## International laboratory of

 statistical and computational genomicsMathematical models in population genomics and their applications

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NATIONAL RESEARCH UNIVERSITY

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## Genomics

Genomics is a multidisciplinary and data-driven science including following fields:

- Biology (genetics)

■ Mathematics

- Computer science

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Today we talk about problems of population genomics.

## What shapes the data?

## Genealogical processes: <br> DNA replication, mutations, recombinations etc.

Sequencing and genotyping: different technologies for reading DNA.


## Wright-Fisher model

Time measured in generations. Constant population size $N$.

## Number of siblings and $p$-th cousins

$p$-th cousins are individuals sharing ancestor $p+1$ generations ago.

## Theorem

The expected proportion of individuals with at least one p-th cousin in a sample of $K$ individuals is approximately $1-e^{-2^{2 p-1} K / N}$ in a diploid dioecious Wright-Fisher population of size $N .{ }^{1}$
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## How lucky was the genetic investigation in the Golden State Killer case?

Posted on May 7. 2018
Last week, police arrested Joseph DeAngelo as a suspect in case of the Golden State Killer, an infamous serial murderer and rapist whose case has been open for over forty years. The arrest is huge news in and of itself, but for people interested in the social uses of genetic data. the wav in which DeAngelo was identified-using genetic genealogv \& genetic data
${ }^{1}$ Shchur, Nielsen (2018) On the number of siblings and p-th cousins in a large population sample. Math. Biol.

## Genealogical and genetic relatives

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## Genealogical and genetic relatives

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## Genealogical and genetic relatives

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## Genetic databases growth



- 2018 by Leah Larkin, www.theDNAgeek.com; Source: ISOGG wiki "Autosomal DNA testing comparison chart" edit history


## Number of genetic cousins

Police found between 10 to 20 genetic $p$-th cousins of Golden State Killer. Then they use civil records to narrow the search to a single extended family.


## What is a genome?

- A DNA molecule is a sequence of four nucleotides: cytosine $(\mathrm{C})$, guanine $(\mathrm{G})$, adenine (A) and thymine ( T ).
- A genome is the genetic material of an organism consisting of DNA (or RNA for some viruses). It includes genes and non-coding regions and packed and organised into chromosomes, each of which is a long DNA molecule.


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## Some numbers

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Maternal

## Coalescent model

- Wright-Fisher model.



## Coalescent model

- Wright-Fisher model.
- Sample genealogy.



## Coalescent model

## 

- Wright-Fisher model.
- Sample genealogy.
- The internal nodes of the tree corresponds to the most recent common ancestors of two lineages.



## Coalescent model <br> limiting distribution of WF model

Backward continuous time. Sample size $K \ll N$.

## Coalescent with recombination

Continuous Markov process.

## Sequentially Markov Coalescent (SMC)

Markov process along the genome.

## Inference under SMC

- Coalescent Hidden Markov Model.
- PSMC method ${ }^{1}$

■ MCMC algorithms.
■ BEAST2 package ${ }^{2}$
${ }^{1} \mathrm{Li}$ and Durbin (2011) Inference of human population history from individual whole-genome sequences. Nature
${ }^{2}$ Bouckaert, R. et al. (2019) BEAST 2.5: An advanced software platform for Bayesian evolutionary analysis. PLoS Comput. Biol.

## PSMC

■ Hidden states: times to the MRCA.
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## Human population size



## Inference under SMC: challenges

- Population structure (migration, non-random mating etc) might affect the inference.
■ Most methods rely on variant calls.
■ We develop three PSMC-inspired methods to infer migration and population split times.



## Covid-19 pandemic

- 211 SARS-CoV-2 sequences (March 11-April 23).
- Including 52 sequences from Vreden Institute of Traumatology.
- Some samples have known travel data.


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## Genomic epidemiology of the early stages of SARS-

 CoV-2 outbreak in RussiaAndrey B Komissarov, © Ksenia R Safina, Sofya K Garushyants, Artem V Fadeev, Mariia V Sergeeva, Anna A Ivanova, Daria M Danilenko, Dmitry Lioznov, Olga V Shneider, Nikita Shvyrev, Vadim Spirin, Dmitry Glyzin, Vladimir Shchur, Georgii A Bazykin
doi: https://doi.org/10.1101/2020.07.14.20150979

## Epidemiology in Russia

■ We combine ML-tree (Russian sequences and 19623 world-wide sequences from GISAID) with travel data.

- We did not find any direct imports from China.
- Expected number of introductions for our dataset is 67 separate events.


## Epidemiology in Russia



## Epidemiology in Russia

a France|Feb-26
Denmark|Mar-10
Non-Russian sequences with later dates (13)

Russia
Algeria
Fujian
North America
NanChang
Europe
Africa
South America
Australia
-IIRussia/StPetersburg-3524/2020|Mar-15
b
Saudi Arabia|Mar-10
Non-Russlan sequences with later dates (35)
Asia
Europe
-Russia/Chechenya-83801/2020|Mar-26

1

C Israel|Mar-17
USA|Mar-13
Australia|Mar-18
Non-Russian sequences with later dates (2)
Austr
Asia
North America

- Russia/StPetersburg-RII4386V/2020|Mar-29
d New Zealand|Mar-02 Asia|Mar-01 North AmericalFeb-27 Australia|Mar-06
Europe|Feb-29
South America|Mar-07
Travel history
I| France
Eermany

Non-Russian sequences with later dates (656)
II Italy

- No travel

Russia/StPetersburg-RII8289S/2020|Apr-21 ERussia/StPetersburg-RII8275S/2020|Apr-21 Russia/StPetersburg-RII7555S/2020|Apr-21 Russia/StPetersburg-RII8955S/2020|Apr-22 Russia/Novosibirsk-84101/2020/Mar-27 Russia/StPetersburg-RII7520S/2020|Apr-20 - Russia/StPetersburg-RII4655S/2020|Apr-05 Russia/StPetersburg-RII8913S/2020|Apr-23 Russia/StPetersburg-RII7505S/2020|Apr-20 Russia/Buryatia-84504/2020|Mar-27 Russia/StPetersburg-R118317S/2020|Apr-21 Russia/SCPM-0-07/2020|Mar-22

- Russia/StPetersburg-RII6056S/2020|Apr-15 Russia/StPetersburg-RII7896S/2020|Apr-21 Russia/StPetersburg-RII6060S/2020|Apr-15 Russia/Perm-82707/2020|Mar-24
Russia/StPetersburg-RII6043S/2020|Apr-14 Russia/Sakha-89702/2020|Apr-01 Russia/Moscow-351/2020|Apr-02 Russia/StPetersburg-RII7656S/2020|Apr-20
- Russia/StPetersburg-RII4328S/20201Mar-25 Russia/StPetersburg-RII6065S/2020|Apr-15 Russia/StPetersburg-RII6065S/2020|
Russia/Ulan-Ude-RII4562V/2020|Mar-25
I| Russia/StPetersburg-RII4332S/2020|Mar-25 Russia/Buryatia-87105/2020|Mar-30 Russia/StPetersburg-64304/2020|Mar-13 Russia/StPetersburg-RII7488S/2020|Apr-20 Russia/Buryatia-87104/2020|Mar-30 Russia/Primorskiy-79001/2020|Mar-22 Russia/StPetersburg-RII7603S/2020|Apr-21 Russia/Vector 84801/2020|Mar-27 Russia/Buryatia-87106/2020|Mar-30 Russia/StPetersburg-RII7545S/2020|Apr-20 Russia/StPetersburg-RII7039V/2020|Apr-16 Ussia/Tatarstan-82208/2020|Mar-24 Russia/Buryatia-84508/2020|Mar-27 Russia/Buryatia-88903/2020|Apr-01 Russia/StPetersburg-RII4532V/2020|Apr-03


## Vreden hospital outbreak

■ At least three separates introductions.
■ Slower spread after quarantine.


## Vreden hospital outbreak

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## International laboratory of statistical and computational genomics

■ Job opportunity for PostDoc/Researcher position.
■ PhD or candidate degree in mathematics, computer science, physics or similar.
■ Please contact me vshchur@hse.ru.

