

A Framework Including Recombination for Analyzing the Dynamics of Within-Host HIV Genetic Diversity

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Short Abstract — Recombination plays important role in shaping within-host HIV genetic diversity, it gives an advantage to the virus to escape the pressures from the immune system and HIV antiviral drugs. I present a novel population genetic model and a computationally tractable framework including recombination for analyzing within-host HIV dynamics at the genomic level. Application of the framework on serial samples of HIV DNA sequences from 9 HIV-infected individuals shows that the model has more power for mimicking within-host HIV dynamics at genomic level and illustrates the interaction of recombination and selection on the dynamics of within-host HIV diversity.

Keywords — modeling HIV recombination, simulation method for serial samples, within-host HIV dynamics, coalescent-recombination model, population genetics.

I. INTRODUCTION

THE recombination has an important role in shaping the dynamics of HIV genetic diversity in HIV-infected individuals, particularly making the virus capable of escaping the pressures of antiviral drugs and immune system [1]. Therefore, it is of great interest to model this process at the HIV genomic level in HIV-infected individuals. In contrast to the existing methods in the literature, this study [2] develops a novel population genetic model and a computationally and statistically tractable framework for explicitly generating the dynamics of HIV diversity at DNA sequence level by including recombination.

Previous methods for analyzing serial samples of HIV DNA sequences from HIV-1-infected individuals were based on computationally tractable frameworks which however might not be suitable for such purposes and also excluded the signature of recombination. For example, in this study I showed that the methods based on the standard coalescent model might be inappropriate for analyzing serial sample of HIV DNA sequences.

Another purpose of this study was the identification and quantification of the signatures of the recombination and selection at the HIV genomic level.

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II. METHODS AND RESULTS

To develop the framework, I first designed a population genetic model that describes within-host HIV population dynamics at DNA sequence level. The model is based on the Wright-Fisher reproduction model with fluctuating population size and generation time, including recombination and mutation explicitly at the DNA sequence level.

Based on this population genetic model I derive a computationally tractable framework as on continuous coalescent-recombination model for simulating the dynamics of HIV genetic diversity at DNA sequence level. Based on this framework I developed analytical formulas as well as simulation algorithms for analyzing genetic diversity in serial samples of DNA sequences.

The method I implemented into a computer program in C programming language and applied to serial sample of HIV DNA sequences from 9 HIV-infected individuals [3]. First I consider the framework in the infinite-sites model and based on the application of the framework to the data sets I also considered the finite-sites model with variable mutation rates at the nucleotide sites. Under the modified framework, I explored the signature of recombination on the dynamics of HIV genetic diversity by using a linkage disequilibrium measure for the observed and simulated data sets under the estimated model.

III. CONCLUSION

The application of the framework on the serial samples of HIV DNA sequences from 9 HIV-infected individuals [3] show that the framework has more power for mimicking the dynamics of HIV genetic diversity in HIV-infected individuals than the previous methods. Furthermore, the framework allows to identify the signature of possible interaction between recombination and selection in shaping the dynamics of within-host HIV genetic diversity.

References

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