

Measure of unevenness in human genomes, described as a self-affine phase transition in a "spin-chain" model.

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1 Abstract

Non-Gaussian distribution of polymorphic positions across a genome can substantially influence the results of any approach to molecular evolution based on a "classical" probability model. The infinite dispersion of non-Gaussian perturbations is a challenge in an attempts to accept it in a probability-based model of evolution.

Here a model is proposed where non-Gaussian distribution is introduced to an exact solution of the "Ising model"; it describes a behavior of one-dimensional chain of spins in an approaching to a phase transition. The distribution of fragments which are identical between two genomes is similar to distribution of islands of spins with the same orientation, in the model where non-integer dimension is introduced.

Application of this model allows to compare the relative contributions of non-Gaussian perturbations for pairs of human genomes from different ethnic groups. An evolution of the three human races in a most compact presentation is considered, rates of development on the separated stages of the evolution are assumed to be proportional to a value of relative unevenness between the appropriate groups of genomes. In the resolved model, the meaningful details of the separation between Asian and European races are clarified, in a period around ten thousands years ago; a particular viewpoint to the separation of the African race is also presented.

2 Introduction

The issues about an unevenness of a genome arose in particular in a distribution of coverage of sequencing reads mapped to a genome [1]. There, the deviations of a reads coverage from a "classical" Lange-Waterman model, which was constructed following a Poisson distribution for short genome fragments, reflects some features of self-affinity for most frequent genome fragments, in addition to the previously observed over-dispersion of a "Poisson" peak. There, the effect was observed stably in several analyzed genomes and is to be treated as a robust enough phenomenon to be discovered further and in deep.

The features of self-affinity in DNA sequences were detected at the very early days of the genomics, in a classical work of Peng et al. [2]; a definition of the fractal dimension for the one-dimensional series was proposed there, and DNA sequences were a model of "fractal"-like series. The self-affinity features in a phenomenon imply an influence of perturbations with infinite dispersion, or a presence of a so-called "fat-tail" in their probability distribution, and these features are difficult to detect and describe.

Here, an approach is proposed to detect and apply a measure to these "perturbations" focusing on the mentioned phenomenon which was observed in coverage distributions. A relevance of a proposed research is demonstrated on a model of evolution of humans restored from some of the present-day human genomes; confusions which are accumulated in solving of this scientific problem were in fact a motif to drive out the research.

3 Methods

Self-affinity features are a property of "transitional" period, and a description of these features is borrowed from approaches to a so-called "Ising model", the model where a phase transition in a mutual orientations of spins in a crystal is explained. A heating of magnetic crystal leads to abrupt disappearance of magnetic momentum, and an approximation of this phenomenon is simulated in the Ising model. In a very simplified form, the interactions in crystal are presented there as an increase of energy if two spins in a linear chain are oriented in the same direction, and a critical temperature of phase transition (T_c) is derived from a strength of these interactions ("coupling constant").

The cooling lead in turn to a sudden appearance of magnetic momentum, and a decrease of a temperature close to a critical temperature leads to accumulation of "islands", long enough fragments where spins are oriented in the same order. Ordered fragments in a one-dimensional spin chain can be compared to identical fragments of genome sequences, and a distribution of these fragments allows to describe there the features of self-affinity.

In the context of statistical physics, an expression for the probability of island of length k was presented in [3], as an applied case of the so-called "Landau-Zener transition": $p(k, \tau) \sim e^{\tau k^2}$

This is a point where a distribution with infinite dispersion can be introduced, assuming that a power coefficient 2 in this Gaussian-like distribution is substituted to some floating power coefficient $D < 2$, a dimension of "intrinsic" self-affinity of the under-laid process. The model constructed above depends on the two flexible parameters, intrinsic dimension D and a parameter τ , a rate of cooling, or a rate of approaching to a transitional phase. This model allows to explain over-dispersion of the genome coverage distributions mentioned above (fig. 1) and to fit the parameters to a measure of unevenness of human genomes, trying to reconstruct most precisely their evolution. The distribution of "islands" for human genomes can be obtained as distribution of lengths of completely identical fragments in the genomes; lists of polymorphic positions from "1000 genomes" project [4] were used as a representation of genomes. Similar distribution of fragment sizes is observed for this data (fig. 2A). The clusters for the three races are clearly seen for both genetic distance and for tails of "island" sizes in genome-genome comparison (fig. 2B). To inter-

pret this, higher unevenness relatively to same genetic distance means higher "equilibration rate", higher mutation rates, and a lesser slope of a fitting line.

4 Results

For the two independent populations, the distance does not depend of heterogeneity in populations; a simple model of exponential development can provide a dependency of average genetic distance within population.

The simplified model of evolution of human ethnic groups is shown in fig. 3, and for further consideration it was reduced to just clarify a separation between three human races. In this case, the model can be further reduced to a system of equations (2). The events which are assumed here as events of separation between races are (a) separation between modern Asians and modern Europeans, which happened nearly just after an expansion to America, about ten thousands years ago; and (b) expansion of modern humans to Eurasia, about fifty thousands years ago.

In the provided equations the mutation rate r for humans is supposed to be fixed, conventionally it is accepted to be about 10^{-9} substitutions per nucleotide per year. The two types of averaged similarities within a race and between races which are clearly seen in fig 2 are provided in table 1 in the appropriate units.

The mutation rate 10^{-9} per nucleotide per year can be transformed as 3 per genome per year = 3000 per genome per t.y., 3000 mutations per 700000 SNP, so that r in the equations above should be about 0.004. Having a requirement that $p_0 \geq 0$, the r should be less than 0.0029. Rates of development are assumed to be unknown, what is only known is a dependency between a rate of development and a linear coefficient m . Values of $b_a, b_e, b_A, p_{ae}, k_{ae}$ which are attributes of a passed history are also assumed to be unknown.

For a marginal but the most confident assumption, $p_0 = 0, p_{ae} = 0.21, k_A = 1.65$ and $k_{ae} = 1.81$. Unevenness in a comparison between groups is a weighted average of evolutionary paths from a time of separation, so that if $k_A = m_A$, $k_e = m_e$, then $k_{ae} \sim (m_{Ae}T + m_A(T + t) + m_e t)/2(T + t)0.0141$. Following a log-linear approximation, k_a and k_e , for modern Asians and Europeans, should be about 1.74 and 1.76.

The genetic diversity of Asians in a time of separation is than estimated as 0.15, much lower than a pool of genotypes just before the separation ($p_{ae} = 0.21$). For Europeans, the pool of genotypes was wider, about 0.20.

What is known is that Eurasia is a continent with good communications, and that it was populated mostly by ancestors of present-day Asian race before the time of last separation, or "crash", in better words. It is also known that ancestors of modern Europeans become to expand to Europe mostly after that "crash", developing slowly before it somewhere in an area of central Asia mountains. The wide expansion to Eurasia, for ancient pre-Asian race, was characterized, instead, by a substantive increase of genome unevenness. Some of it now is lost, some is kept in native Americans, and, for modern Asians, the instabilities in diverged genomes were neutralized by a long enough period of a stable slow development after the crash.

5 Conclusions

Selection of individuals was almost the same as in [5], the difference with that model is that non-Gaussian features in genomes are considered here explicitly. This has a substantial influence to a reconstructed history of the three human races. Dealing with self-affine phenomena is difficult and risky, but it by no way can be ignored in any of valuable challenges to a present-day science.

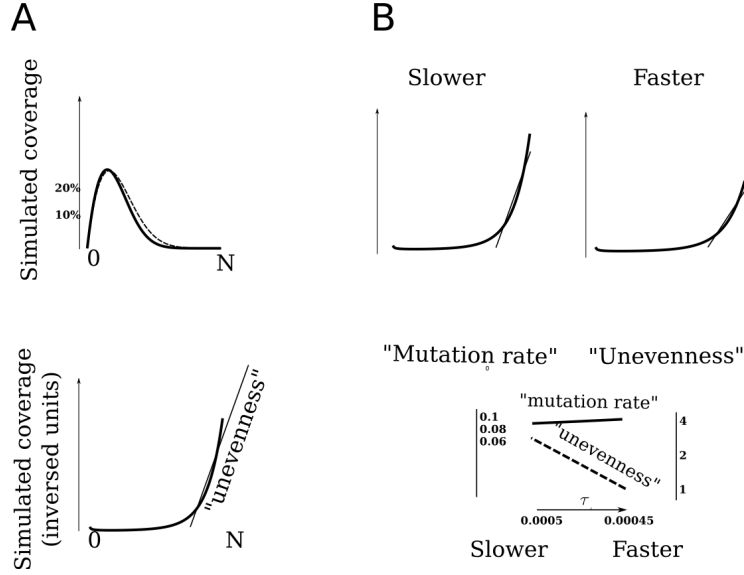
6 Formal declarations

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- Acknowledgements are intentionally omitted.
- Source codes of the scripts and intermediate data are deposited to zenodo.org (10.5281/zenodo.4362224).

7 References

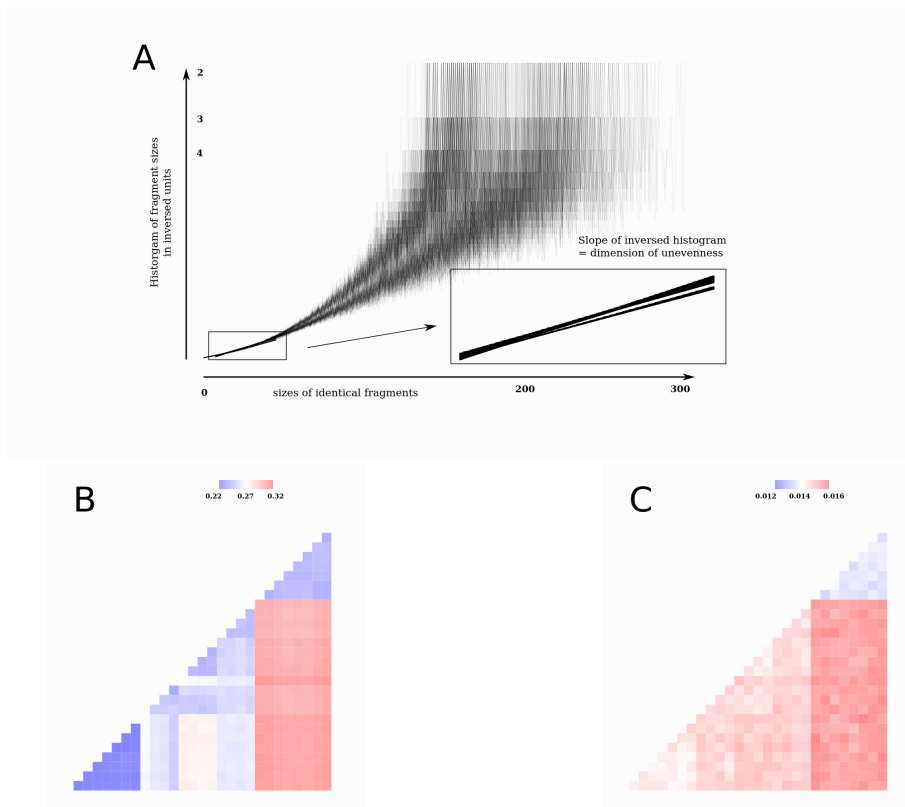
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Figure 1



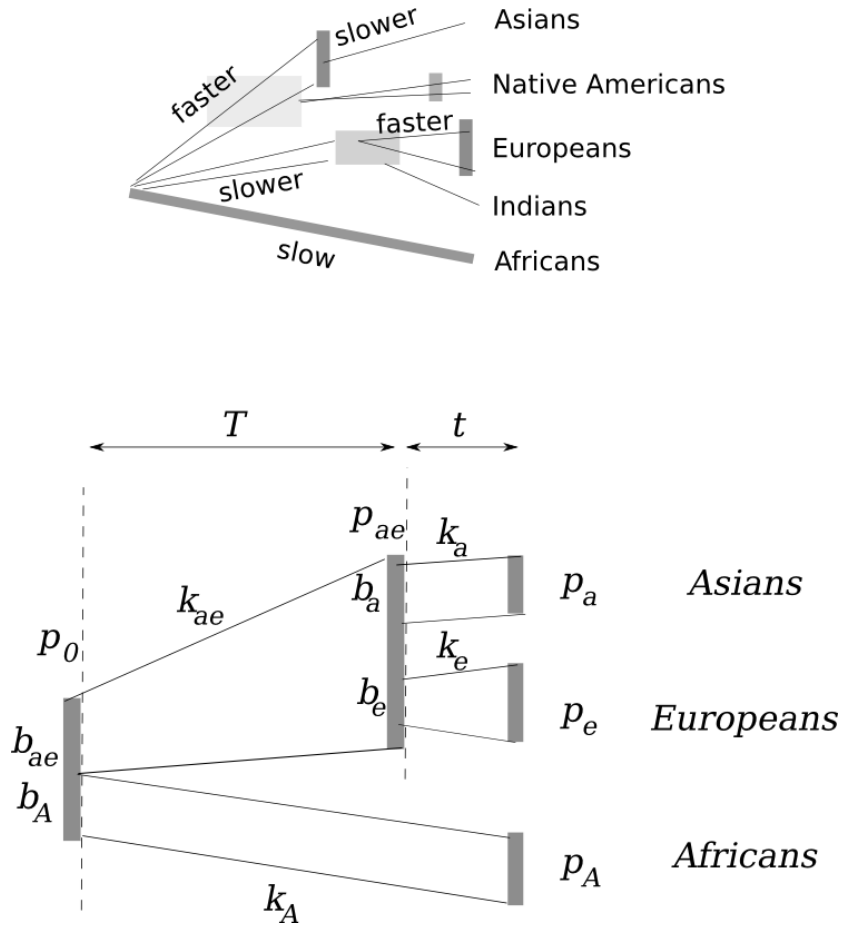
(A) Simulation of over-dispersion effect in a genome following modified Ising model of islands in a chain of spins. Here, $D = 1.9$, $\tau = 0.0005$, number of spins $N = 200$. Dashed line, $ke^{\tau k^2}$, emulates an ordinary Poisson distribution, τ is the same. (B) Dependency between estimated fitting coefficient, average of distribution, and underlying closeness to "phase transition".

Figure 2



(A) Distribution of fragments sizes in human genomes in a pairwise comparison. (B,C) Measures of closeness between genomes: genetic distance (B) and unevenness of fragment sizes (C). Here, races are, from left to right, from bottom to top: Asia, Mexico, Europe, India, Africa.

Figure 3



Simplified presentation of human evolution. p_a, p_e, \dots - heterogeneity of genomes within a communicating group; d_{ae}, \dots - distance between genomes of separated groups; b_e, b_a, \dots - relative heterogeneity of a group in the events of separation between groups. k_a, k_e, \dots - rates of "exponential" development.

Table 1

Approximated averaged similarities between human races and within a race, accordingly to the detailed chart in Fig. 2.

Races		"unevenness" m	genetic distance p
Europe	Europe	0.0138	0.25
Europe	Asia	0.0144	0.27
Asia	Asia	0.0137	0.22
Europe	Africa	0.0152	0.29
Asia	Africa	0.0153	0.29
Africa	Africa	0.0131	0.24