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Spatial Genetic Heterogeneity Assessment - a regional case study

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Genetic Heterogeneity

Genetic epidemiology

Evolution

Clinical studies

Pharmacogenetics

allele frequency

F-statistics

cluster analysis

wombling

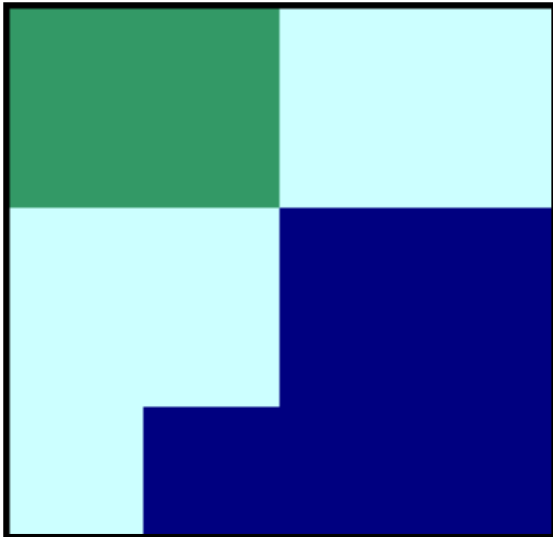
principal component analysis

spatial structure

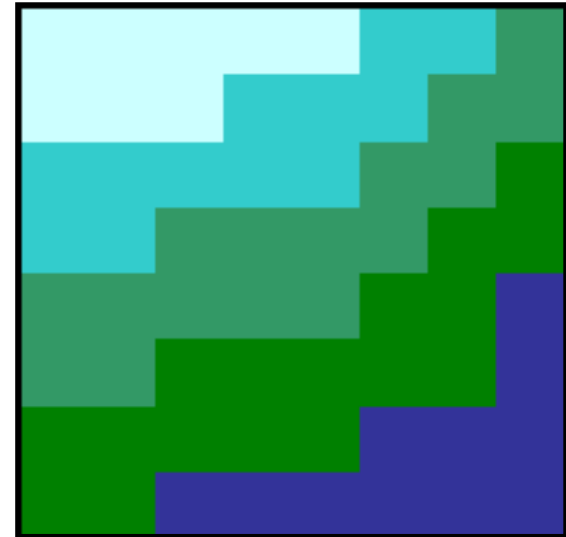
Genetic landscapes

Genetic landscapes

Clusters



Clines



Genetic Landscapes

KORA S4

Probands

- 700 probands
- ethnicity and socioeconomic information

Markers

- randomly selected markers
- 212 SNPs
- autosomal and X-chromosomal
- 1:2 intragene / intergene position

Steffens et al., 2006, SNP-Bases Analysis of Genetic Substructure in the German Population, *Hum Hered* (in press)

http://www.gsf.de/KORA/projekt_survey2000.html

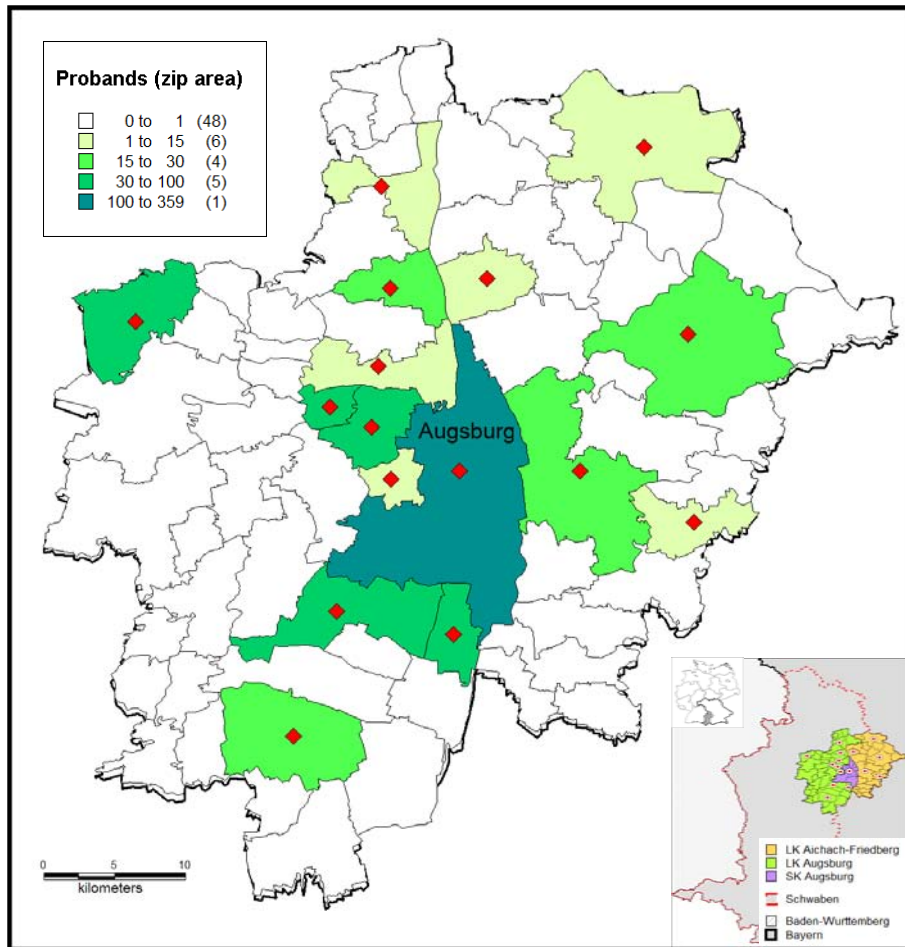


GRASS

Geographic Resources Analysis Support System

*Spatial modelling and
analysis
of genetic information*

KORA S4



Data

726 Probands

29 zip areas

187 SNPs

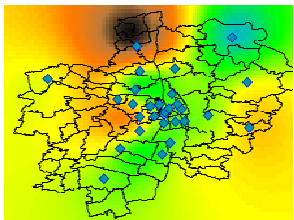
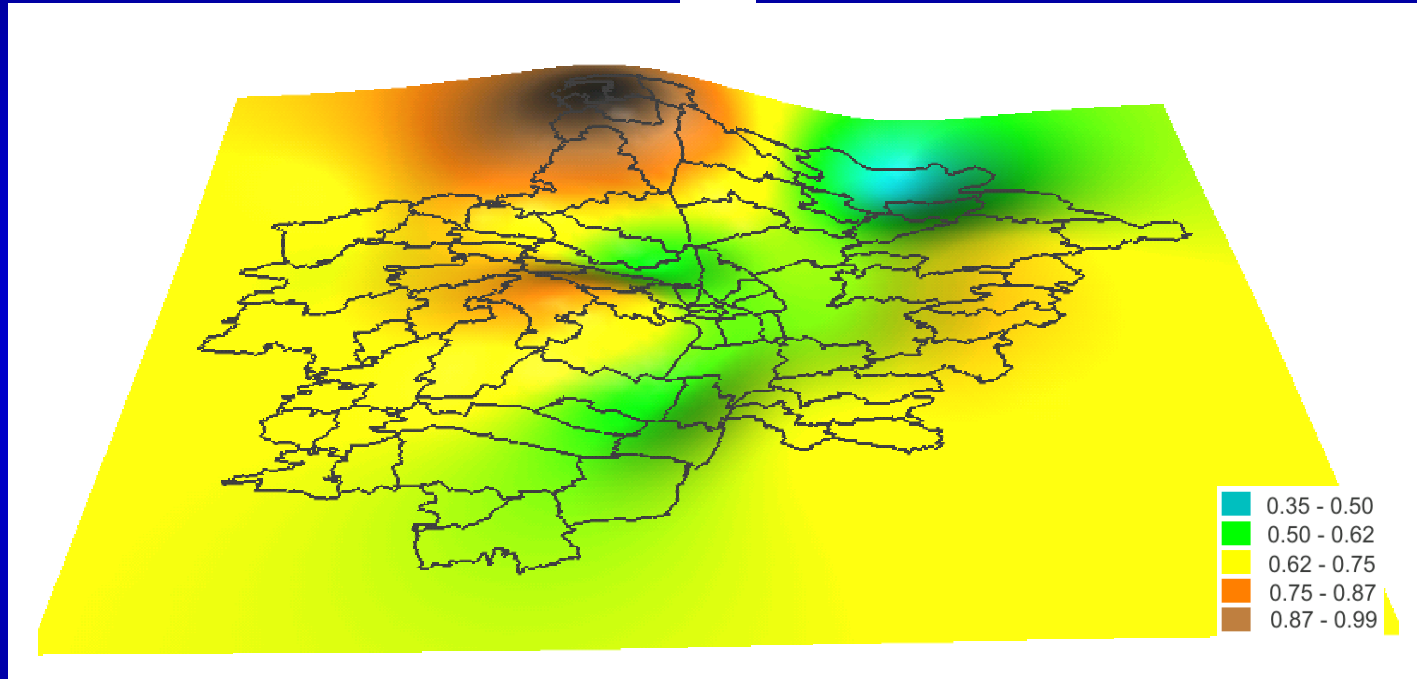
- count (minor allele)
- q = minor allele frequency
→ $f = \arcsin(\sqrt{q})$

Spatial Differentiation of Allele Frequency

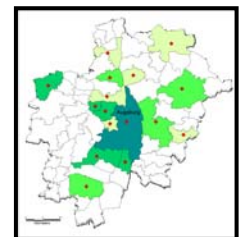
rs3625 (count)		
PLZ	ALLELE1	ALLELE2
86150	324	364
86316	20	24
86343	41	41
86356	36	52
86368	8	2
86391	5	7
86399	48	54
86405	8	14
86450	51	45
86462	14	30
86482	33	29
86495	6	10
86508	11	11
86551	31	11
86554	9	13
86830	15	17

MARKER	p-value	Postion (gene)
rs1860300	0,0062	inter
rs1997660	0,0324	intra
rs2242046	0,0174	intra
rs3625	0,0138	intra
rs4379869	0,0631	intra
rs461311	0,0128	inter
rs597354	0,0076	inter
rs717477	0,0018	inter

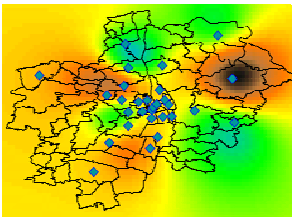
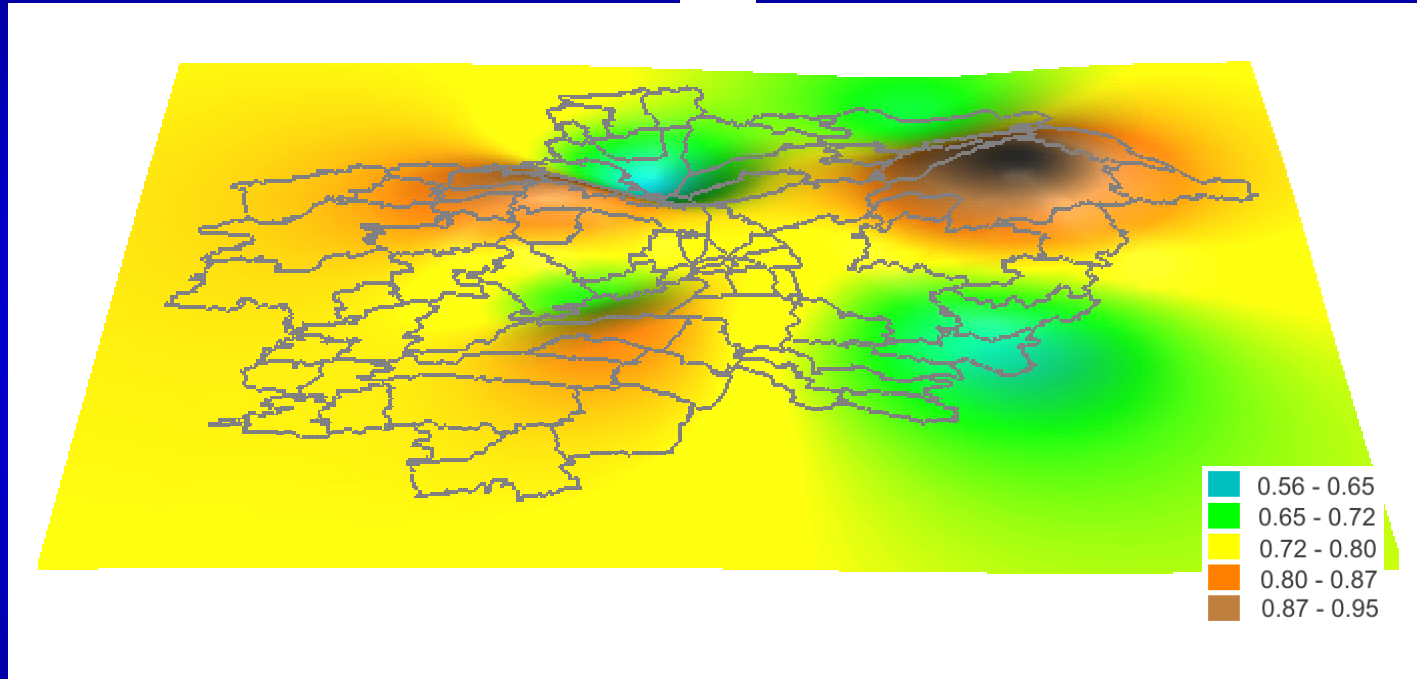
Genetic Landscapes



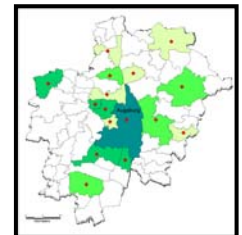
Allele Frequencies - rs717477



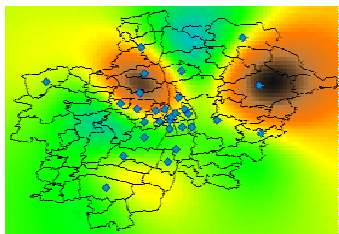
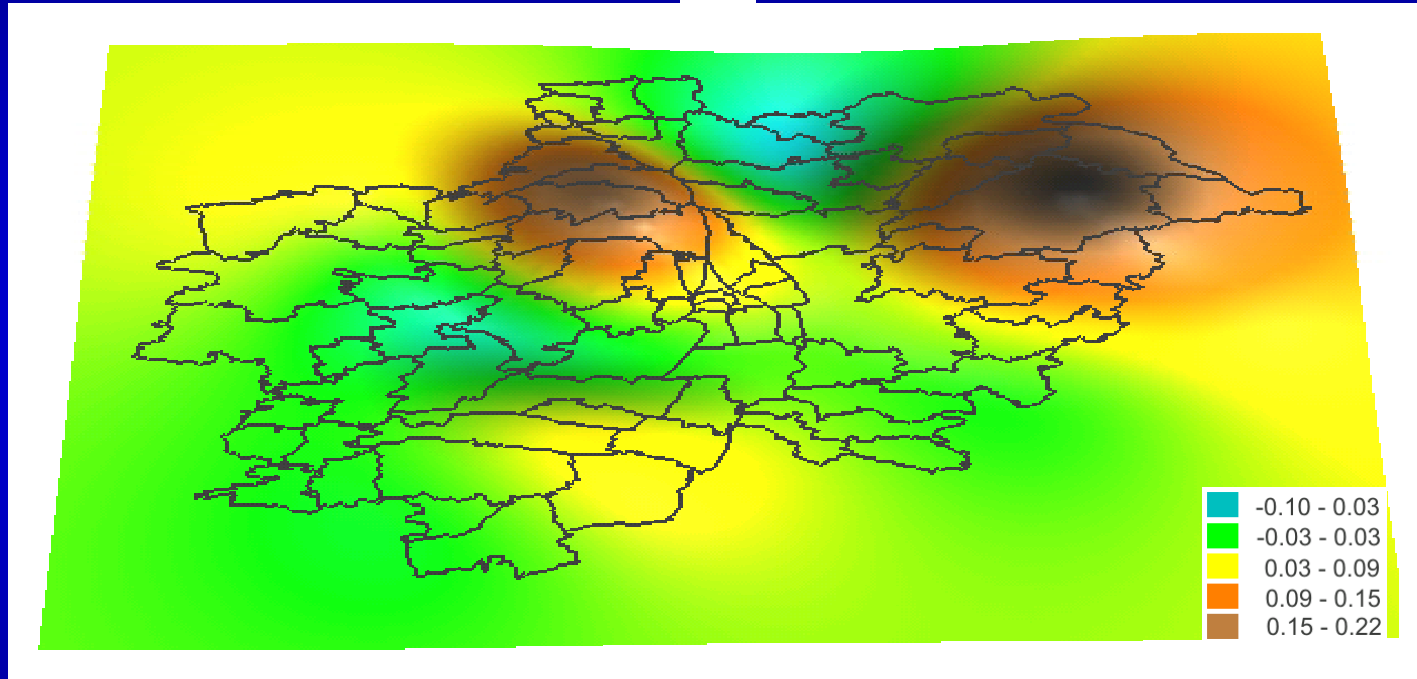
Genetic Landscapes



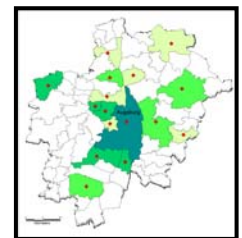
Allele Frequencies - rs3625



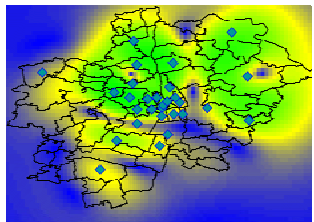
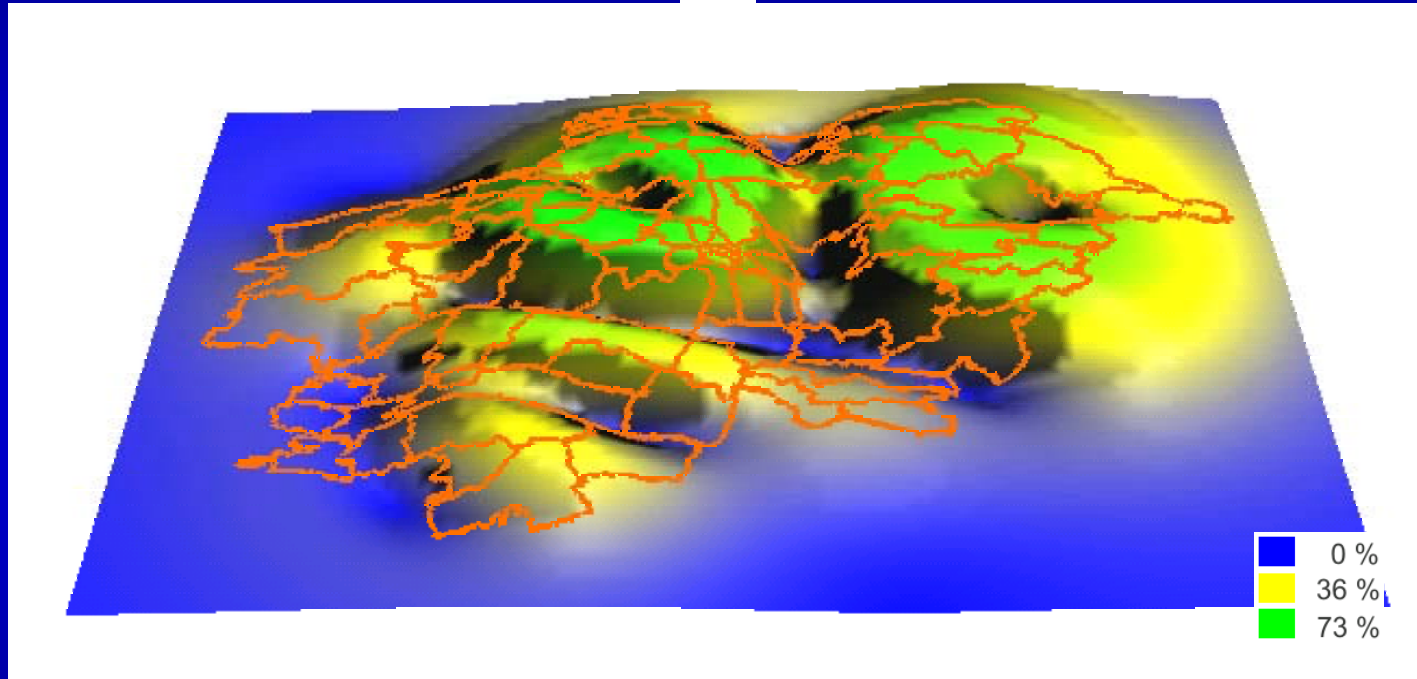
Genetic Landscapes



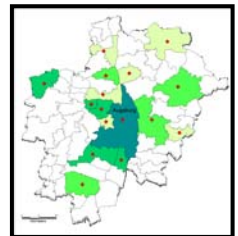
Population Specific F_{IS} - rs3625



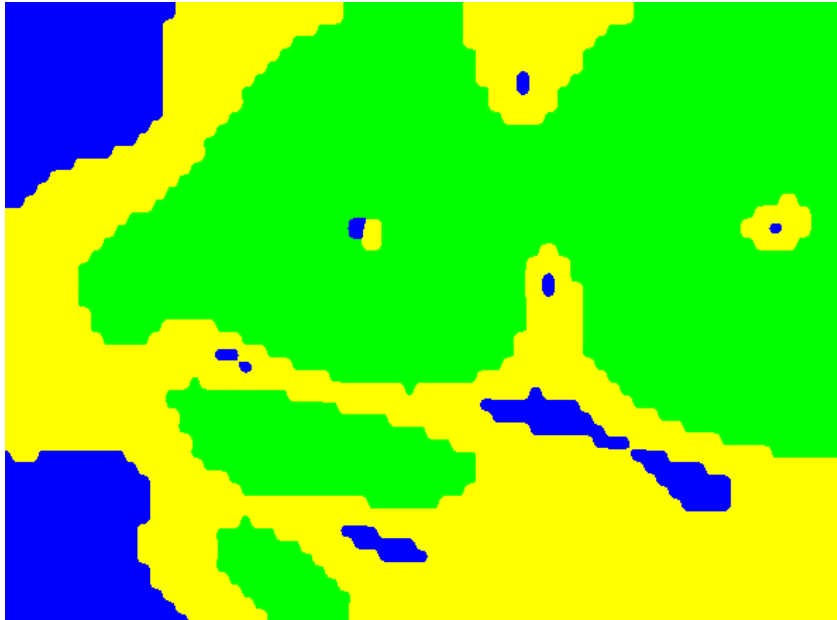
Genetic Landscapes



Slope of Population spc. F_{IS} - rs3625

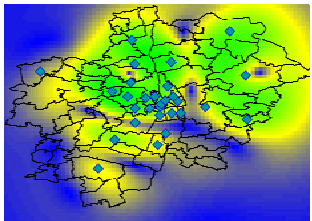


Genetic Landscapes

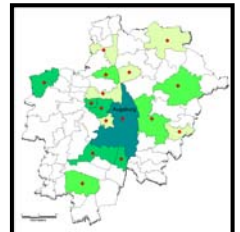


Class	Slope (%)	Pixel
1	Low < 10	100
2	Medium 10 - 30	633
3	High ≥ 30	2501

Landscape Index	Score
Patchiness (1:2:3)	high (10:3:3)
Connectivity (class: 1)	low
Fragmentation (class: 1)	high



Slope of Population spc. F_{IS} - rs3625



Conclusions

A Genetic Geographical Information System is a powerful tool for detecting, modelling and analysing genetic heterogeneity along a study region.

Spatially limited populations may contained significant genetic heterogeneity for a single allele.

The wide spread assumption of homogeneity by genetic studies should be evaluated case specifically.

Aknowledgments

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*GenGIS opens the GATE to the
third dimension in genetic studies.*

...Thank you