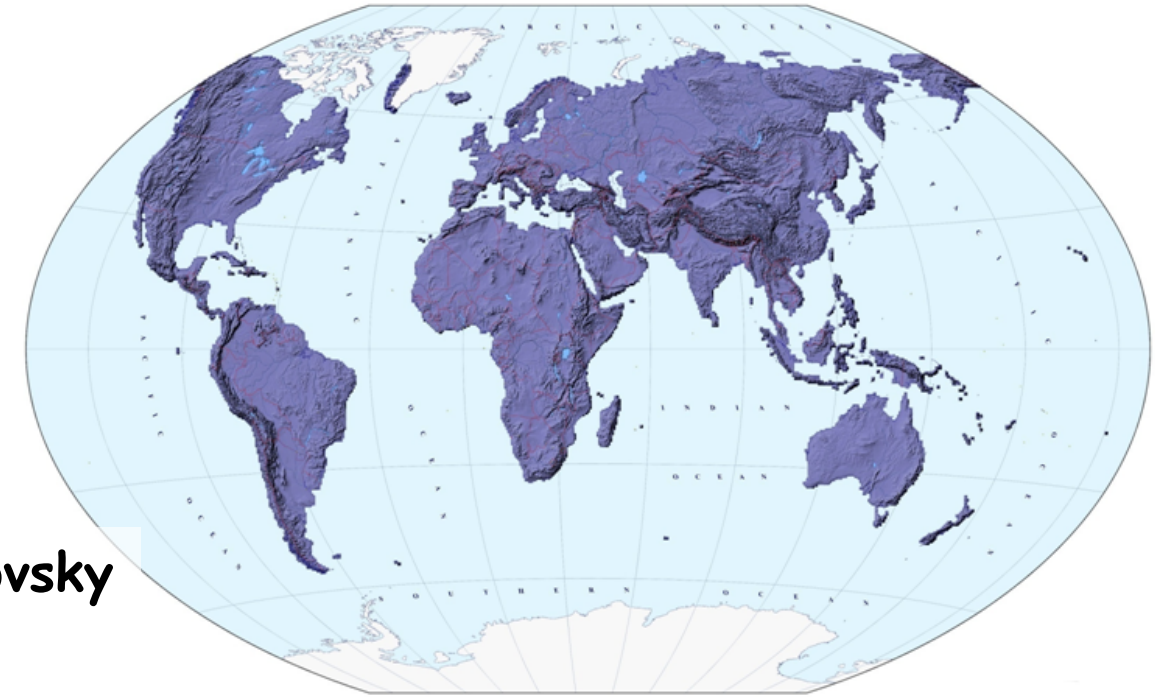
The Microevolution Processes in Human Populations:

The Emerging Portrait of Global Gene Pool Structure



Oleg Balanovsky

The 10th International Conference on Bioinformatics:
"Genomics and Evolution of Pathogens and Hosts"
November 19-21, 2015, Atlanta, USA.

Centenary of Gene Geography
1914 (1919) - 2015

1914: THE DISCOVERY OF THE UNEQUAL DISTRIBUTION OF HUMAN BLOOD GROUPS ACROSS THE GLOBE

1919: THE FIRST PUBLICATION

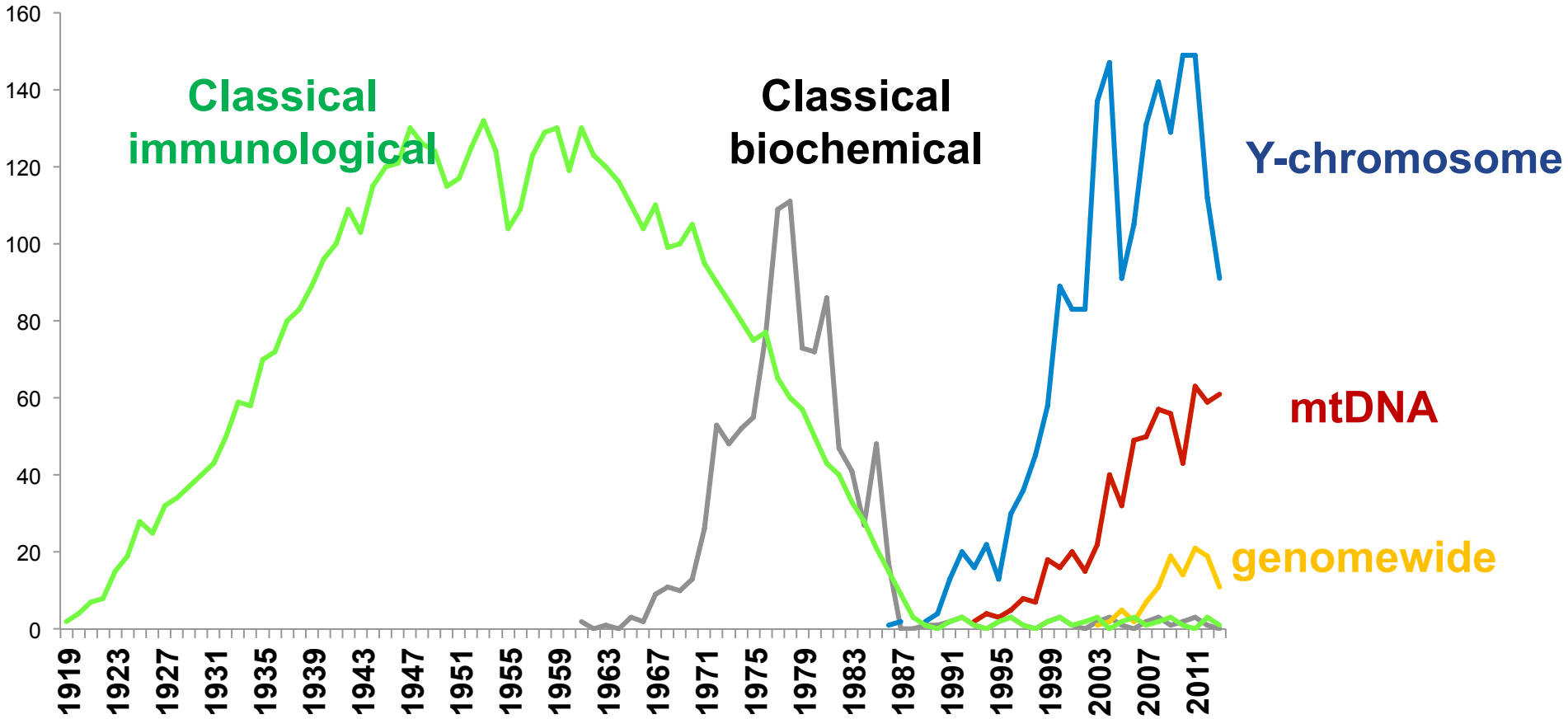
The tragedy of the World War I revealed the dramatic differences in frequencies of blood groups between soldiers of different races and ethnic groups.

Hirsfeld L., Hirsfeld H. Serological differences between the blood of different races. The results of researches on the Macedonian front// Lancet. 1919. P. 675.

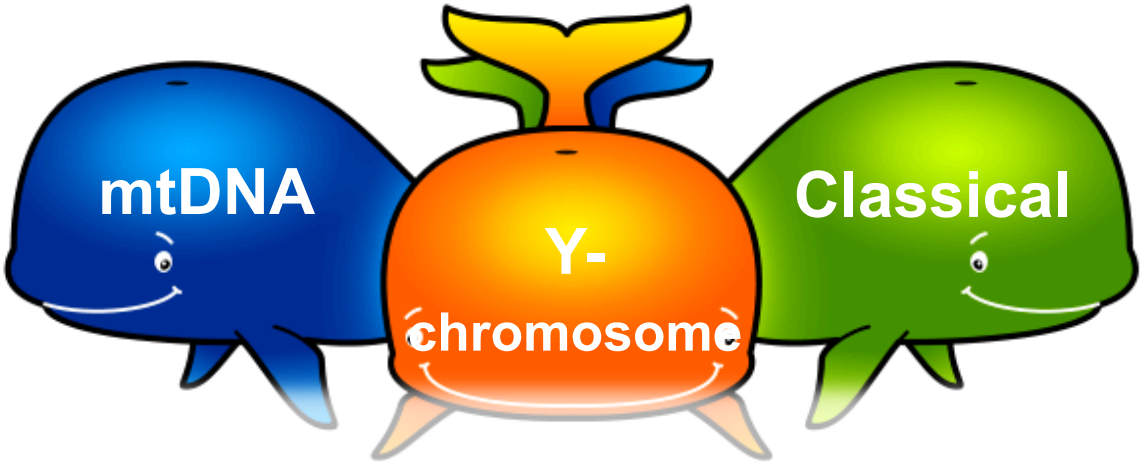
Hirszfeld, L., and H. Hirszfeld. 1919. Essai d'application des methodes au probleme des races. Anthropologie 29: 505-537.

Genetic markers in fashion: dynamics

Number of papers per year is plotted for 5 principal systems of genetic markers



The “polysystem approach”

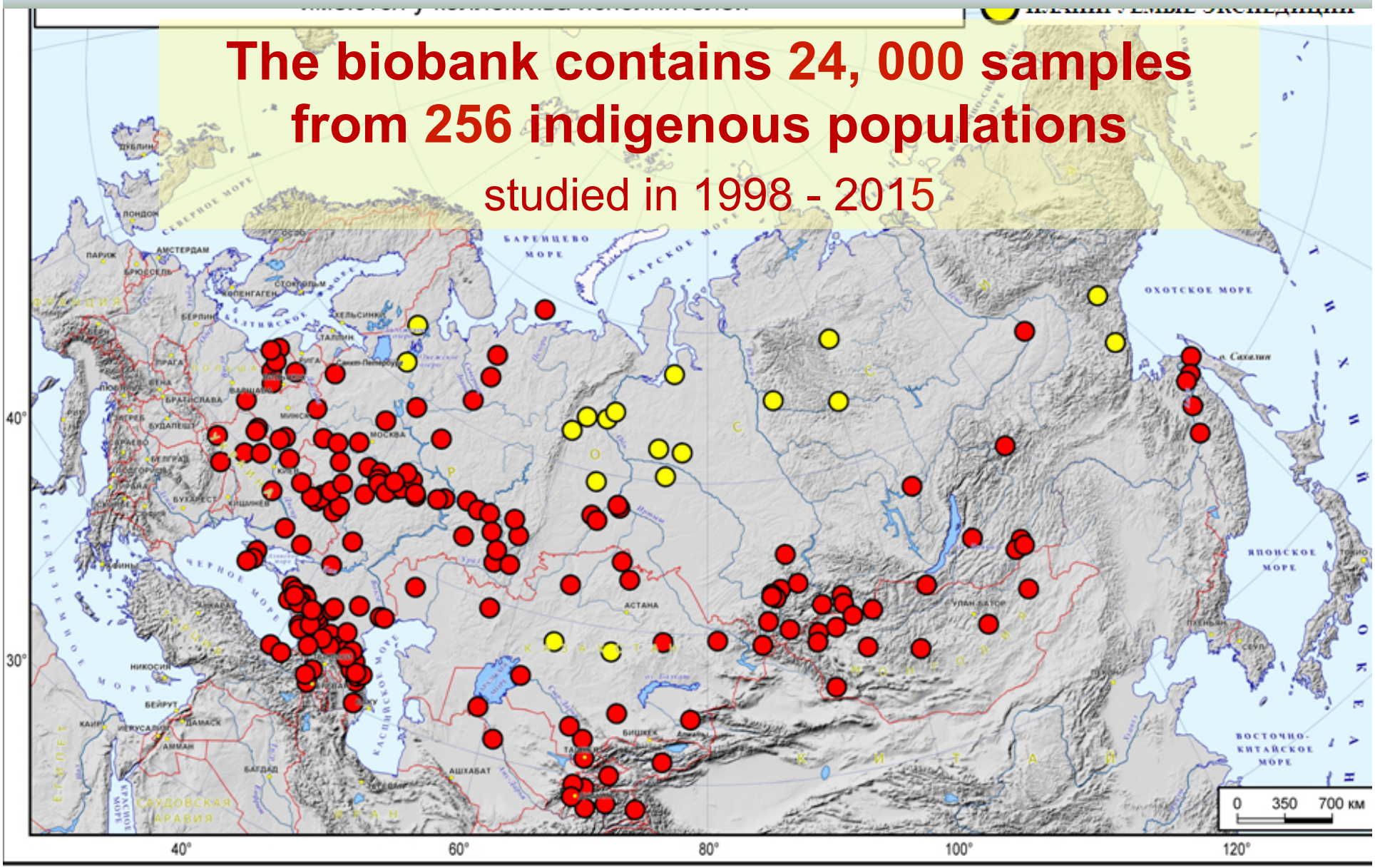


- **To study a gene pool reliably one needs to analyze different genetics systems in parallel;**
- **The most reliable patterns are those which are revealed by each system.**
- **Once this general genetic structure is drawn, each system might add its own details on this genetic portrait of the populations.**

Our expeditions

The biobank contains 24, 000 samples from 256 indigenous populations

studied in 1998 - 2015



DATA SETS USED

Classical markers	• Cavalli-Sforza et al., 1994. • «Gene Pool» databank (Balanovska, Rychkov, 1990-2000)
mtDNA	MURKA database: (Balanovsky, Zaporozhchenko, Balanovska, 2003-2014)
Y-Chromosome	Y-base. (Balanovsky, Pshenichnov, Sychev, Balanovska, 2008-2014)
Genome wide	Li et al., 2008

The atlases of gene pool

Were created by our GeneGeo cartographic software

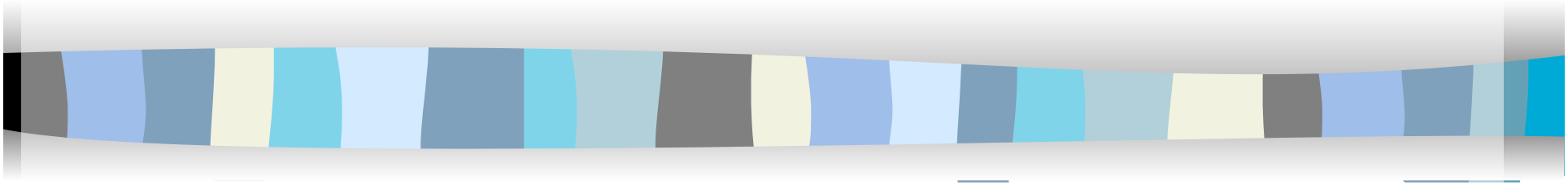
Maps of separate haplogroups (hundreds)

A separate map for each allele

Synthetic maps (dozens)

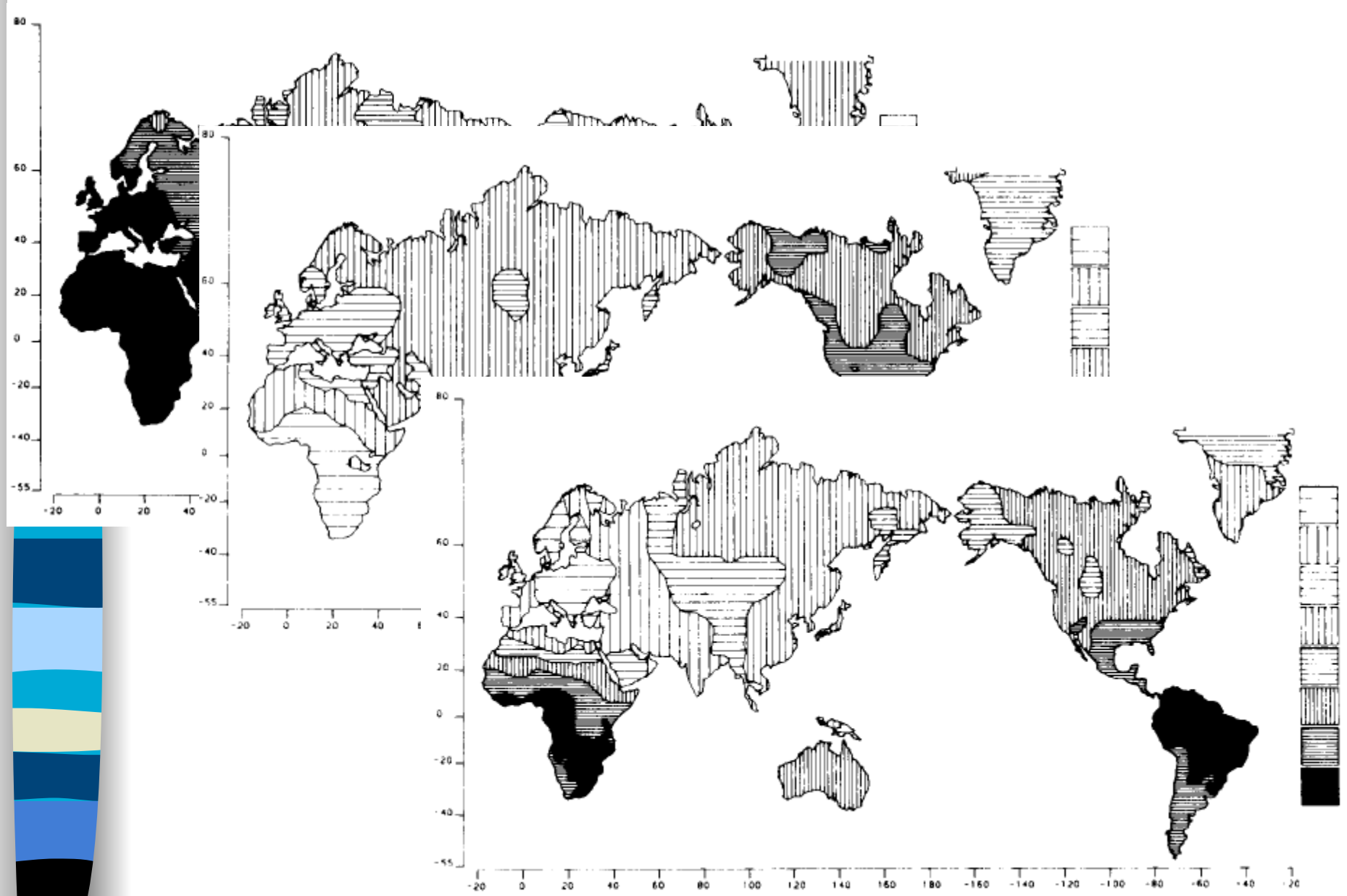
- Maps of principal compondents
- Diversity maps
- Genetic distances maps
- Summarized maps
- Genetic boundaries maps

Summary # 1:

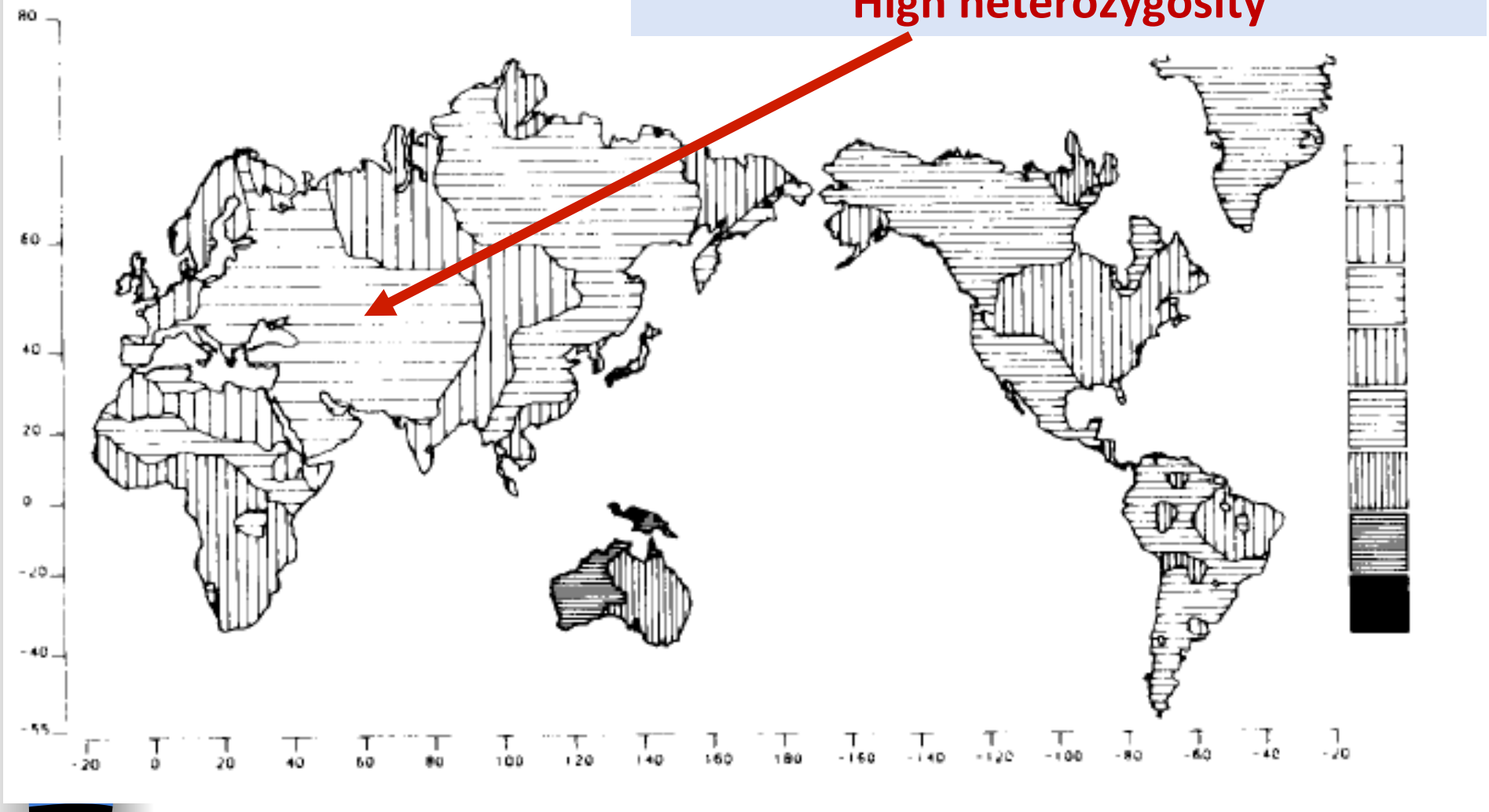


World gene pool
in the mirror of classical markers

Maps of the principal components



Map of intra-population diversity (heterozygosity)



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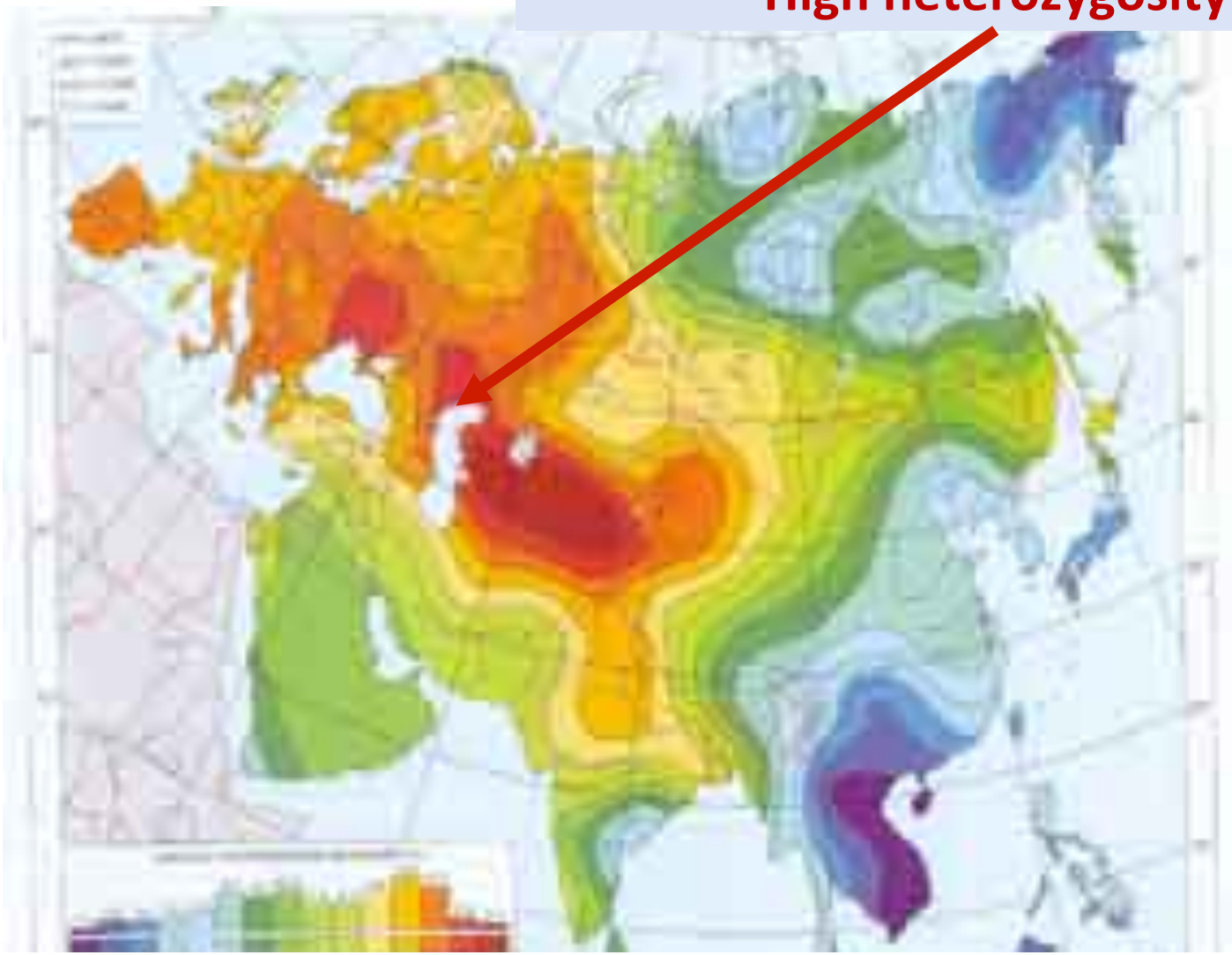
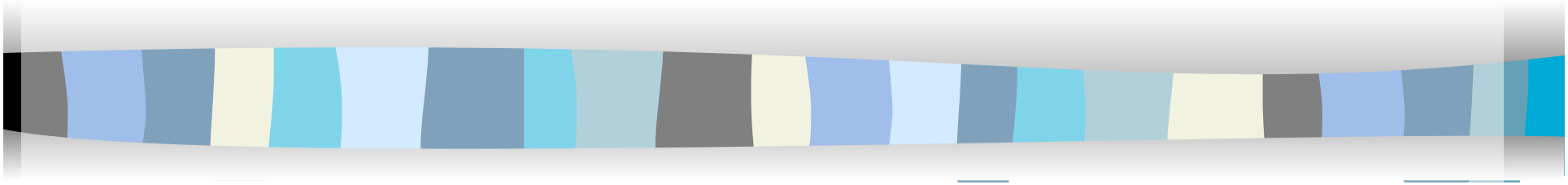


Summary # 2:

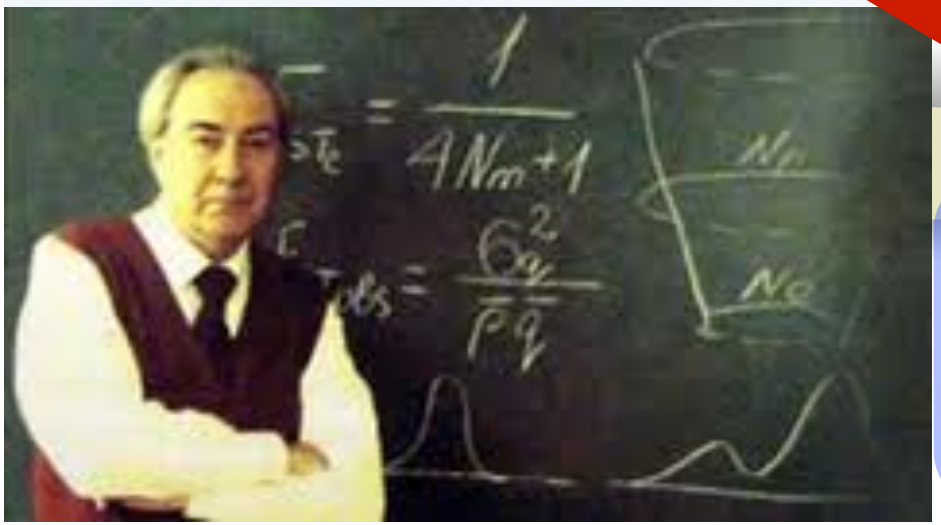


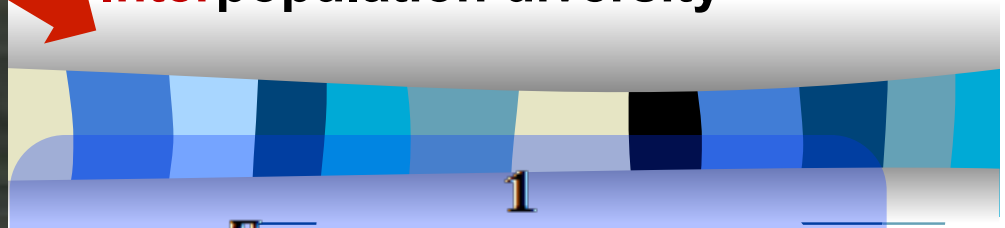
World gene pool
in the mirror of Y-chromosome

Diversity maps

Intrapopulation diversity

Interpopulation diversity





$$F_{ST} = \frac{1}{4NM + 1}$$

Revealing the geographic areas with high interpopulation diversity

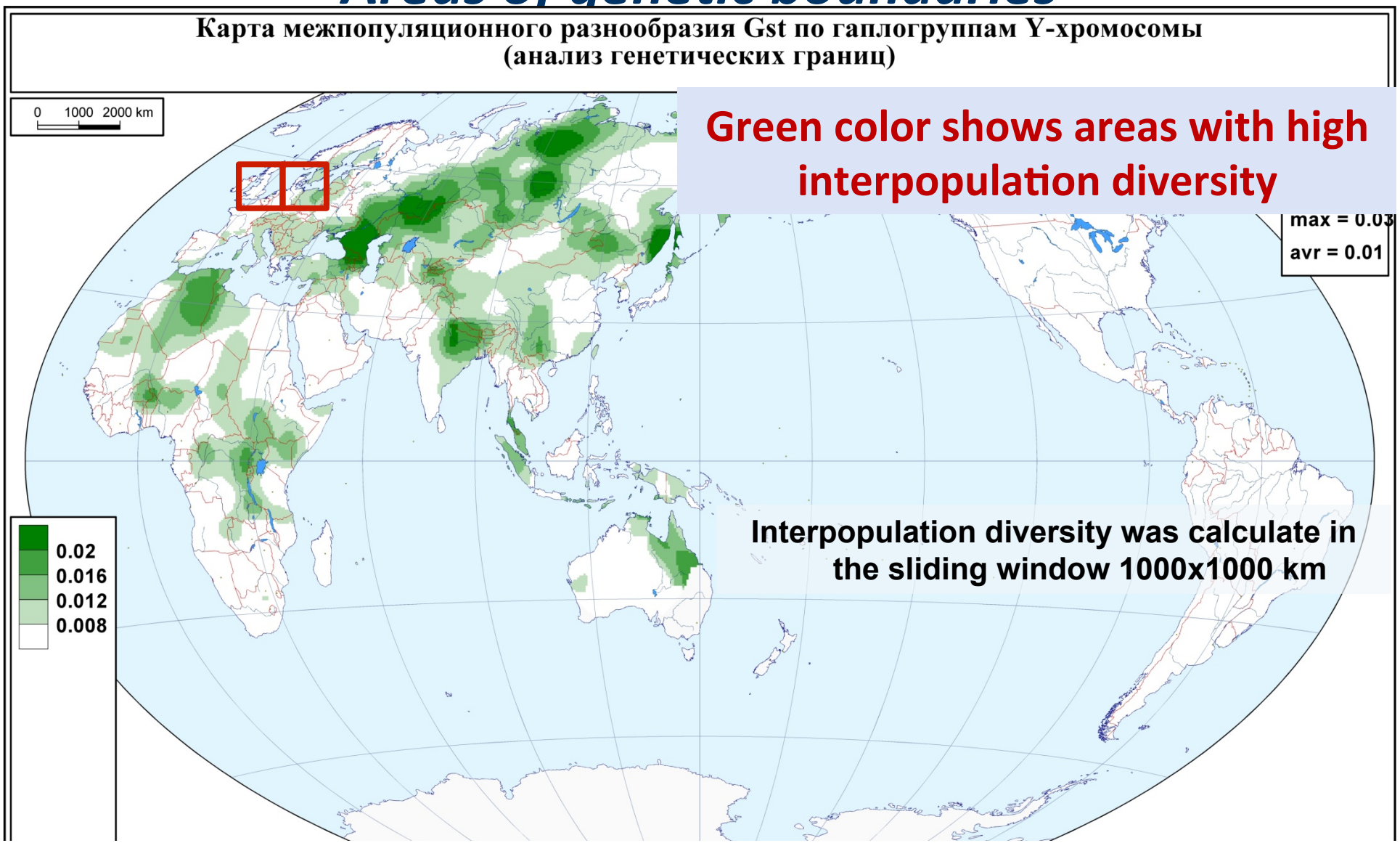
High diversity is expected at the boundaries of the contrasting gene pools

Map of interpopulation diversity = Map of genetic boundaries

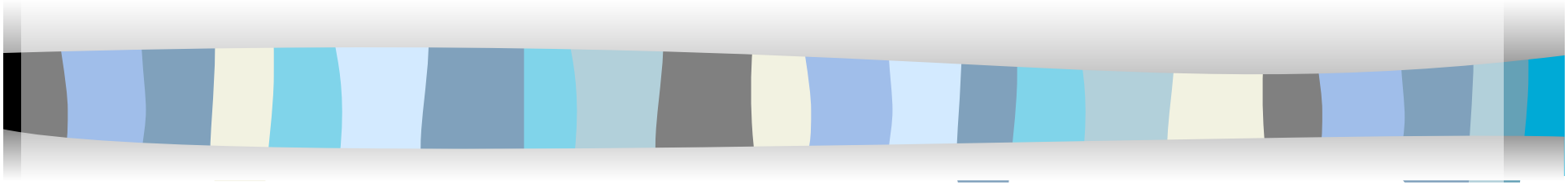
Map showing levels of interpopulation diversity

Y-chromosome

Areas of genetic boundaries



Summary # 3:



World gene pool
in the mirror of genome-wide data

Genome wide

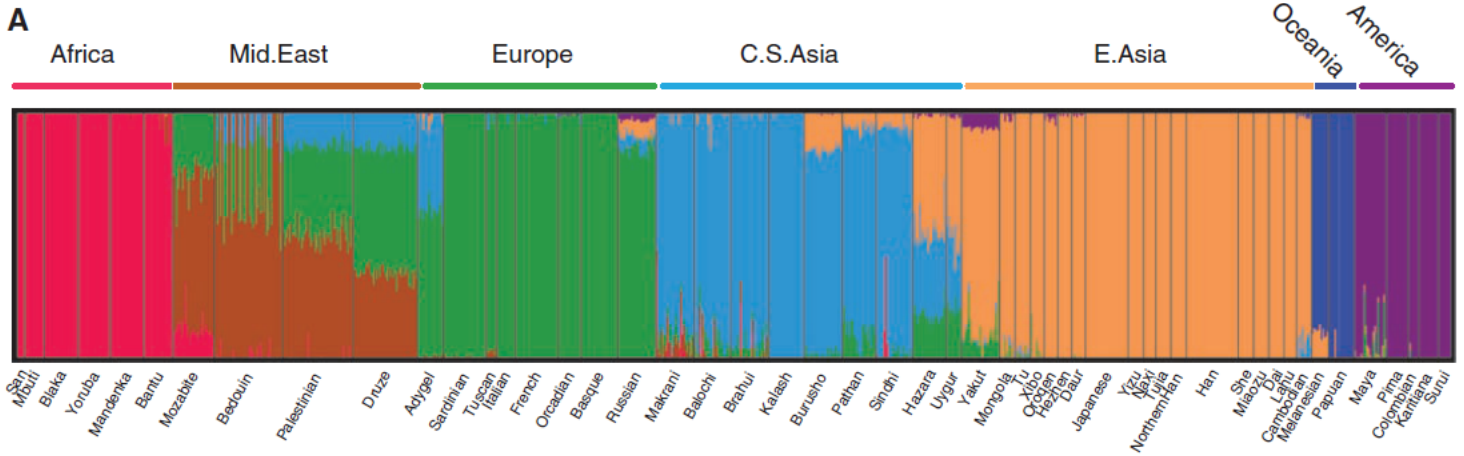
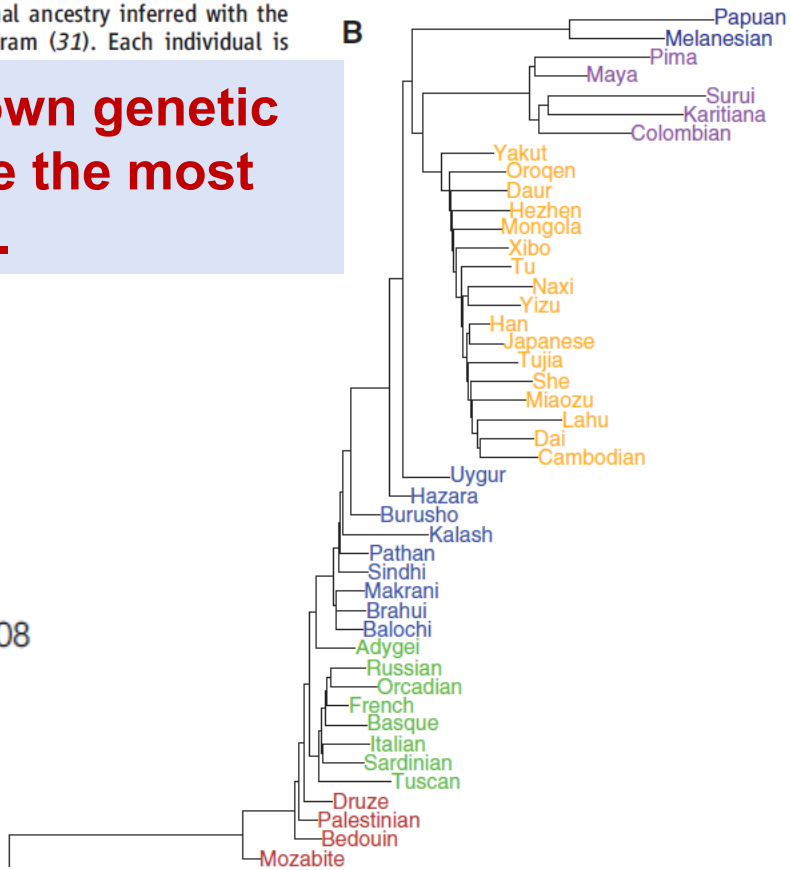


Fig. 1. Individual ancestry and population dendrogram. (**A**) Regional ancestry inferred with the *frappe* program at $K = 7$ (*13*) and plotted with the Distruct program (*31*). Each individual is



Most geographic regions have their own genetic component; Europe ad Near East are the most intermixed with each other.

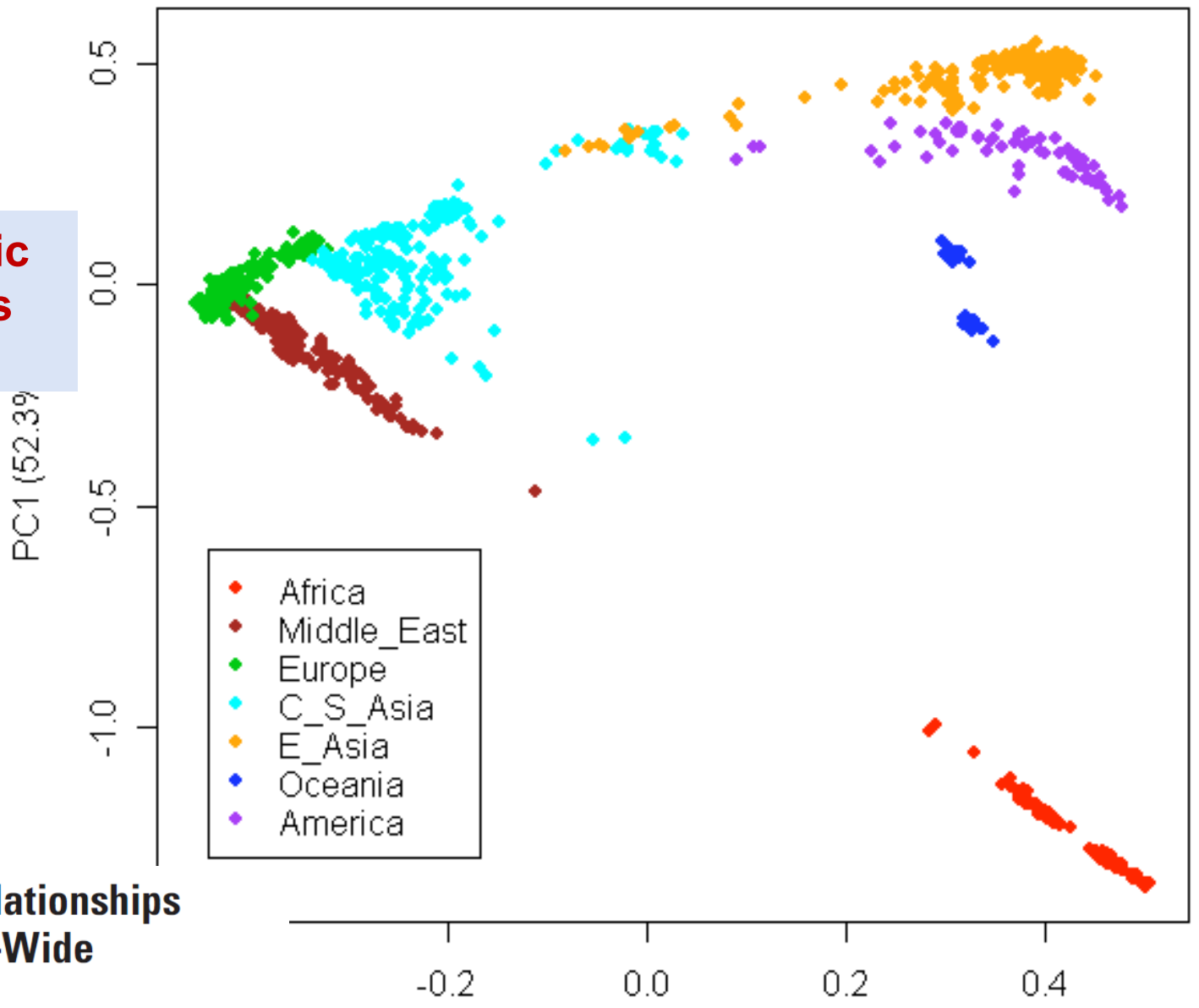
Worldwide Human Relationships Inferred from Genome-Wide Patterns of Variation

Jun Z. Li,[1,2]*† Devin M. Absher,[1,2]* Hua Tang,[1] Audrey M. Southwick,[1,2] Amanda M. Casto,[1] Sohini Ramachandran,[4] Howard M. Cann,[5] Gregory S. Barsh,[1,3] Marcus Feldman,[4]‡ Luigi L. Cavalli-Sforza,[1]‡ Richard M. Myers[1,2]‡

www.sciencemag.org **SCIENCE** VOL 319 22 FEBRUARY 2008

Genome wide

Clear geographic structuring was observed.



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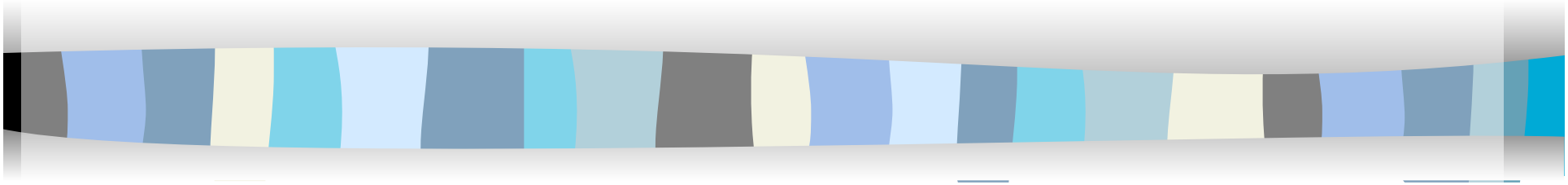
www.sciencemag.org SCIENCE VOL 319 22 FEBRUARY 2008

Summary # 4:



World gene pool
in the mirror of mtDNA

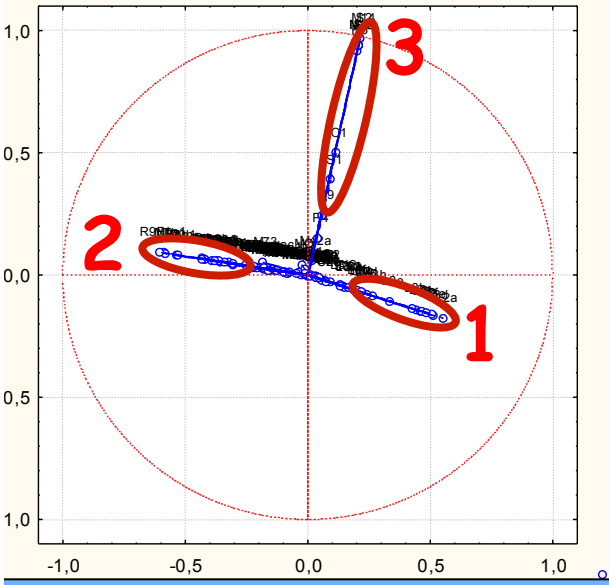
PC analysis

mtDNA

Dataset:

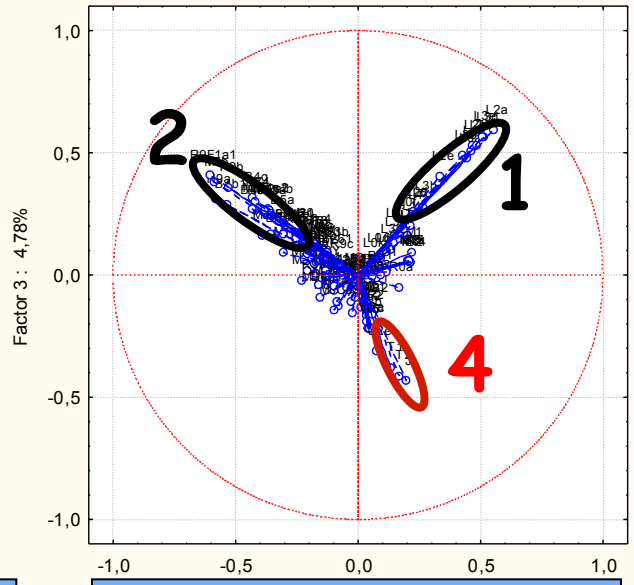
Frequencies of 118 haplogroups in 619 populations worldwide.
Plots shows haplogroups rather than populations.

Factors 1 and 2



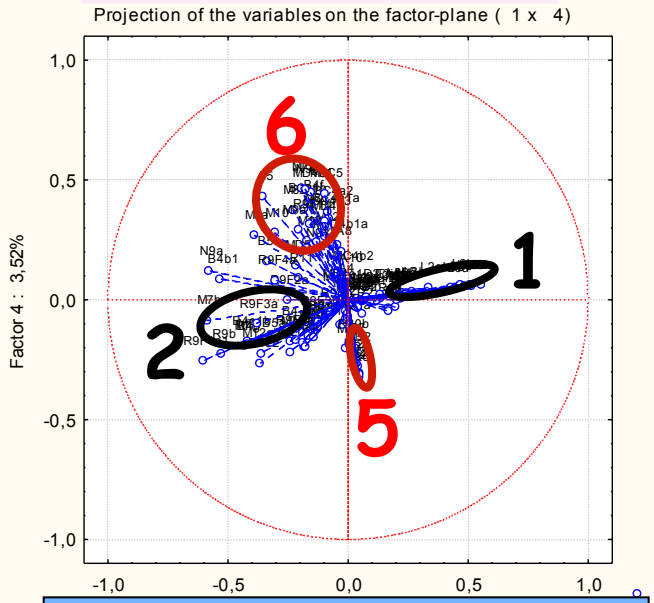
Three clusters are obvious

Factors 1 and 3



The same two clusters plus one new one

Factors 1 and 4

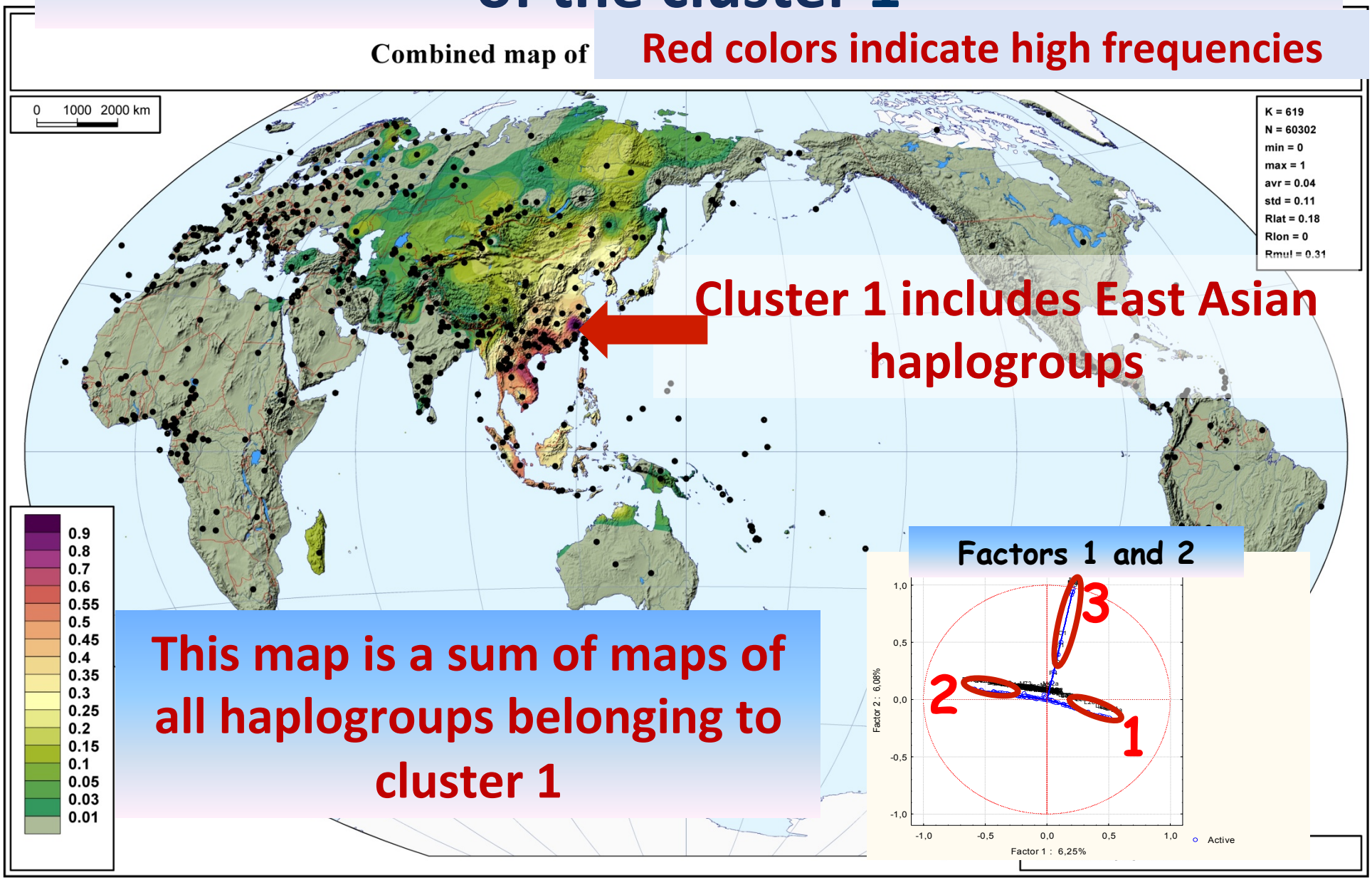


Two new clusters

Summarized frequencies of haplogroups of the cluster 1

mtDNA

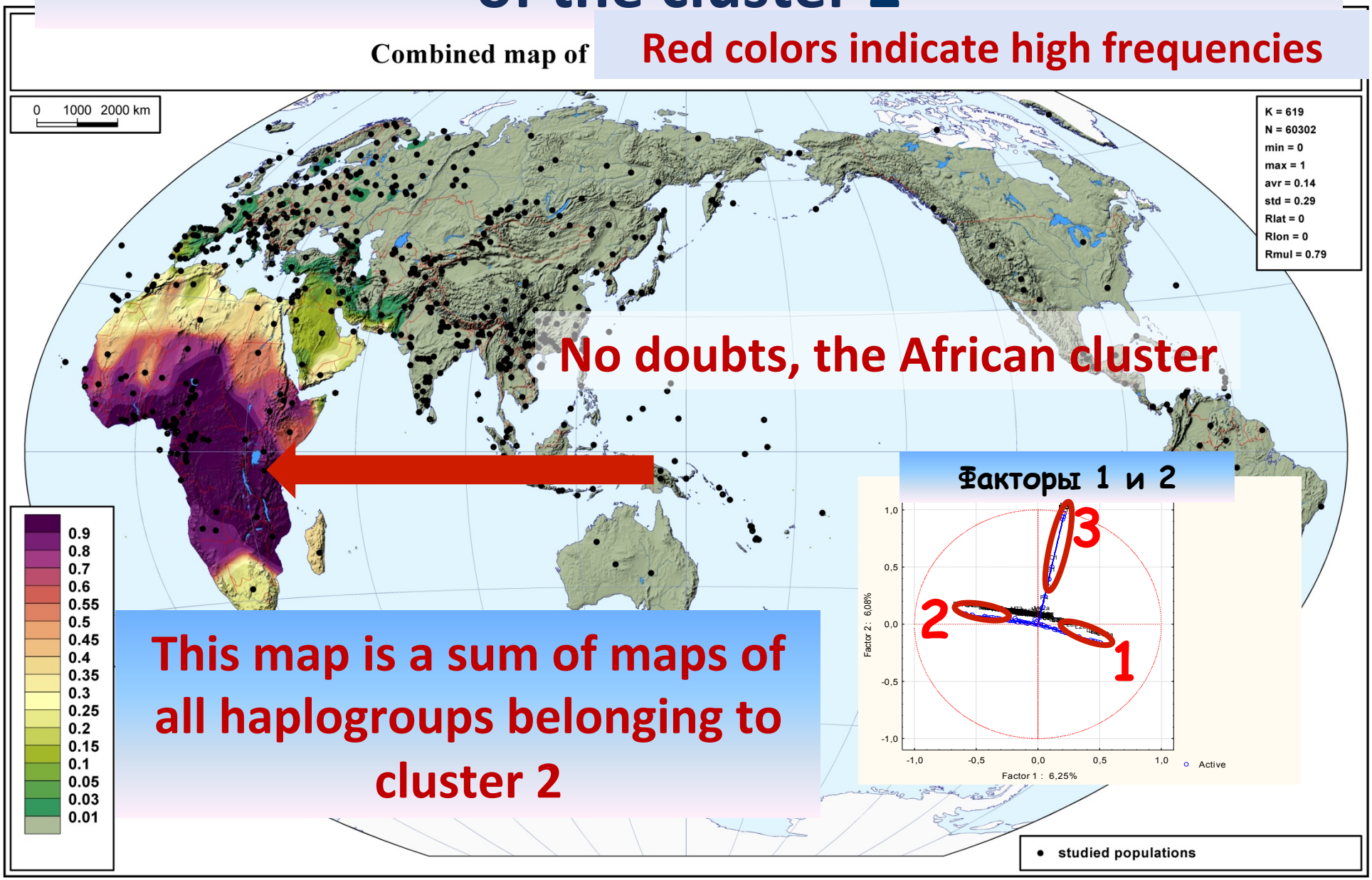
Red colors indicate high frequencies



Summarized frequencies of haplogroups of the cluster 2

mtDNA

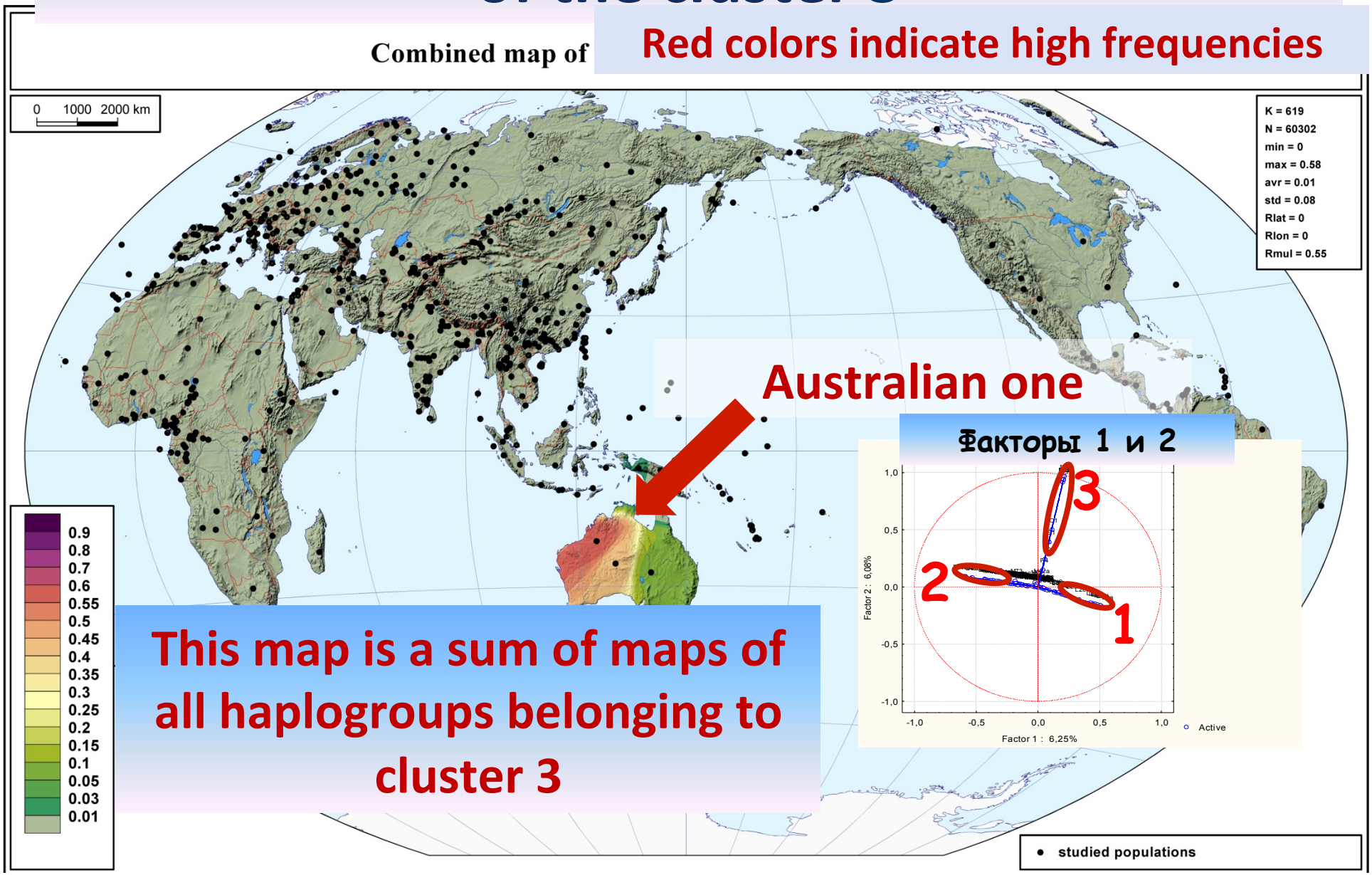
Red colors indicate high frequencies



Summarized frequencies of haplogroups of the cluster 3

mtDNA

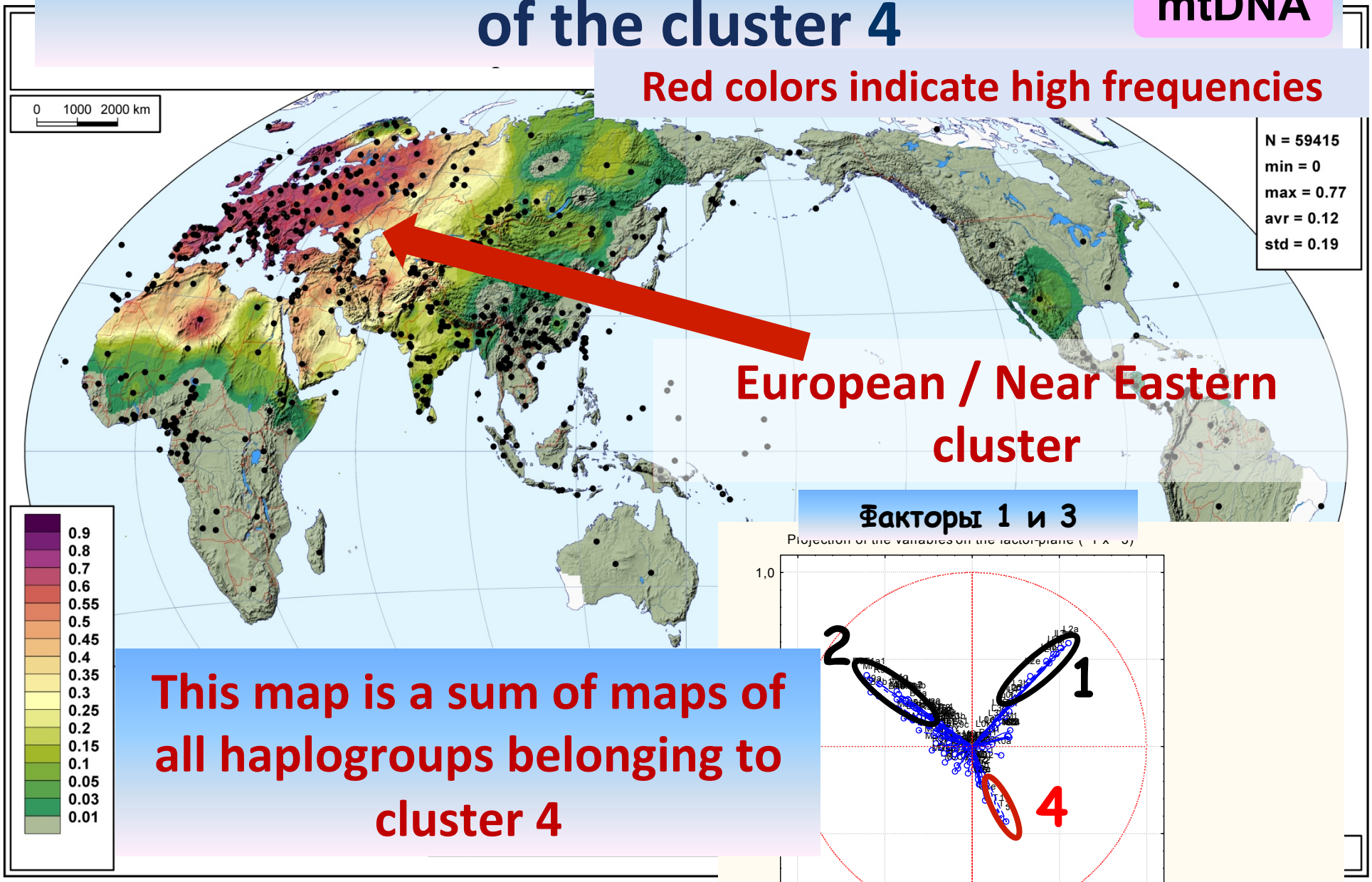
Red colors indicate high frequencies



Summarized frequencies of haplogroups of the cluster 4

mtDNA

Red colors indicate high frequencies



European / Near Eastern cluster

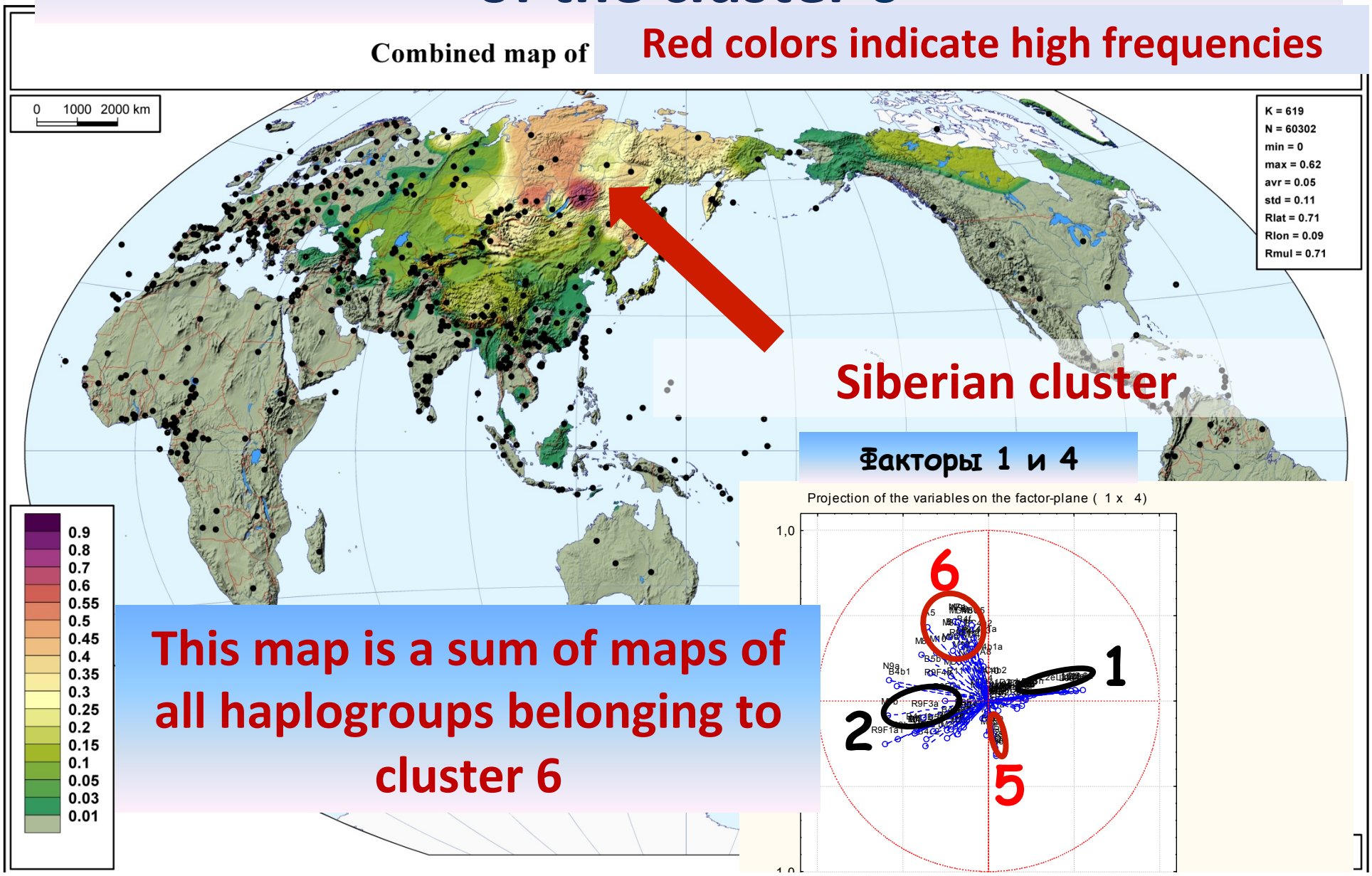
This map is a sum of maps of all haplogroups belonging to cluster 4

Факторы 1 и 3

Summarized frequencies of haplogroups of the cluster 6

mtDNA

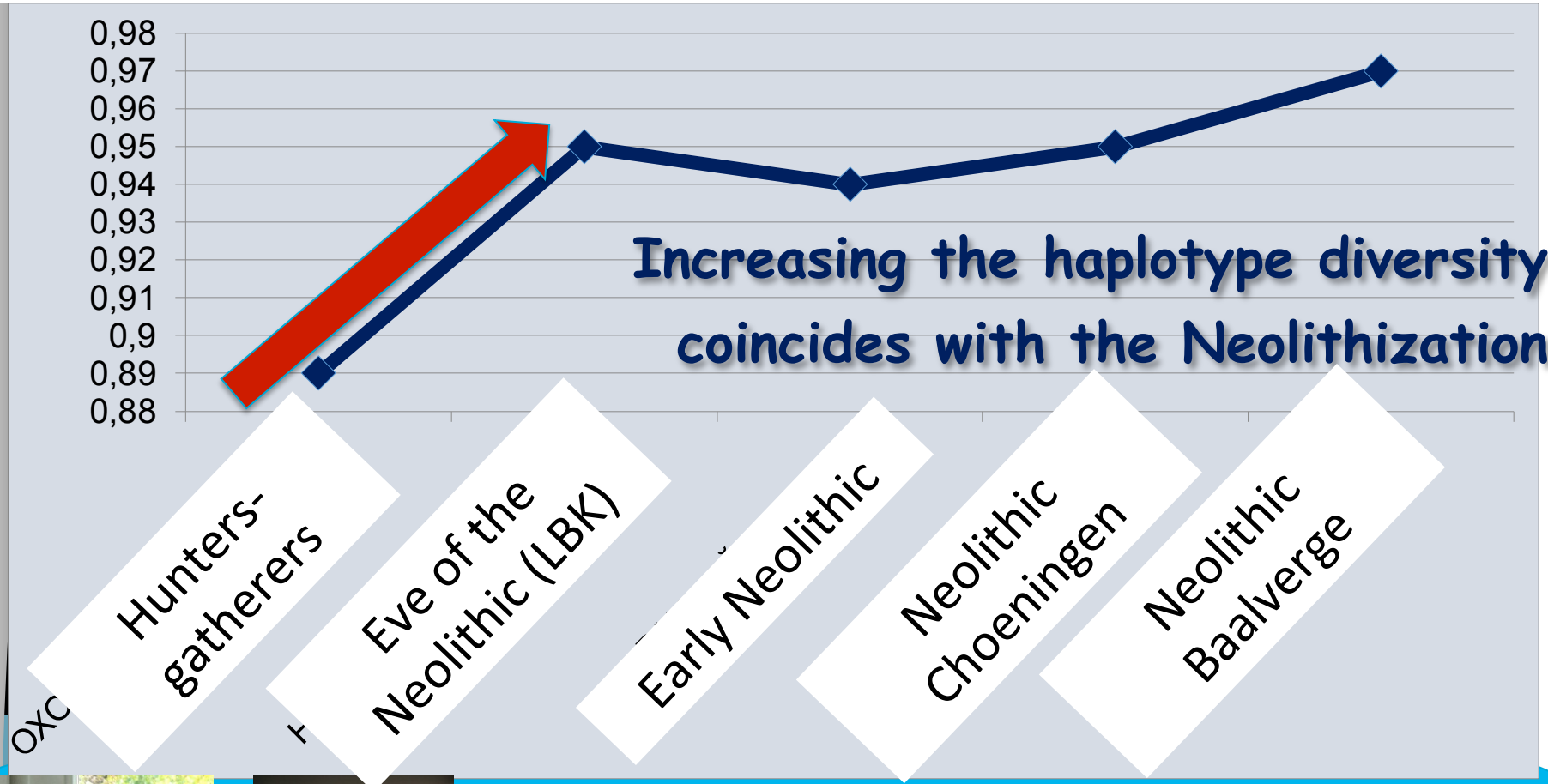
Red colors indicate high frequencies



Siberian cluster

This map is a sum of maps of all haplogroups belonging to cluster 6

Факторы 1 и 4



collaboration:

Guido Brandt Prof. Kurt W. Alt Dr. Wolfgang Haak Dr. Oleg Balanovsk

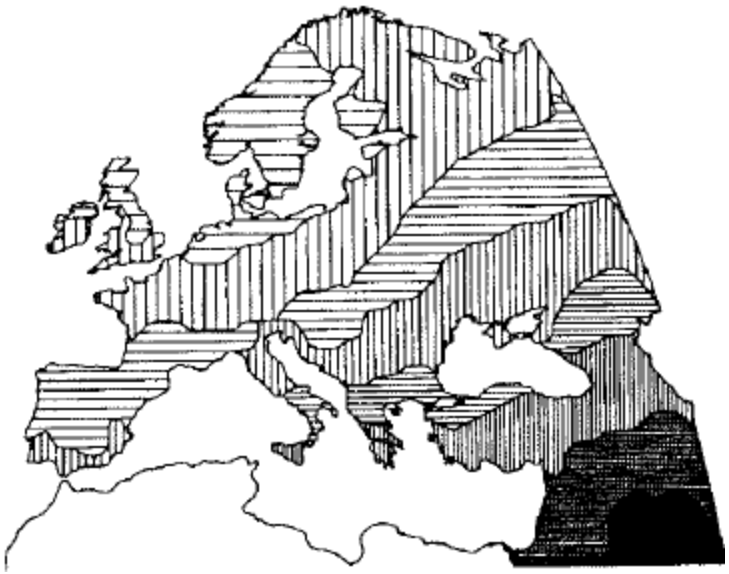
Institute of Anthropology,
Johannes Gutenberg University, Germany

BRANDT ET AL., 2013. Science.

ORIGIN ON THE EUROPEANS

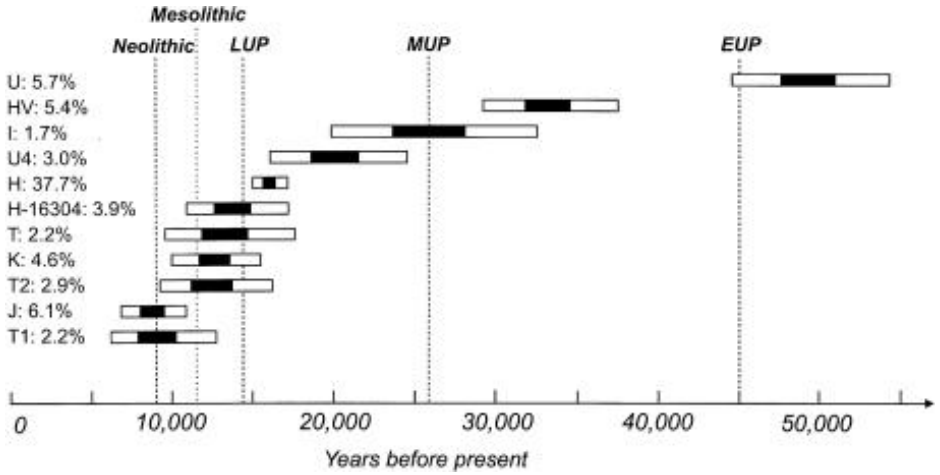
NEOLITHIC VS PALEOLITHIC AGE OF THE EUROPEAN GENE POOL

- **First synthetic map summarizing genetic variation in Europe**

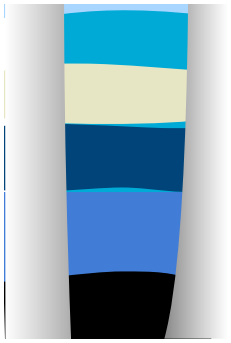


(Cavall-Sforza et al., 1994)

- **Ages of major mitochondrial haplogroups in Europe**



(Richards et al., 2000)



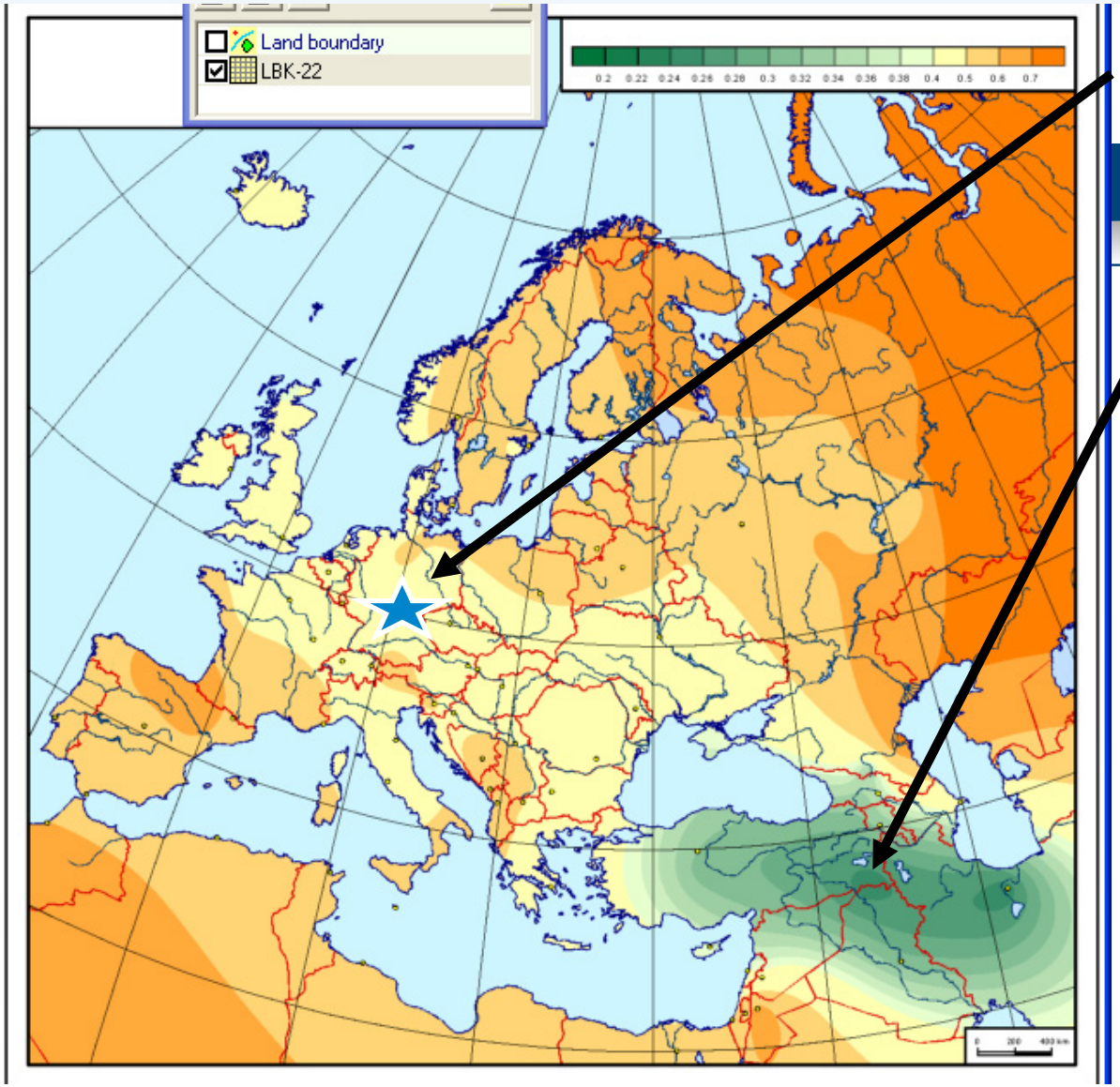
Neolithisation **<<** **Paleolithic initial settlement**

Demic diffusion

Neolithisation by cultural diffusion

Analysis of the ancient (Neolithic DNA)

Map of genetic distances from Neolithic Europeans



Location of the sampled Neolithic Europeans

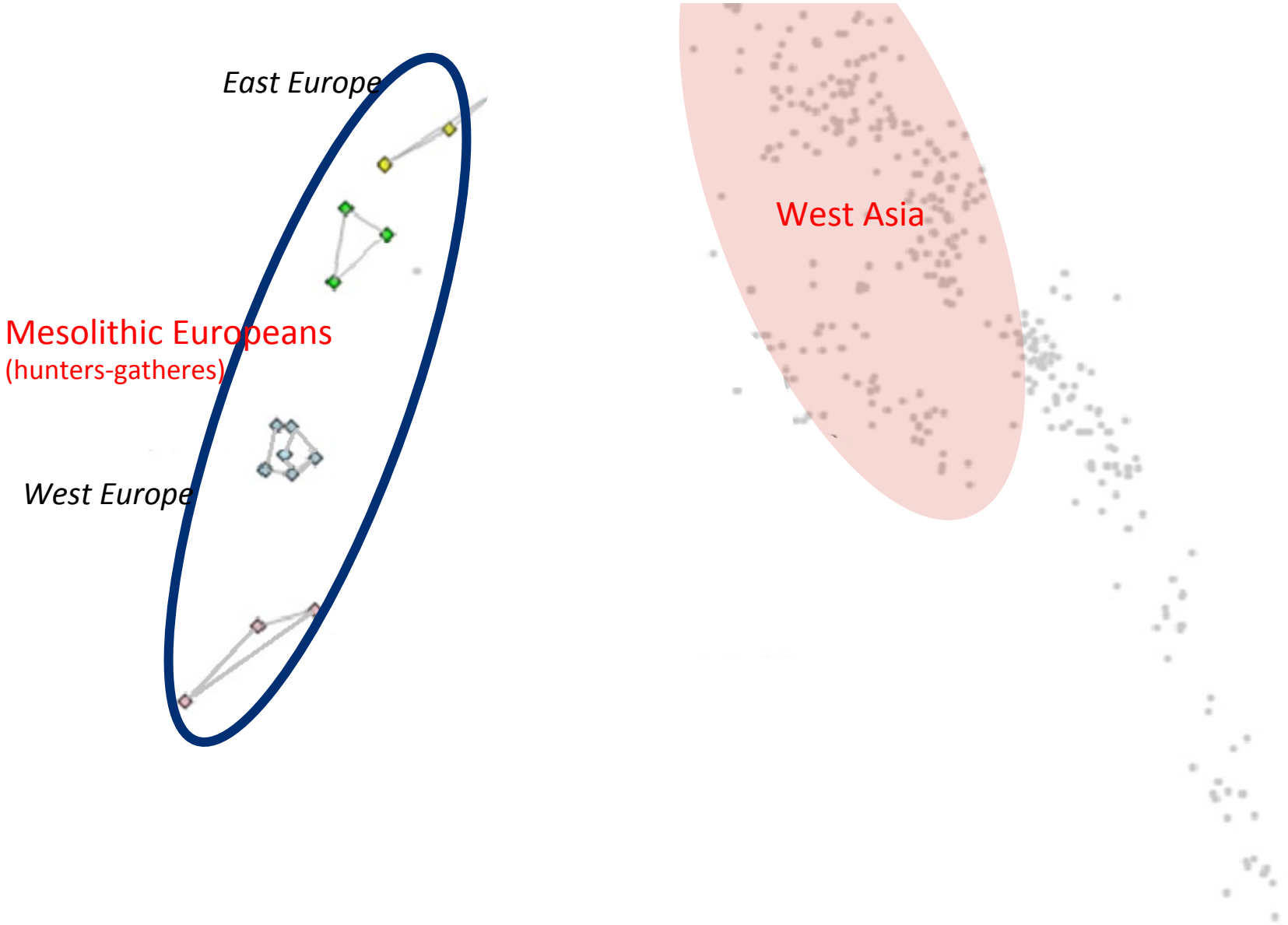
The present-day genetically similar populations are in the Near East

The present day Europeans are genetically distant from the Neolithic Europeans

Thus, the migrations of Neolithic farmers from Near East took place indeed, but these gene pool of farmers then dissolved in the local gene pool of hunder-gatherers.

Ancient DNA unravels history of Europeans

(based on papers from David Reich lab, 2013 - 2015, Nature)



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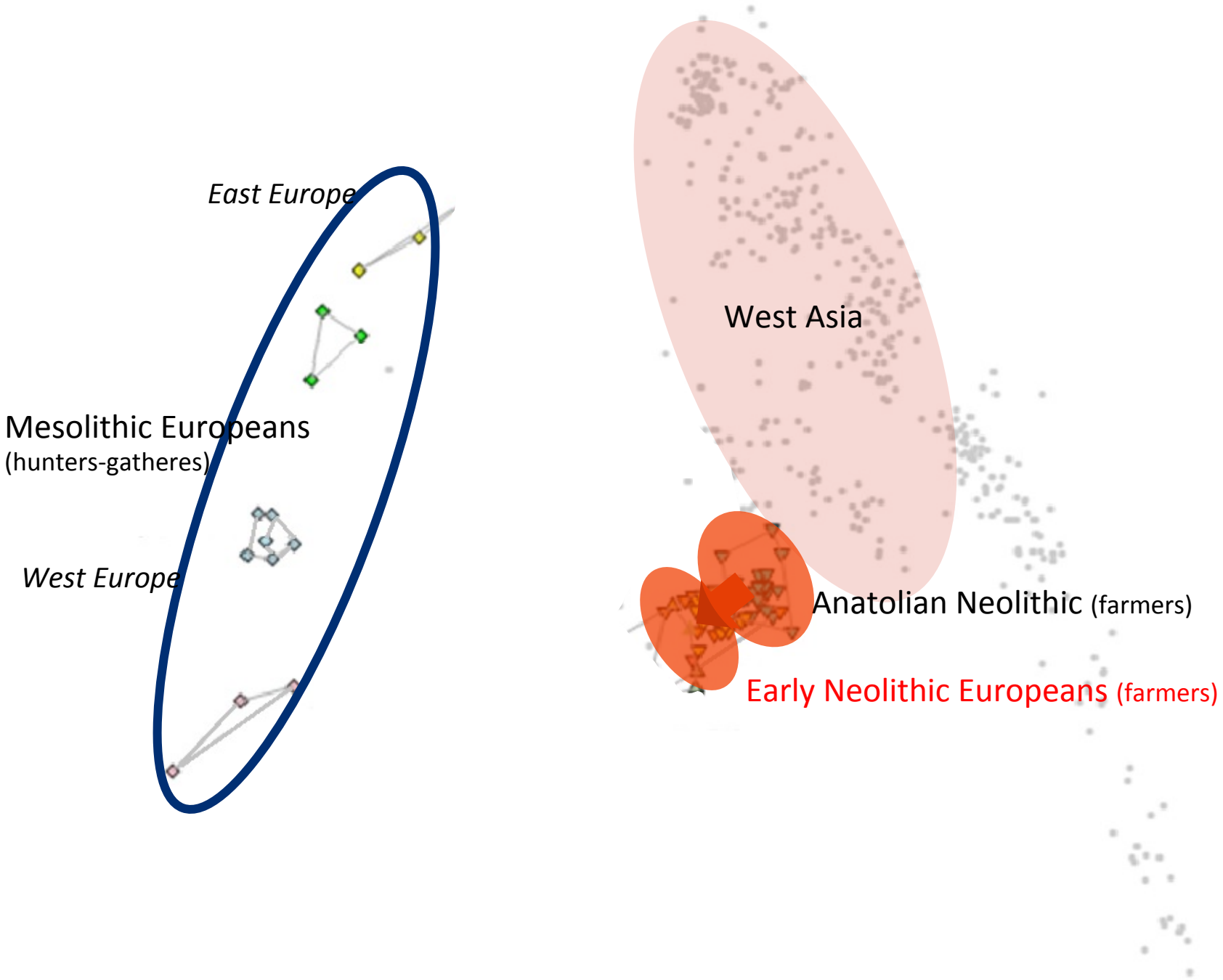
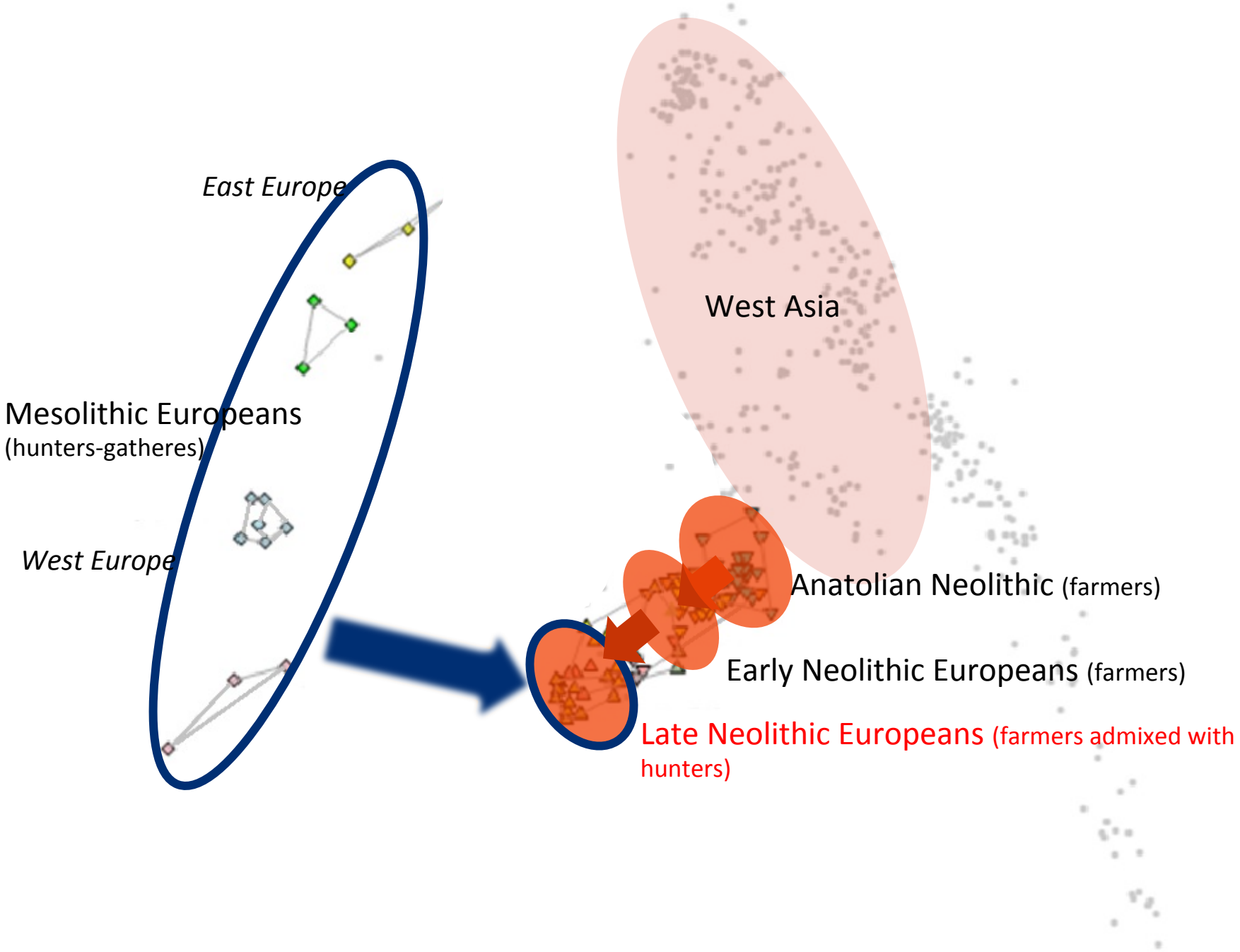
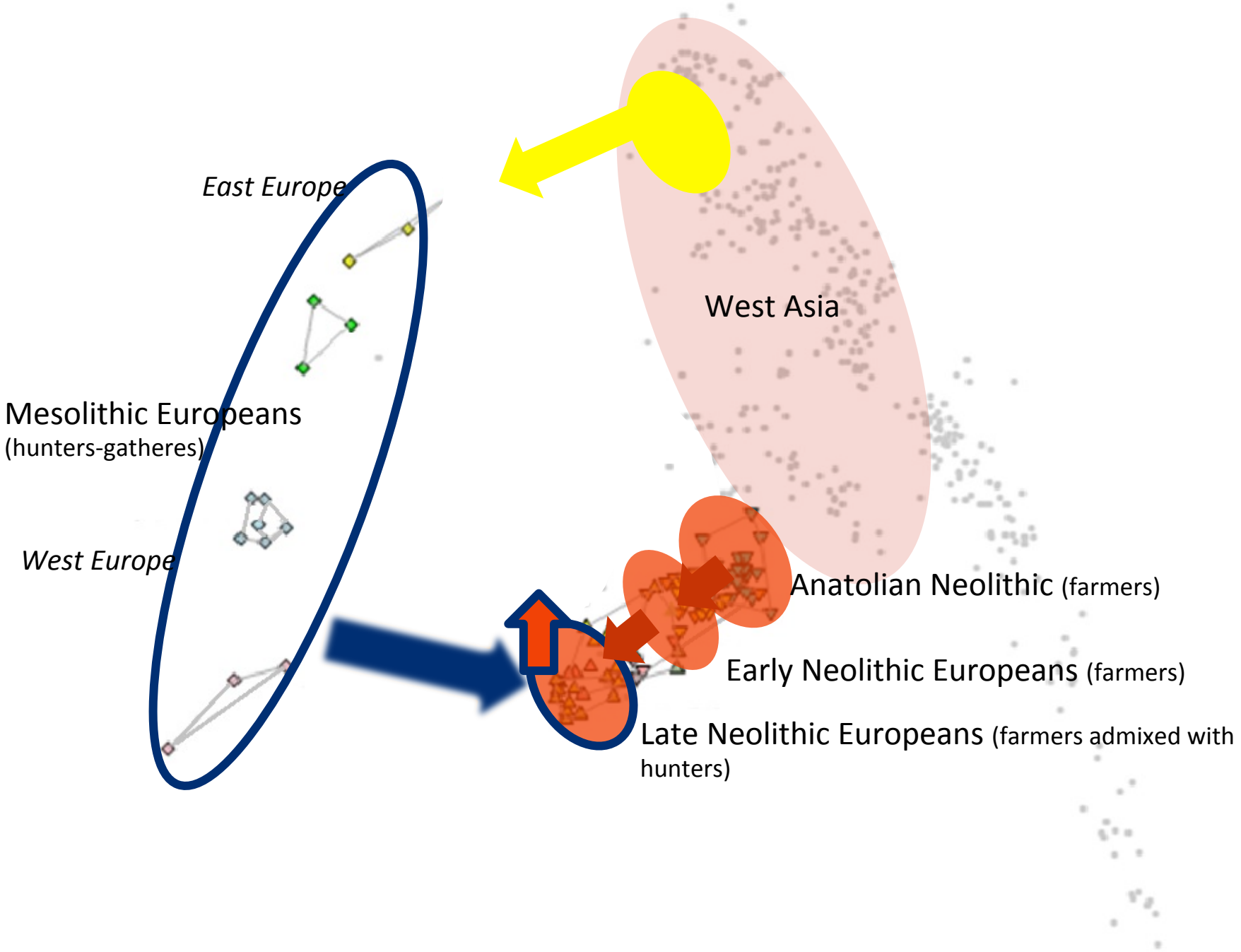

East Europe
Mesolithic Europeans
(hunters-gatheres)
West Europe
West Asia
Anatolian Neolithic (farmers)
Early Neolithic Europeans (farmers)


East Europe
West Asia
Mesolithic Europeans
(hunters-gatheres)
West Europe
Anatolian Neolithic (farmers)
Early Neolithic Europeans (farmers)
Late Neolithic Europeans (farmers admixed with hunters)


East Europe
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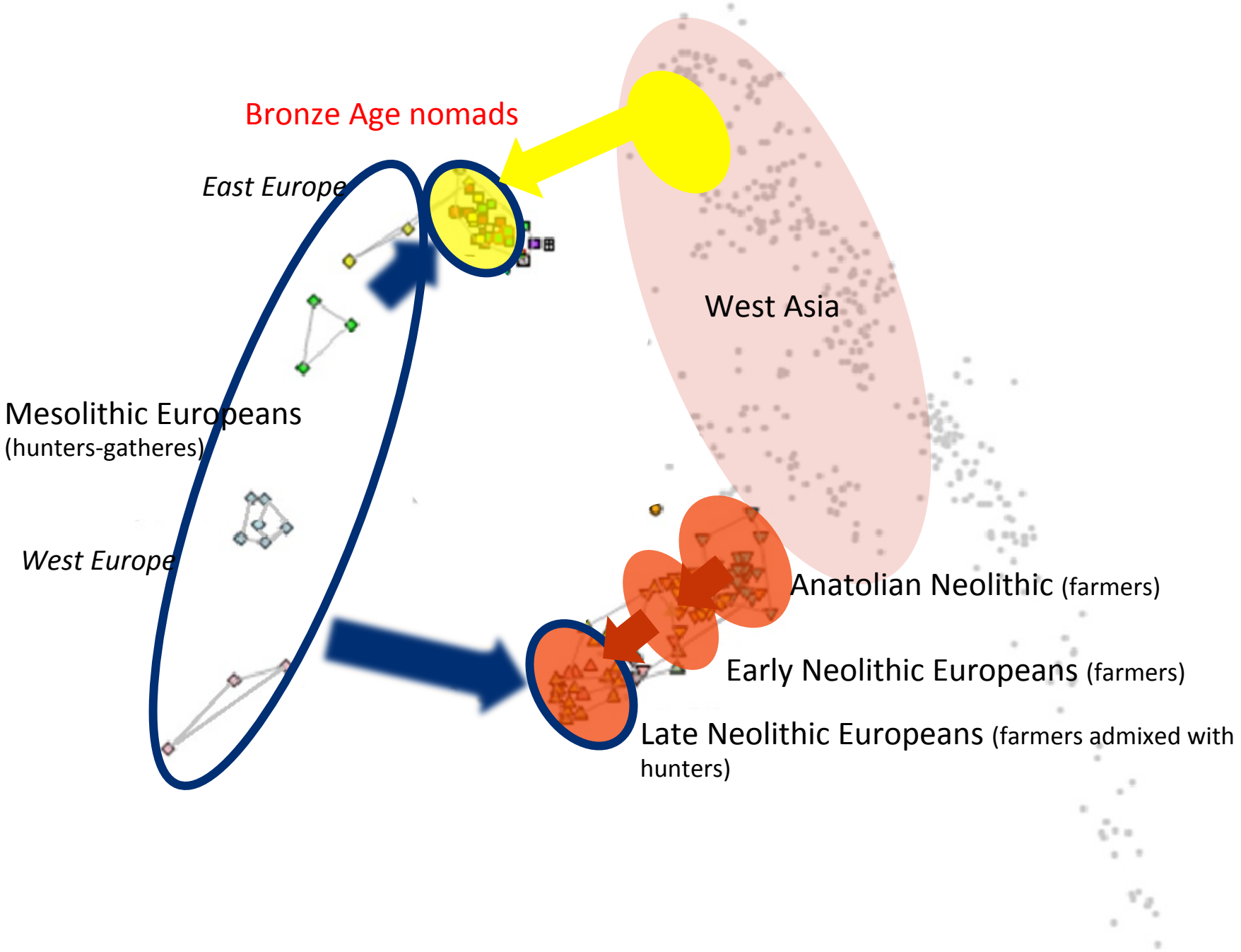
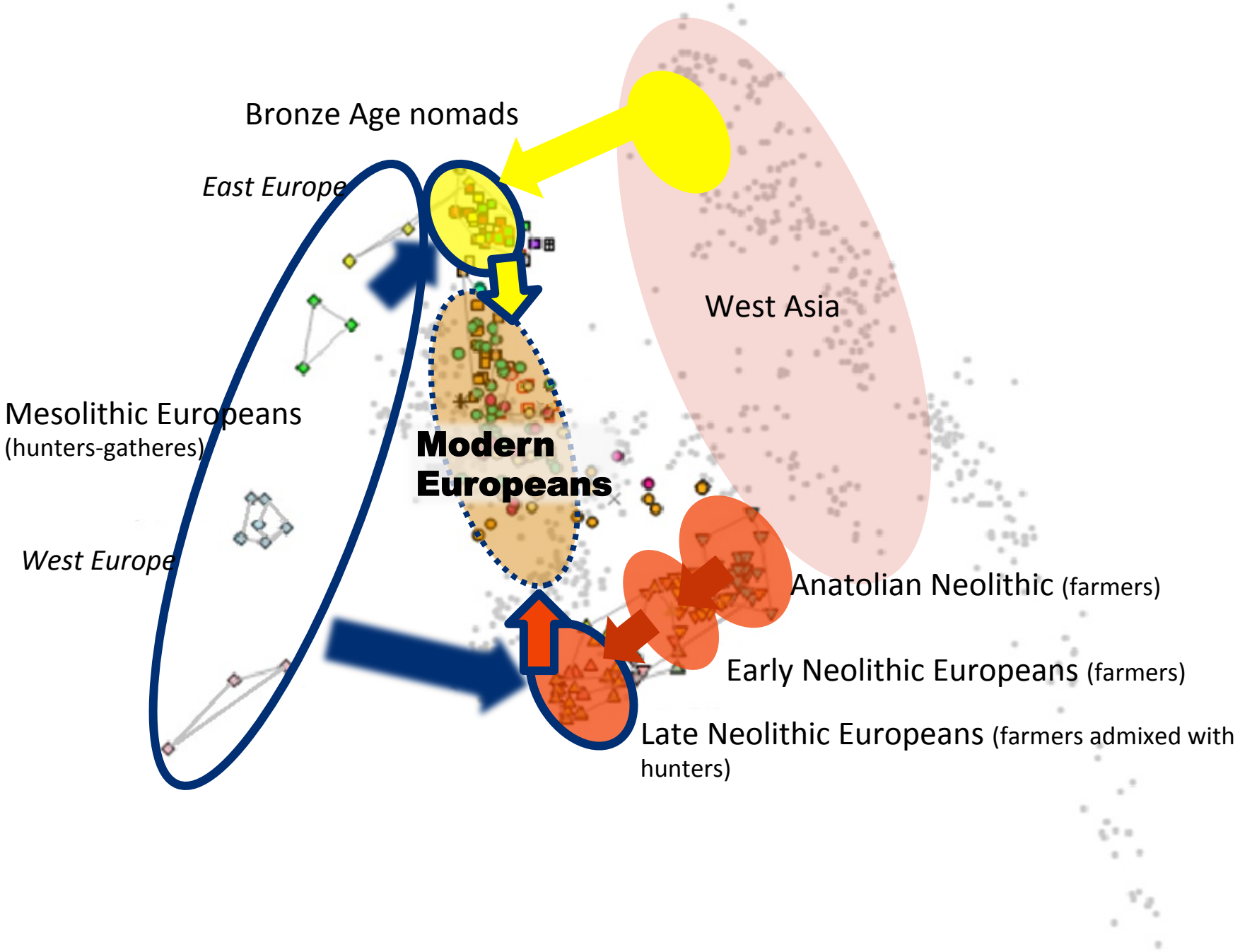
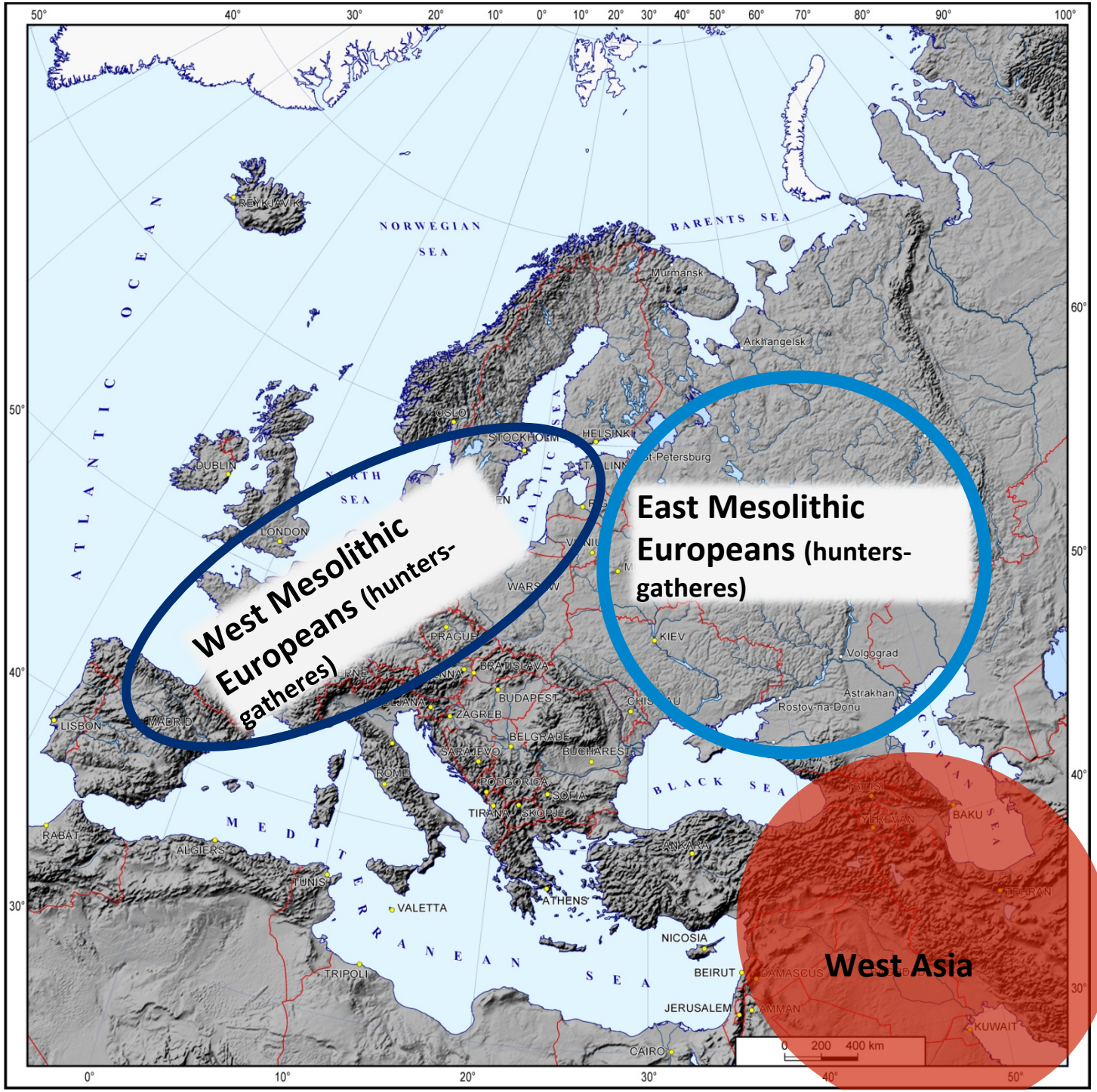
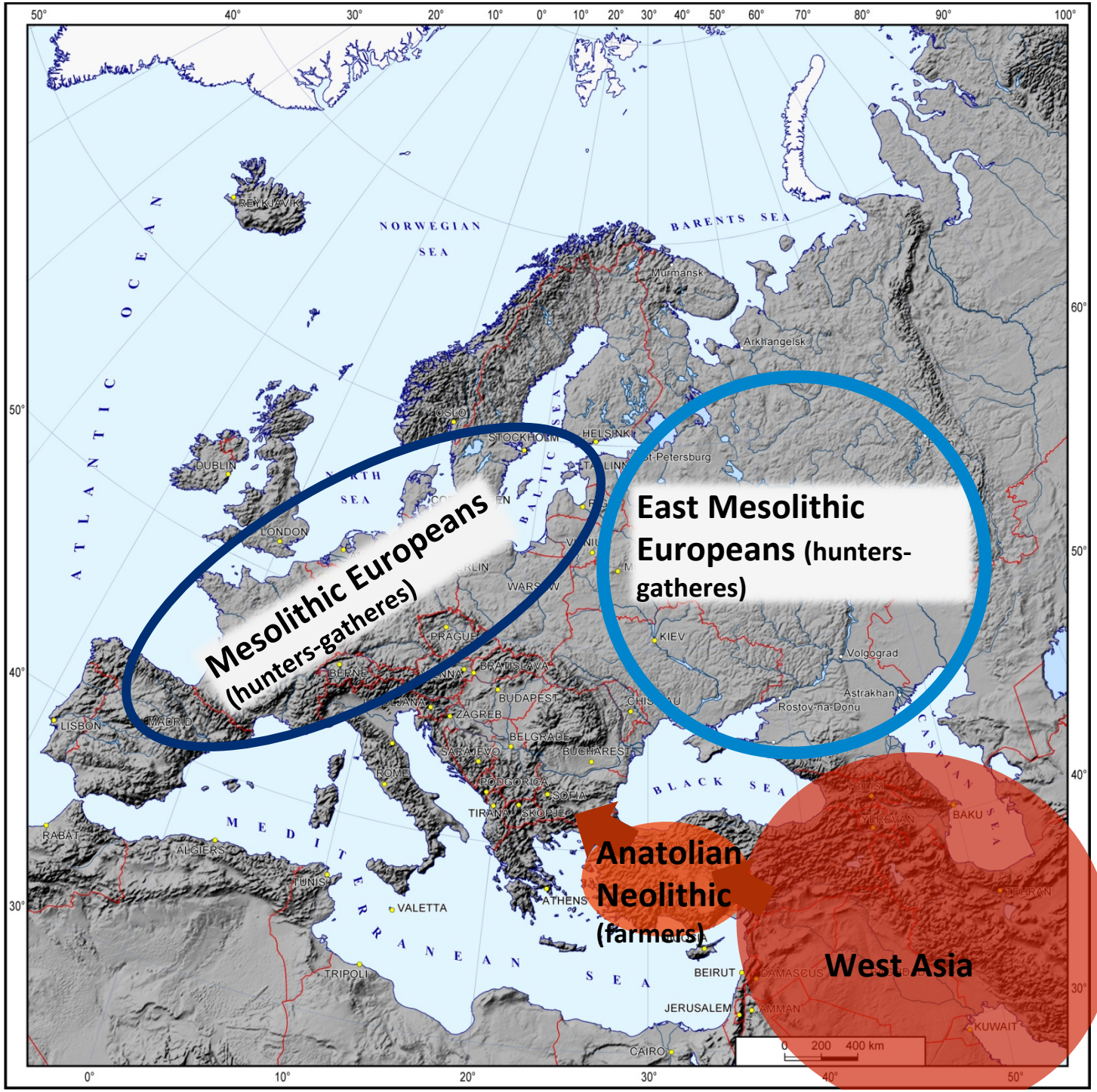

Bronze Age nomads
East Europe
West Asia
Mesolithic Europeans
(hunters-gatheres)
West Europe
Anatolian Neolithic (farmers)
Early Neolithic Europeans (farmers)
Late Neolithic Europeans (farmers admixed with hunters)


Bronze Age nomads
East Europe
West Asia
Mesolithic Europeans
(hunters-gatheres)
Modern
Europeans
West Europe
Anatolian Neolithic (farmers)
Early Neolithic Europeans (farmers)
Late Neolithic Europeans (farmers admixed with
hunters)


West Mesolithic Europeans (hunters-gatheres)
East Mesolithic Europeans (hunters-gatheres)
West Asia
ATLANTIC OCEAN
NORWEGIAN SEA
BARENTS SEA
BALTIC SEA
BLACK SEA
CASPIAN SEA
MEDITERRANEAN SEA
REYKJAVIK
Murmansk
Arkhangelsk
OSLO
STOCKHOLM
HELSINKI
St-Petersburg
DUBLIN
LONDON
WARSAW
PRAGUE
BRATISLAVA
BUDAPEST
ZAGREB
BELGRADE
SARAJEVO
BUCHAREST
PODGORICA
SOFIA
TIRANA
SKOPJE
ROME
KIEV
Volgograd
Astrakhan
Rostov-na-Donu
LISBON
MADRID
RABAT
ALGIERS
TUNIS
VALETTA
TRIPOLI
ATHENS
ANKARA
NICOSIA
BEIRUT
DAMASCUS
JERUSALEM
AMMAN
CAIRO
KUWAIT
TEHRAN
BAKU
YEREVAN
0 200 400 km


Mesolithic Europeans
(hunters-gatheres)
East Mesolithic
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SARAJEVO
BUCHAREST
PODGORICA
SOFIA
TIRANA
SKOPJE
ROME
LISBON
MADRID
RABAT
ALGIERS
TUNIS
VALETTA
ATHENS
TRIPOLI
BEIRUT
DAMASCUS
JERUSALEM
AMMAN
KUWAIT
CAIRO
TEHRAN
BAKU
YEREVAN
0 200 400 km


East Mesolithic Europeans (hunters-gatheres)
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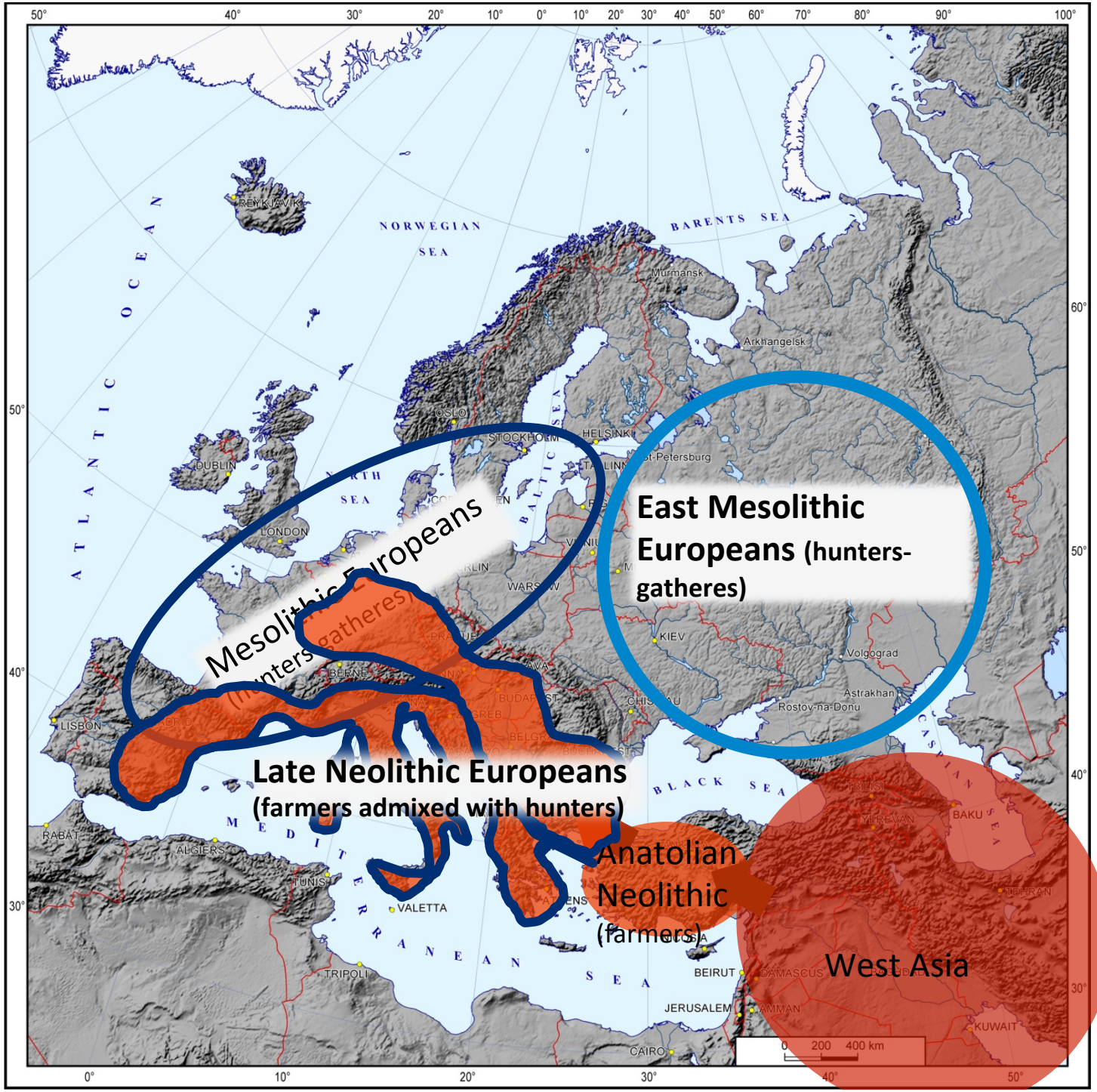
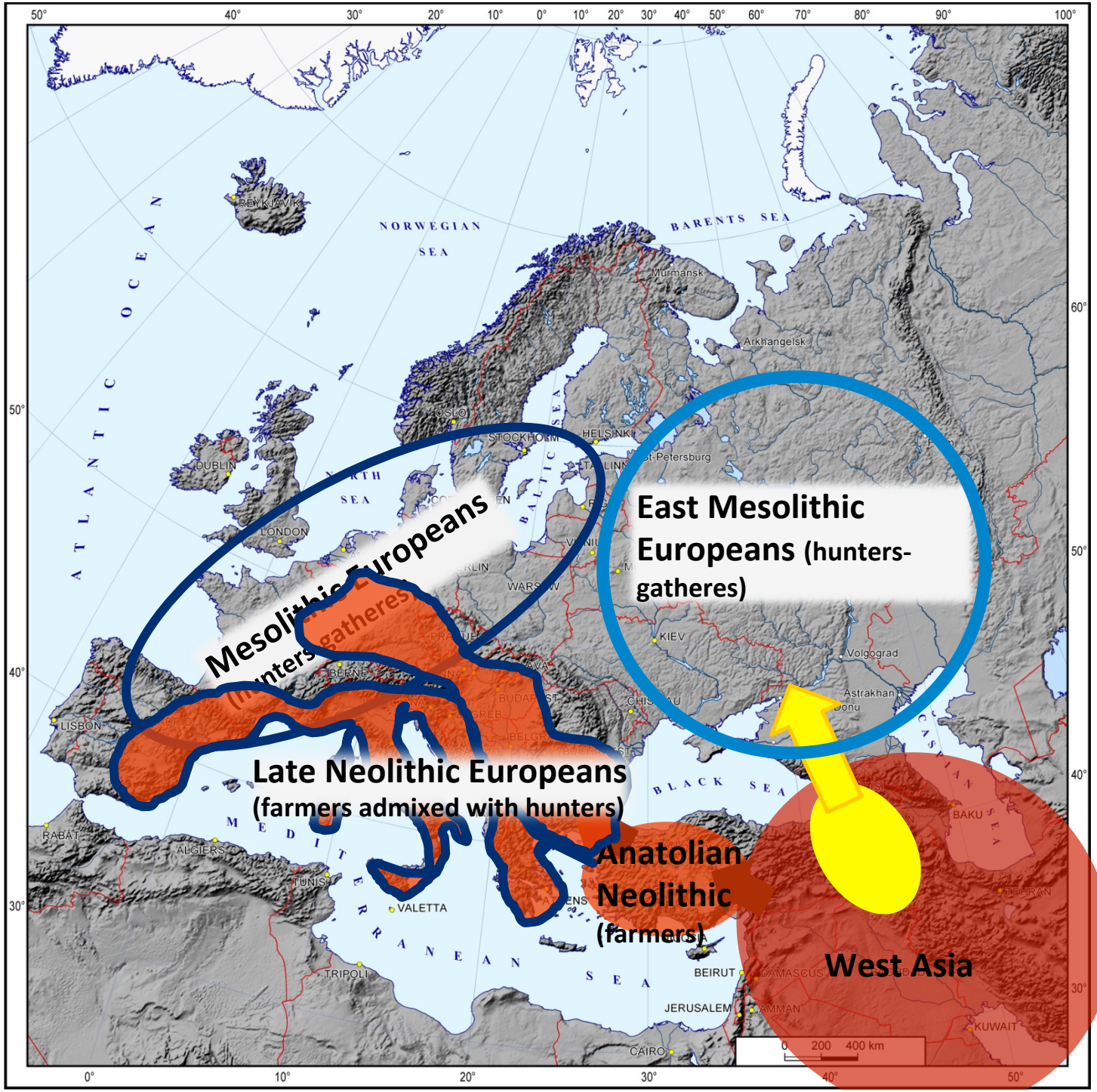
TUNIS
VALETTA
TRIPOLI
BEIRUT
DAMASCUS
JERUSALEM
CAIRO
BAKU
TEHRAN
KUWAIT
0 200 400 km


East Mesolithic Europeans (hunters-gatheres)
Late Neolithic Europeans
(farmers admixed with hunters)
Anatolian Neolithic
(farmers)
West Asia
ATLANTIC OCEAN
NORWEGIAN SEA
BARENTS SEA
BALTIC SEA
BLACK SEA
MEDITERRANEAN SEA
REYKJAVIK
OSLO
STOCKHOLM
HELSINKI
Murmansk
Arkhangelsk
DUBLIN
LONDON
BERNE
WARSAW
KIEV
Volgograd
Astrakhan
Rostov-na-Donu
LISBON
RABAT
ALGIERS
TUNIS
VALETTA
TRIPOLI
BEIRUT
JERUSALEM
CAIRO
BAKU
TEHRAN
KUWAIT
0 200 400 km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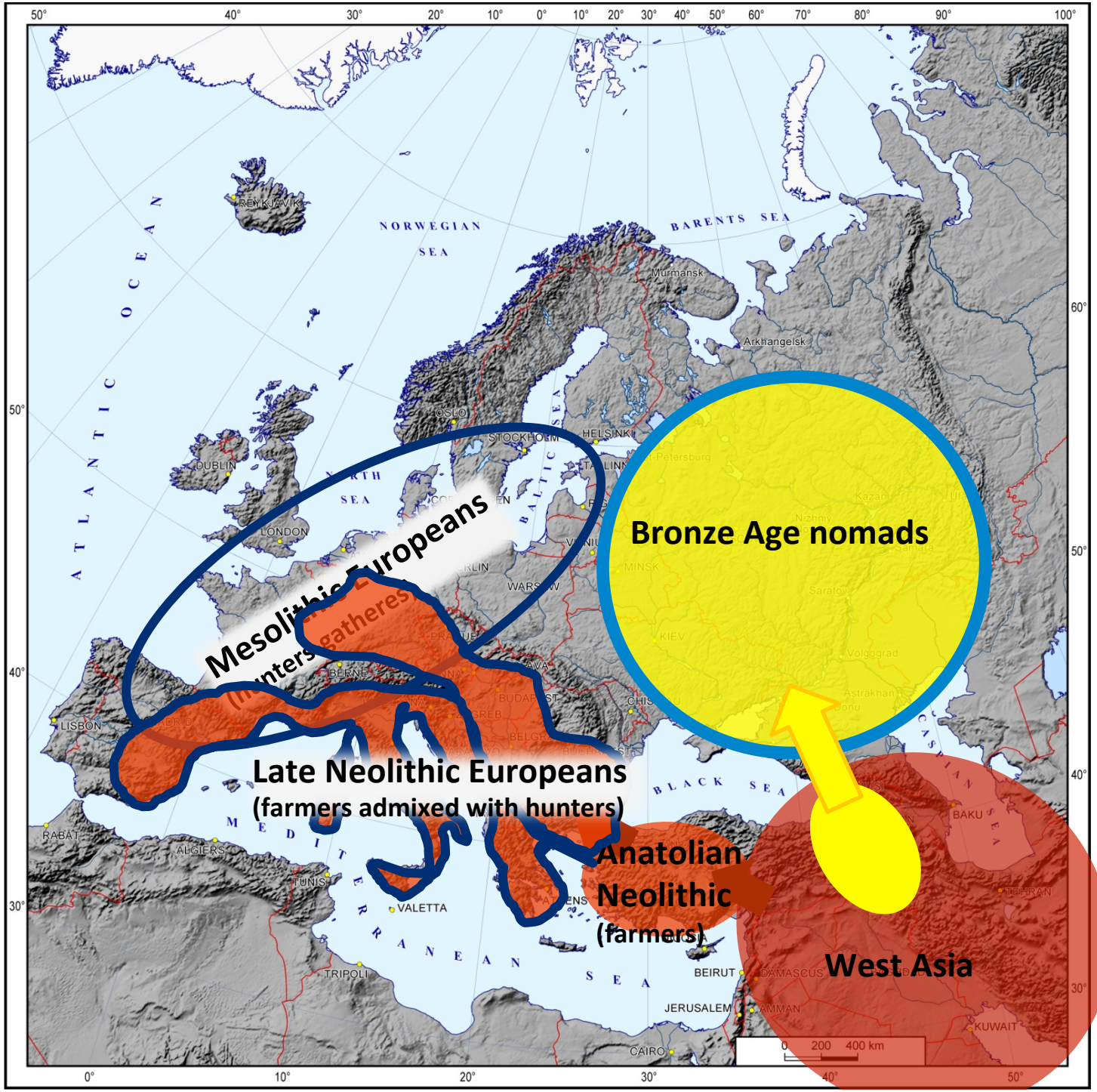
Bronze Age nomads
Late Neolithic Europeans
(farmers admixed with hunters)
Anatolian
Neolithic
(farmers)
West Asia
ATLANTIC OCEAN
NORWEGIAN SEA
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Murmansk
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OSLO
STOCKHOLM
HELSINKI
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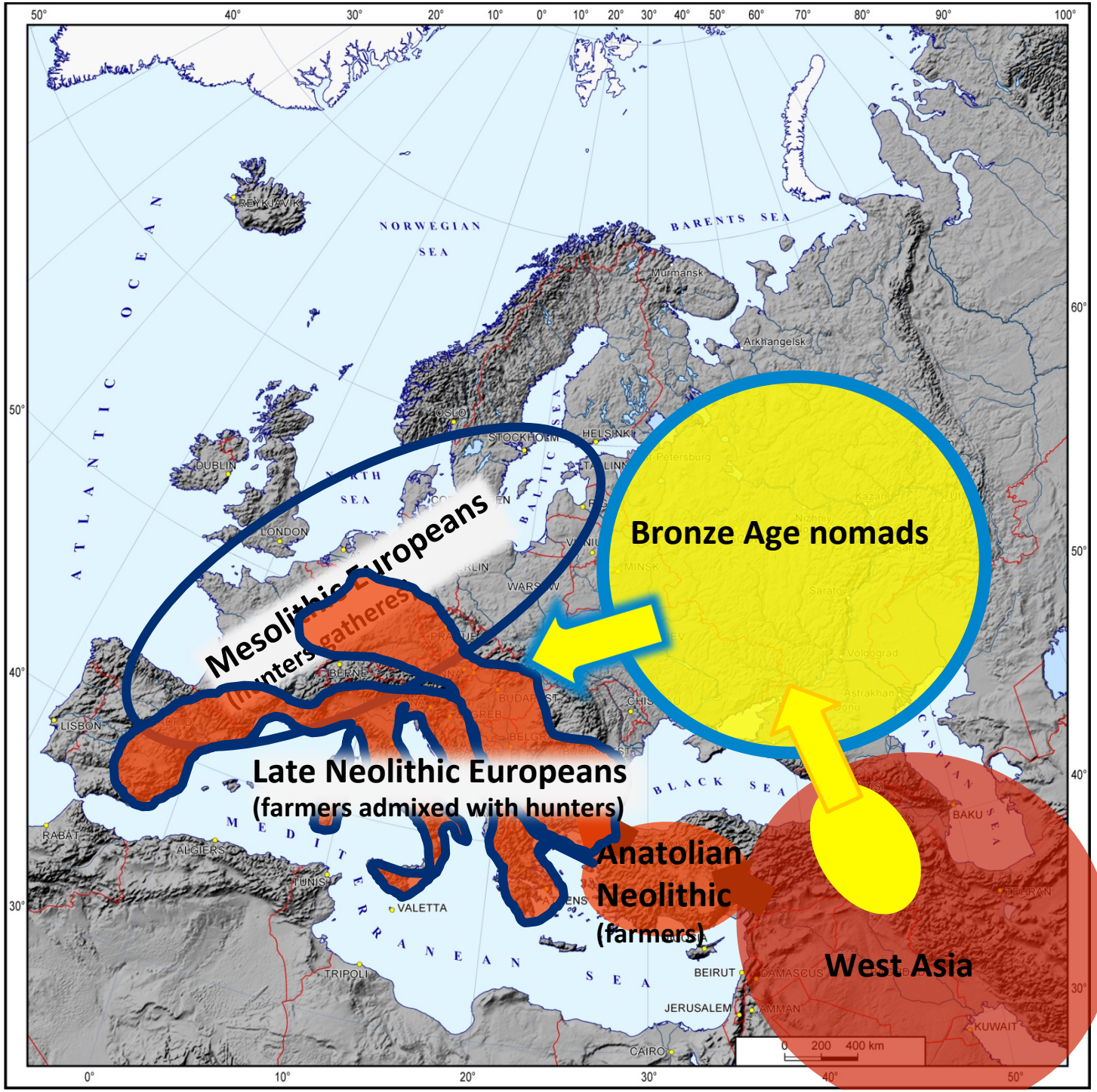
BERLIN
WARSAW
MINSK
KIEV
Volgograd
Astrakhan
BERNE
BUDAPEST
LISBON
BELGRADE
RABAT
ALGIERS
TUNIS
VALETTA
TRIPOLI
BEIRUT
DAMASCUS
JERUSALEM
AMMAN
CAIRO
KUWAIT
BAKU
TEHRAN
0 200 400 km


Bronze Age nomads
Mesolithic Europeans
(hunters gatheres)
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(farmers admixed with hunters)
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(farmers)
West Asia
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NORWEGIAN SEA
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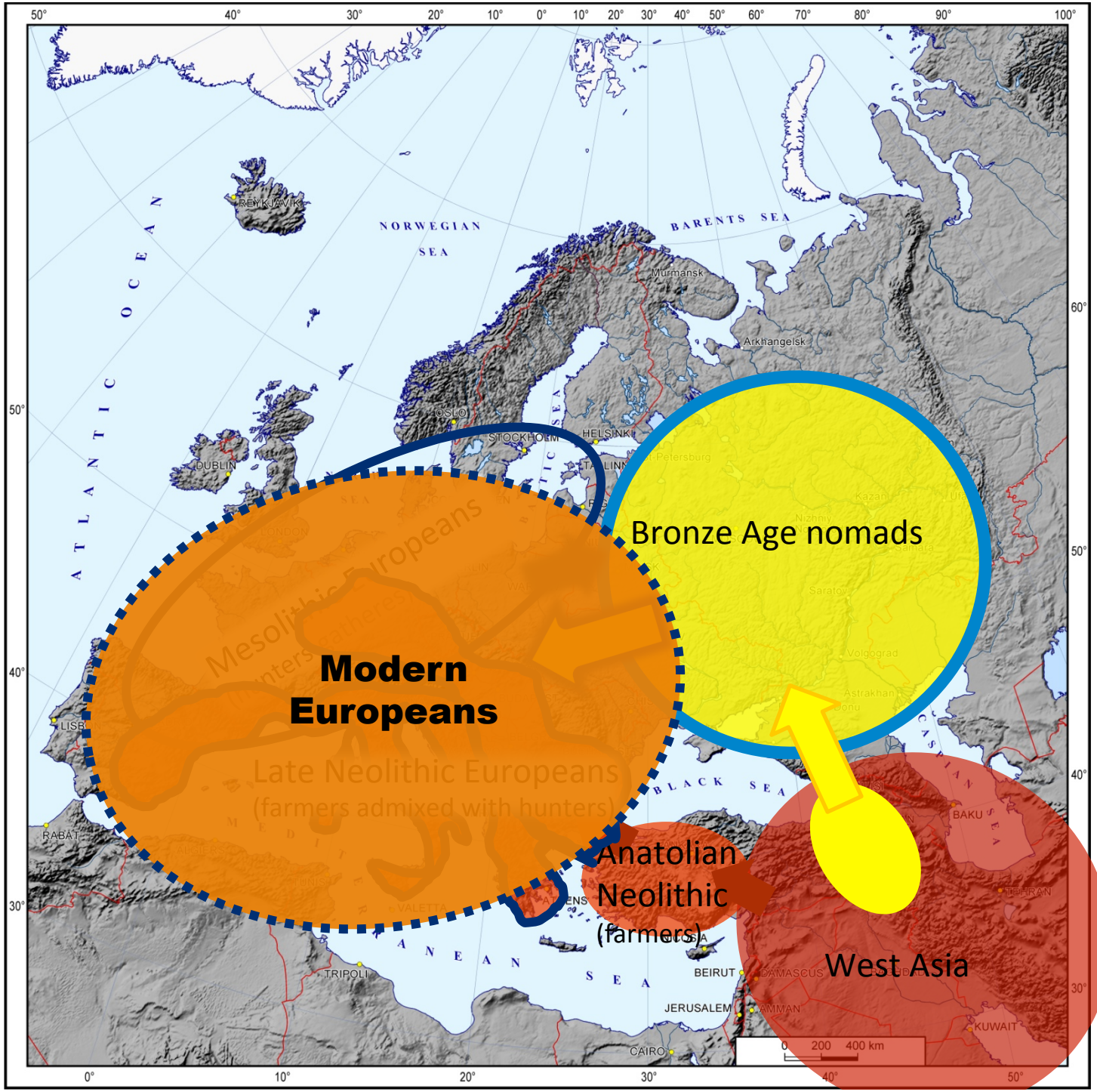
Modern Europeans
Late Neolithic Europeans
(farmers admixed with hunters)
Bronze Age nomads
Anatolian Neolithic
(farmers)
West Asia
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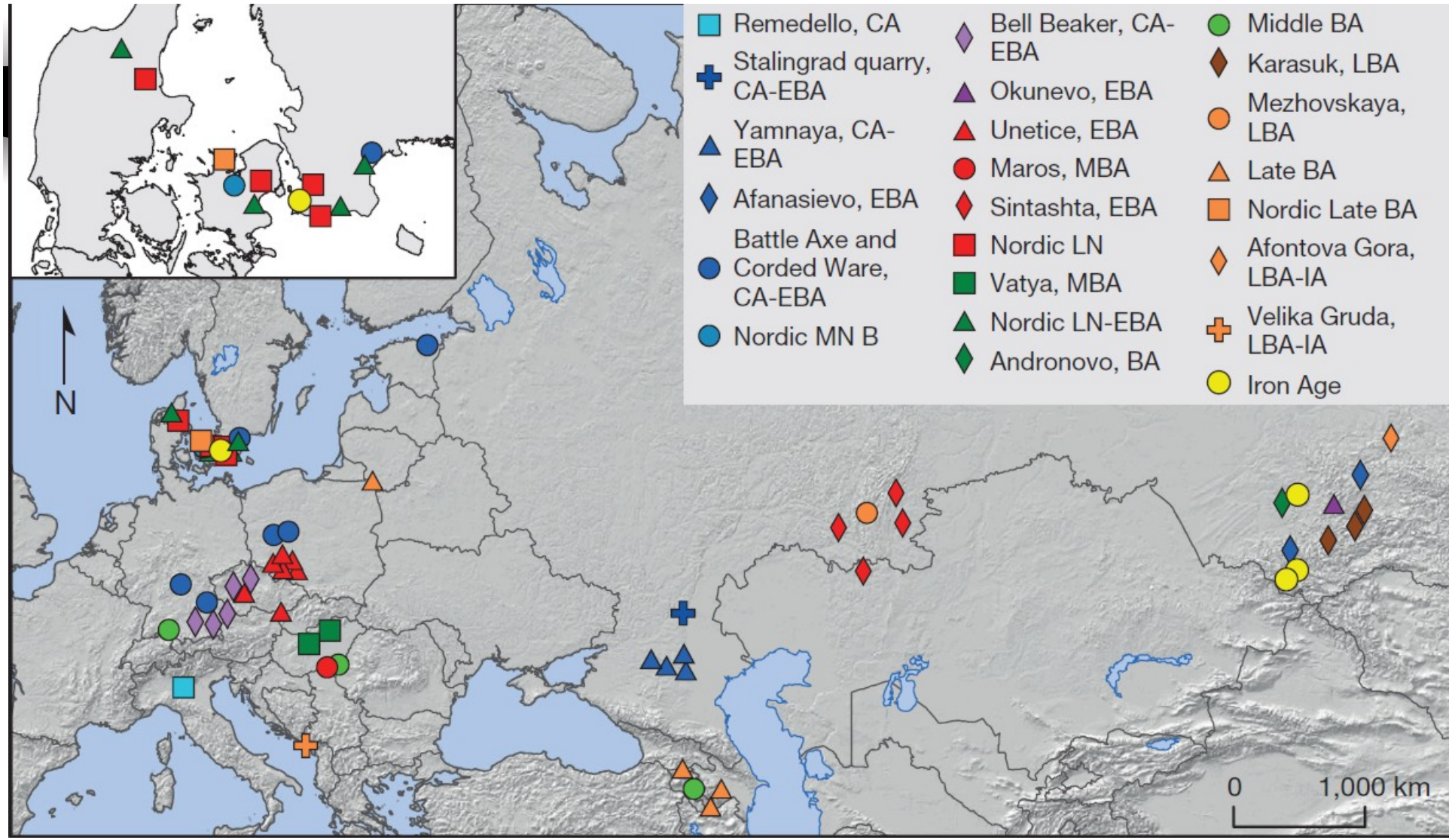
Another study, the same result
(Allentoft et al., 2015, Nature)



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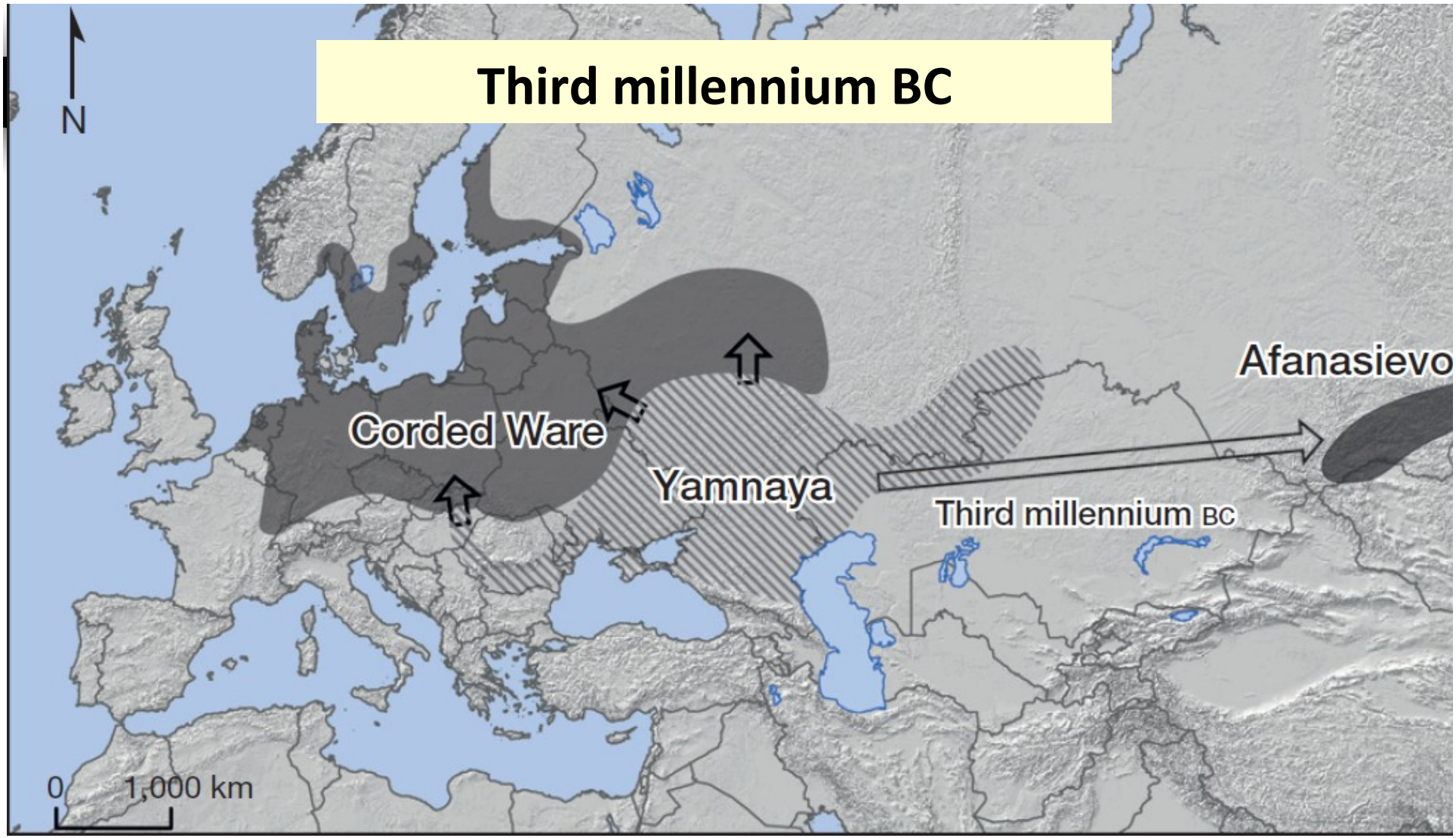

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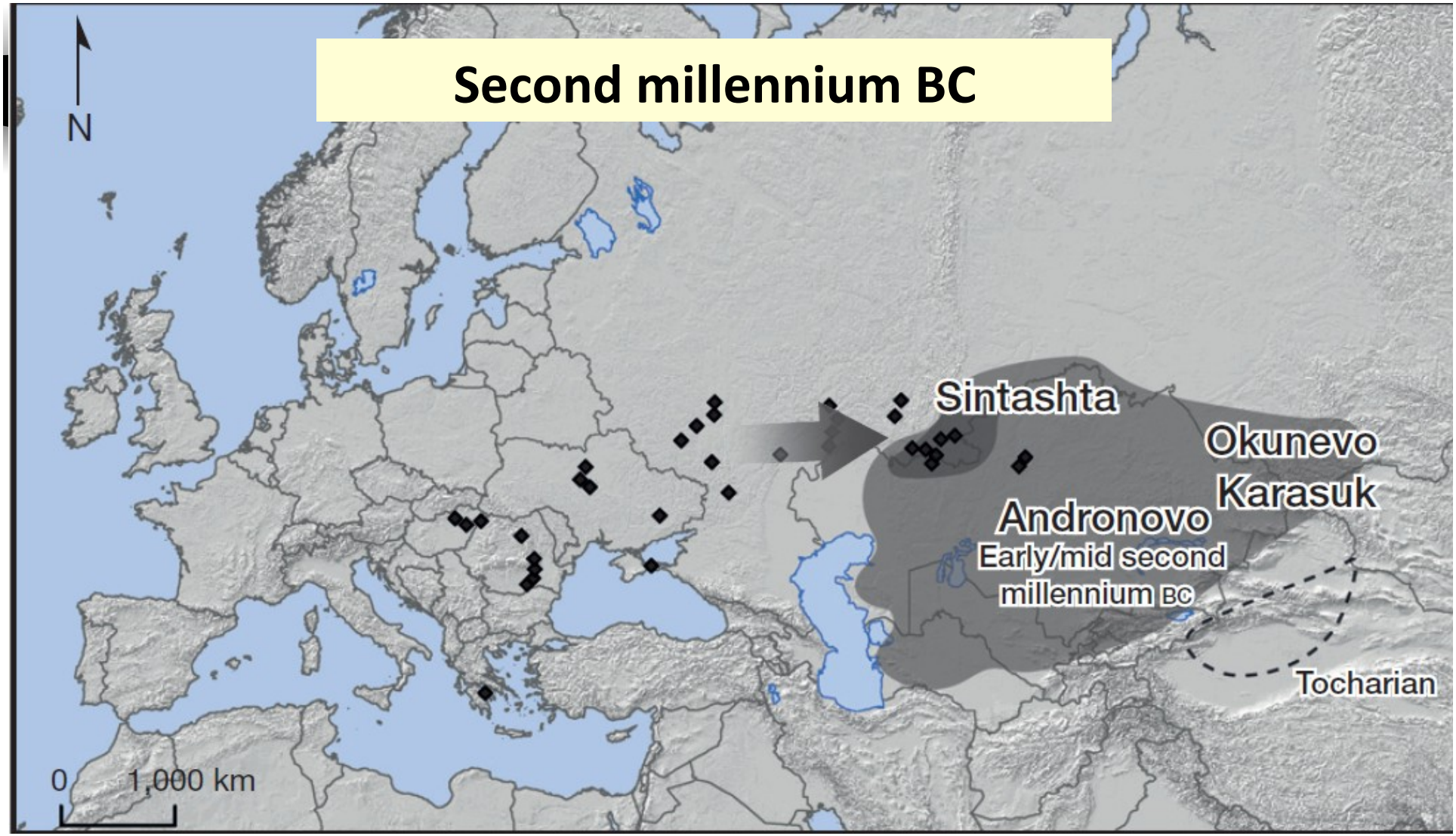


Plague in Bronze Age Eurasia

(Rasmussen et al., 2015, Cell)

The same ancient human samples have been tested for *Yersinia pestis.*

7 out of 102 samples were positive.

Comparing Bronze Age, Medieval and Contemporary *Yersinia pestis* genomes.

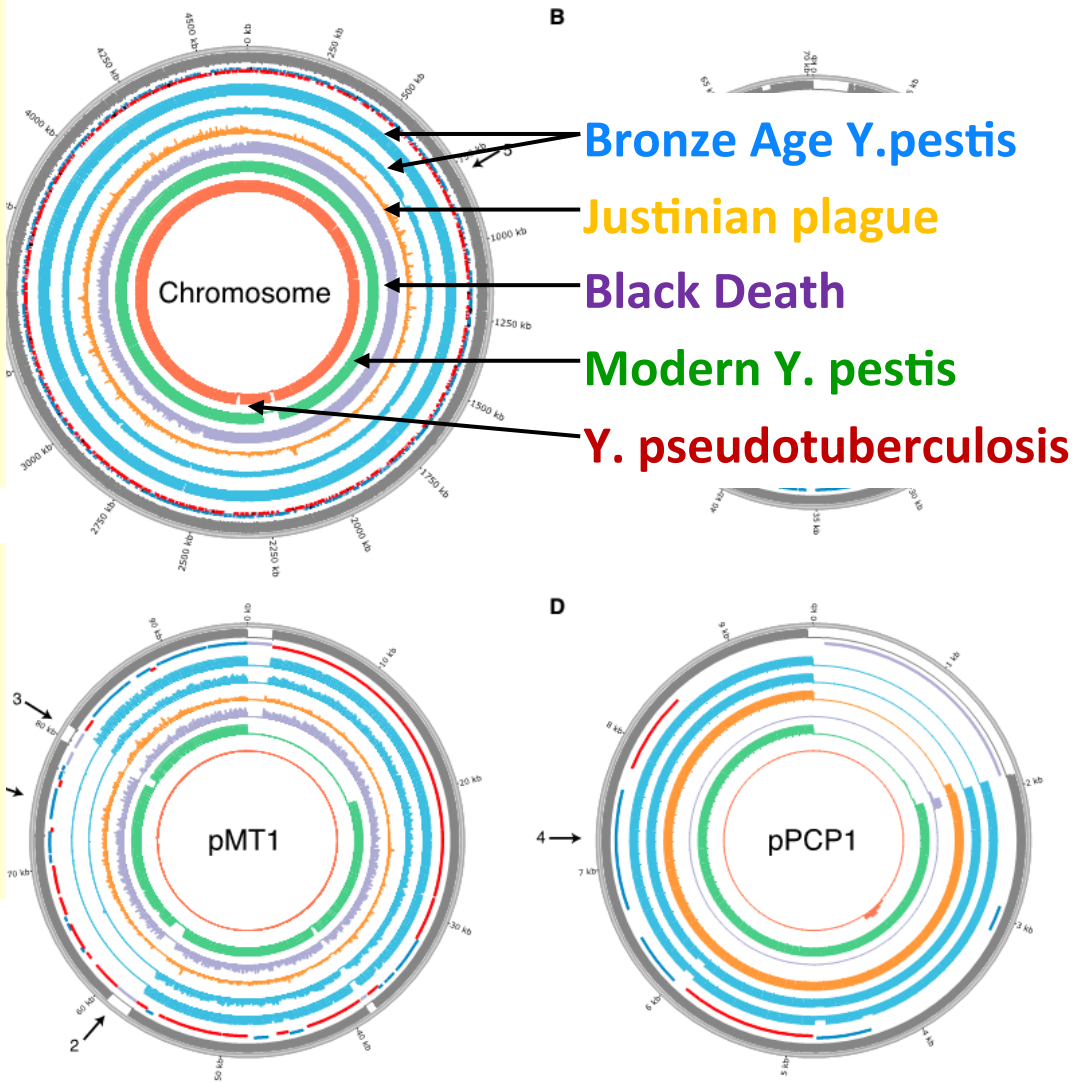
1) Bronze Age samples lacked the ymt gene on pMT1 plasmide.

The gene allows Y.pestis to be spread by rat flea.

ymt gene is first recorded in single sample dated 1700 BC, but since 1000 AD it is omnipresent (98% of Y. pestis samples) – natural selection?!

2) Bronze Age samples also lacked the I259T mutation on the pla gene.

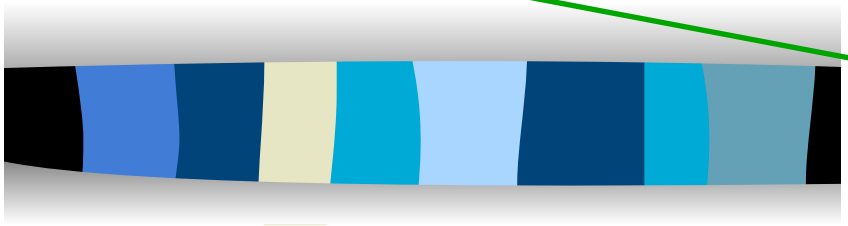
This mutation causes the bubonic form of plague.



Origin and diversity of *Yersinia pestis*

Y. Pseudotuberculosis (in blue)

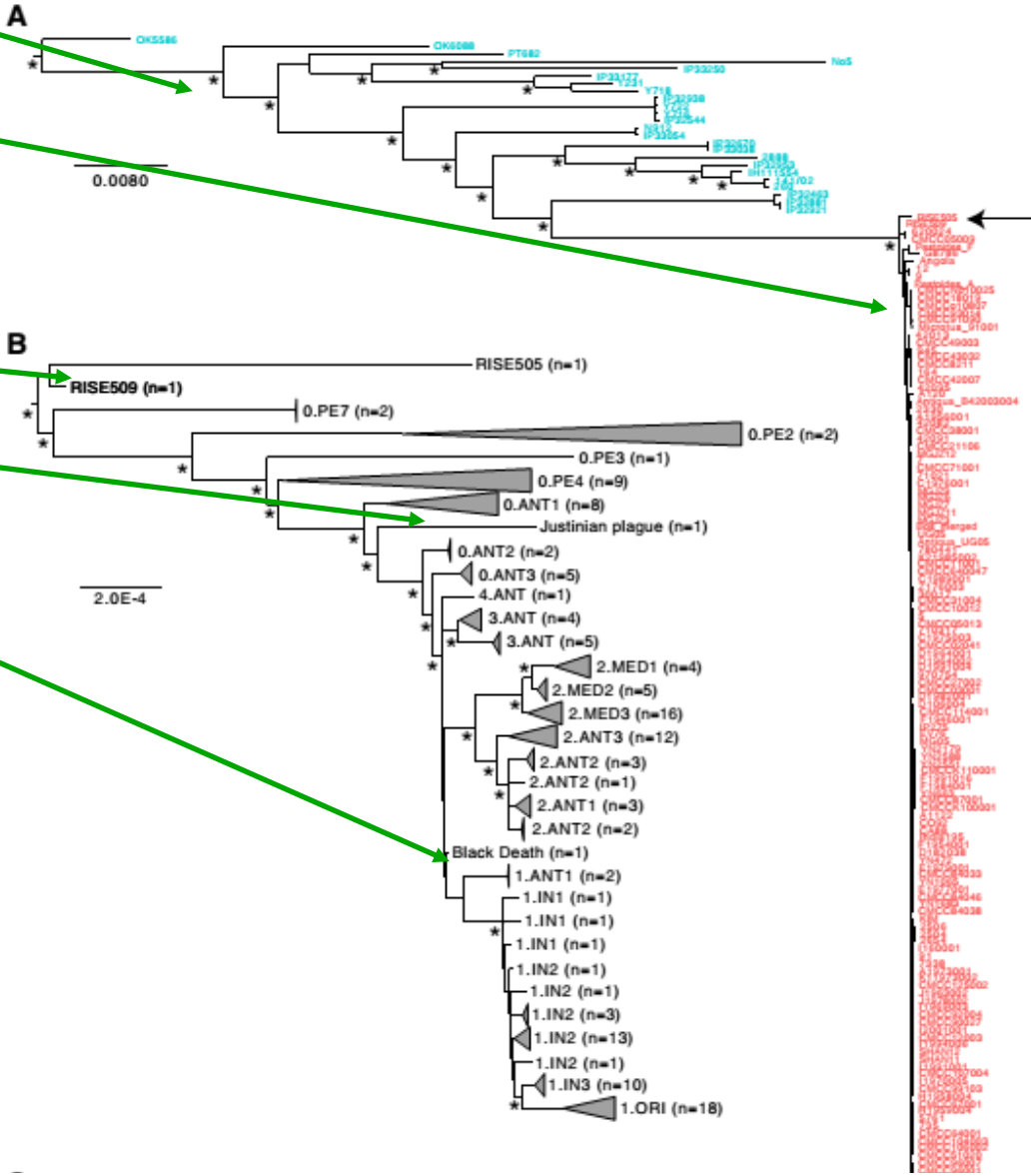
Y.pestis (in red)



Bronze Age plague (1700-2900 BC)

Justinian plague (600 AD)

Black Death (1350 AD)



Due to analysis of ancient DNA, one can directly see the evolution of Yersinia pestis:

from less virulent and less see Bronze Age samples lacked the ymt gene on pMT1 plasmide.

The gene allows Y.pestis to be spread by rat flea.

Ancient DNA and *Yersinia pestis*

Now one can directly see the evolution of *Yersinia pestis*:

from the frequent, less virulent and less dangerous disease in Bronze Age

to the medieval BLACK DEATH.

Many archeologists, linguists and geneticists believe, that Bronze Age nomads from Eurasian Steppe spoke proto-Indo-European language

– the common root of languages spoken by 3 billion people today.

Were the same nomads responsible for triggering the evolution of Y. pestis to higher virulence?

"It is plausible that plague outbreaks could have facilitated—or have been facilitated by—these highly dynamic demographic events" (Rasmussen et al., 2015).

Then, these Bronze Age events exemplifies interrelated evolution of pathogen and host.

Our team (on the geographical map) thanks your for your attention