveler/California/HKWF96/2007|USA|H10N7
2003|Avian|A/mallard/Alberta/209/2003|Canada|H10N7
2004|Avian|A/sanderling/New_Jersey/279/2004|USA|H10N7
2003|Avian|A/mallard/Maryland/210/2003|USA|H10N7
2007|Avian|A/northern_shoveler/California/44287-162/2007|USA|H10N7
2000|Avian|A/mallard/Alberta/127/2000|Canada|mixed|N7
2001|Avian|A/mallard/Maryland/161/2001|USA|H10N7
2001|Avian|A/ruddy_turnstone/Delaware/1057/2001|USA|H10N7
2000|Avian|A/pintail/Alberta/202/2000|Canada|H10N7
2000|Avian|A/northern_shoveler/TX/56/2000|USA|H10N7
2000|Avian|A/blue-winged_teal/Texas/108/2000|USA|H10N7
1999|Avian|A/mallard/Minnesota/17/1999|USA|H7N7
1999|Avian|A/chicken/California/755/1999|USA|H10N7
1999|Avian|A/quail/California/1022/1999|USA|H10N7
1996|Avian|A/mallard/ALB/196/1996|Canada|H10N7
1996|Avian|A/emu/California/2092/1996|USA|H10N7
1993|Avian|A/pintail/Alberta/129/1993|Canada|H10N7
1991|Avian|A/duck/Alaska/658/1991|USA|H10N7
1991|Avian|A/turkey/VA/31409/1991|USA|H10N7
1995|Avian|A/quail/NJ/25254-22/1995|USA|H10N7
1996|Avian|A/shorebird/Delaware_Bay/31/1996|USA|H9N7
1989|Avian|A/mallard/Ohio/122/1989|USA|H10N7
1988|Avian|A/ruddy_turnstone/DE/2378/1988|USA|H7N7
1988|Avian|A/green-winged_teal/LA/169GW/1988|USA|H10N7
1987|Avian|A/ruddy_turnstone/DE/2764/1987|USA|H10N7
1989|Avian|A/red_knot/NJ/325/1989|USA|H7N7
1986|Avian|A/herring_gull/Delaware/471/1986|USA|H2N7
1986|Avian|A/laughing_gull/New_Jersey/798/1986|USA|H2N7
1984|Avian|A/redhead_duck/ALB/767/1984|Canada|H10N7
1979|Avian|A/mallard_duck/Minnesota/19/1979|USA|H10N7
1977|Avian|A/pintail_duck/ALB/303/1977|Canada|H10N7
1977|Equine|A/equine/Argentina/1/1977|Argentina|H7N7
1977|Equine|A/equine/Santiago/77|Chile|H7N7
1976|Equine|A/equine/Sao_Paulo/4/1976|Brazil|H7N7
1976|Equine|A/equine/Uruguay/1063/1976|Uruguay|H7N7
1975|Equine|A/equine/Kentucky/1a/1975|USA|H7N7
1974|Equine|A/Cor/16/1974|USA|H7N7
1966|Equine|A/equine/Lexington/1/1966|USA|H7N7
1956|Equine|A/equine/Prague/2/1956|Czech_Republic|H7N7
1956|Equine|A/equine/Prague/1/1956|Czech_Republic|H7N7
H7N7
①
②
eastern avian
western avian
1850.0
1900.0
1950.0
2000.0

g

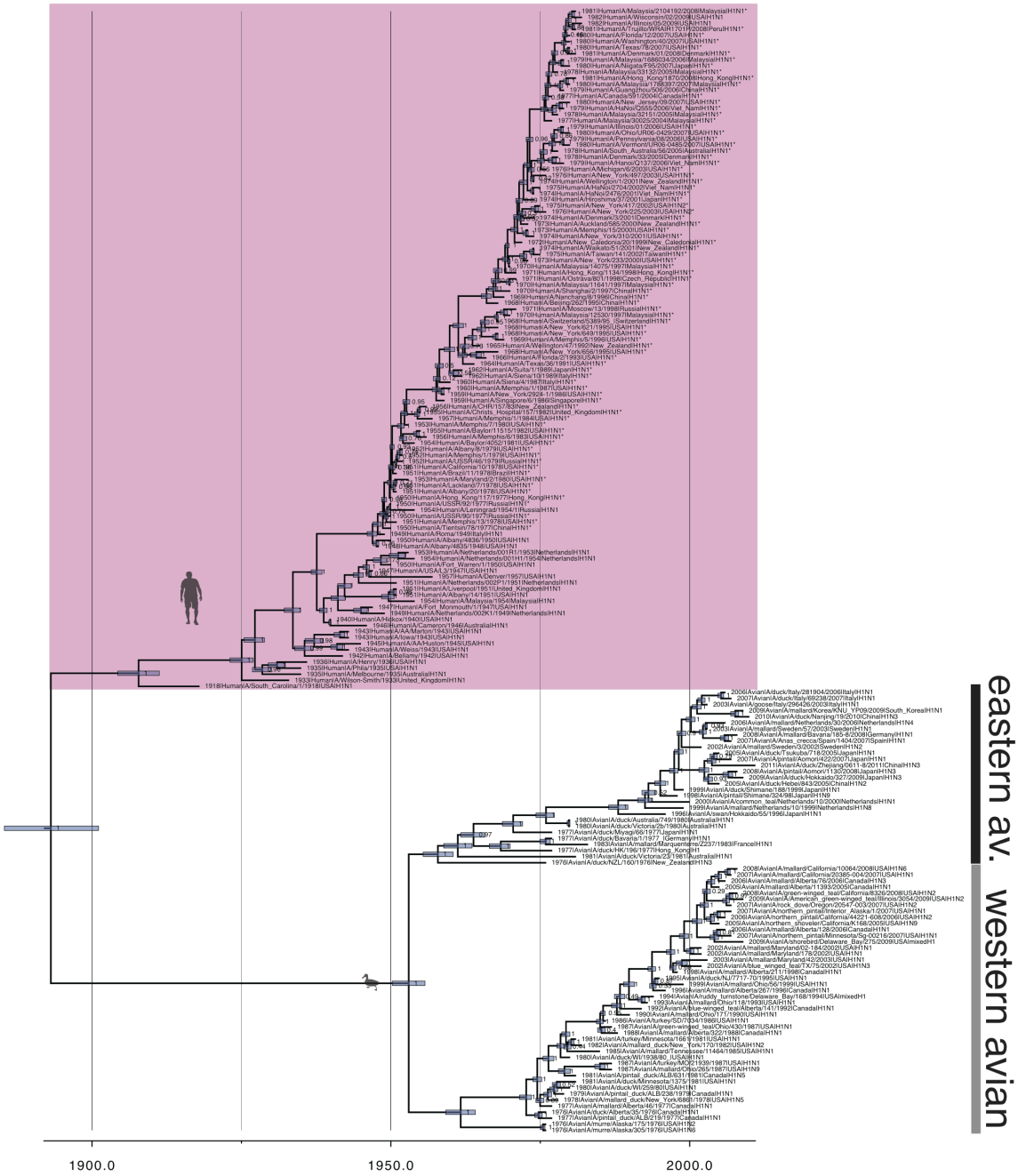

M1/2 (Fig.2 results)
1872
eastern av.
western avian
H3N8
H7N7
①
②
1850.0
1900.0
1950.0
2000.0

h

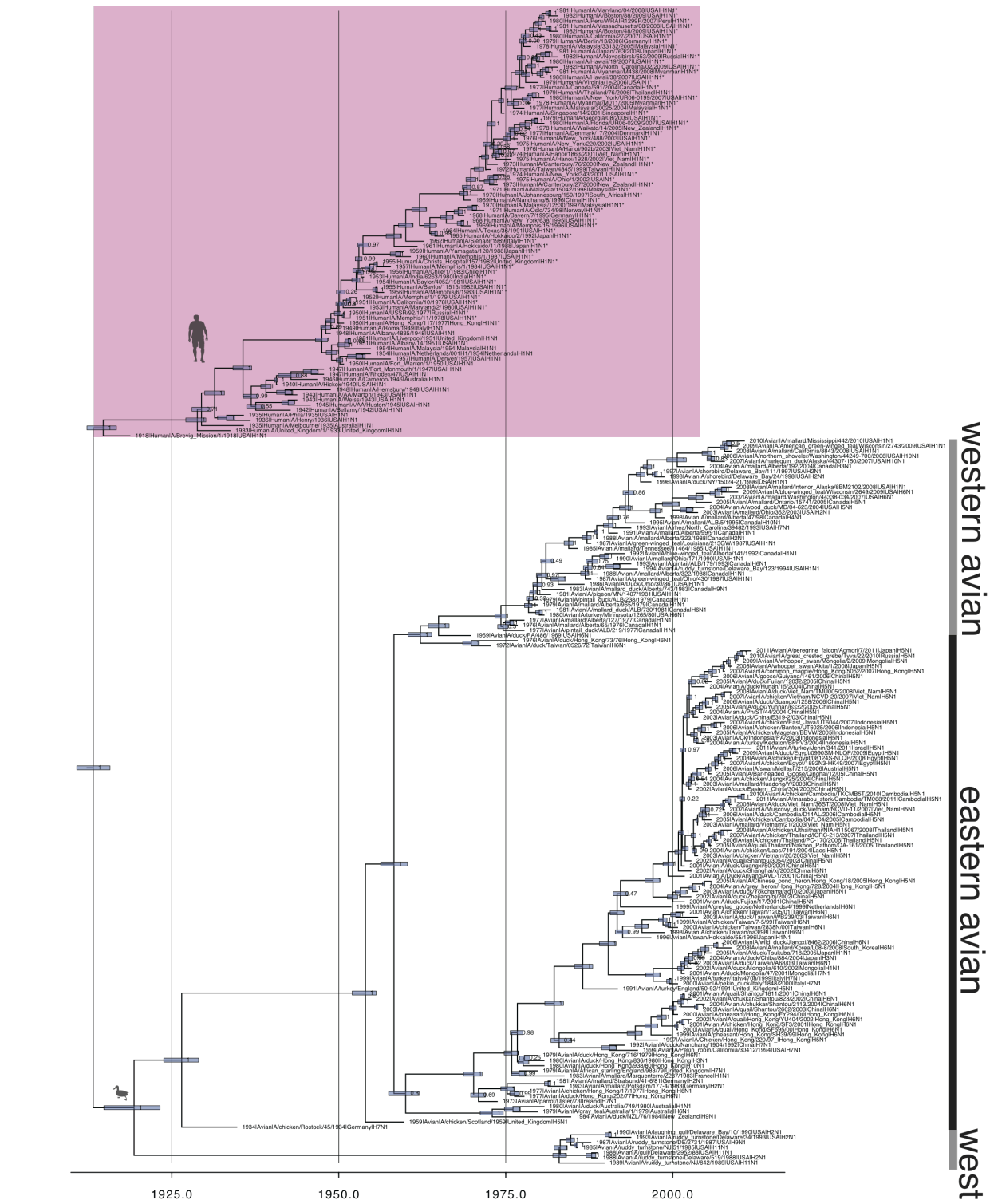

NS1/2 (Fig.2 results)
1872
West-2
H3N8
2009-2013 Western Hemisphere AIV (separate analysis):
NS A West-1: 1.1%
NS A West-2: 98.9%
2
1
H7N7
1750.0
1800.0
1850.0
1900.0
1950.0
2000.0
eastern avian
NS lineage A
western avian (West-1)
NS lineage B

i

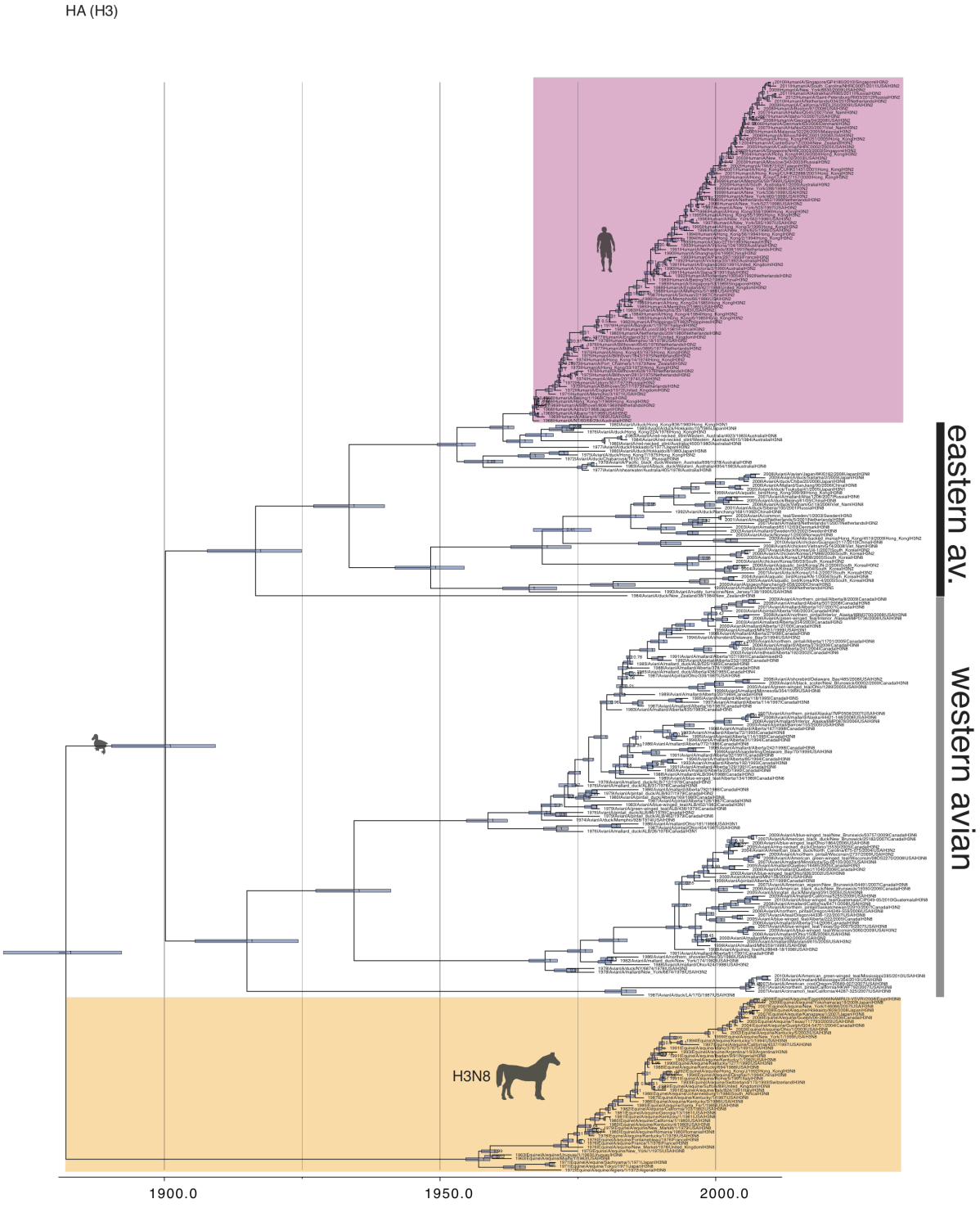
HA (H1)



j


NA (N1)
western avian
eastern avian
west
1925.0
1950.0
1975.0
2000.0

k



I

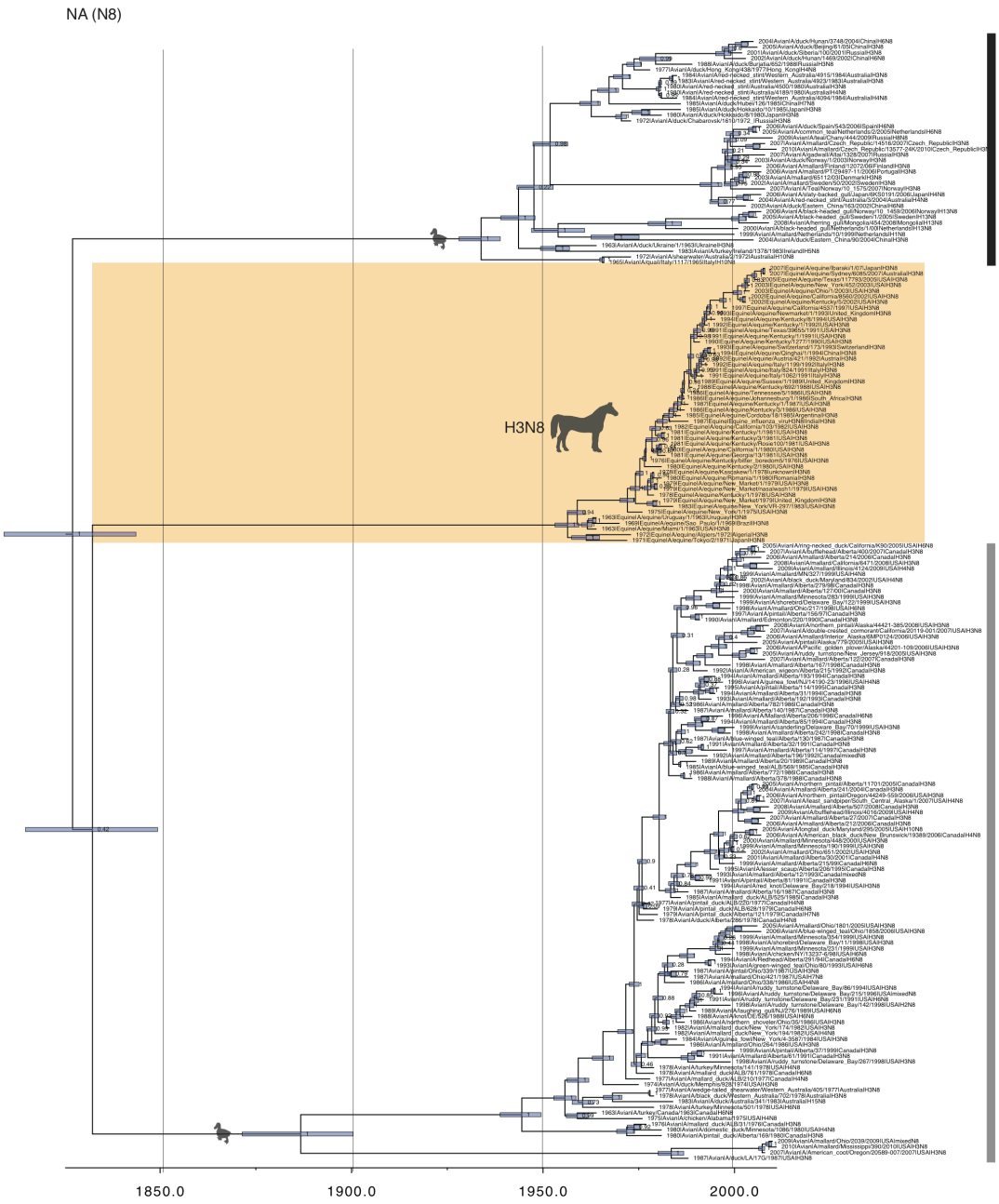


Figure S1 | Host-specific local clock model results (full trees corresponding to Fig. 2 and Extended Data Fig. 6). a through **h,** MCC trees for *PB2*, *PB1*, *PA*, *HA* (H7), *NP*, *NA* (N7), *M1/2*, and *NS1/2*, respectively. Branch lengths are in years. Posterior probability and 95% CI for each node date are indicated. These are the complete trees corresponding to Fig. 2. The inset boxes in **b**, **c**, **e**, and **h** indicate the percentages of 'West-2' and 'West-3' sequences in a sample of Western Hemisphere sequences from 2009-2013. **i** through **l,** MCC trees for H1, N1, H3, and N8, respectively. These are the complete trees corresponding to Extended Data Fig. 6.