RESEARCH

Real-time strain typing and analysis of antibiotic resistance potential using Oxford Nanopore MinION sequencing

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Abstract

Clinical pathogen sequencing has significant potential to drive informed treatment of patients with unknown bacterial infection. However, the lack of rapid sequencing technologies with concomitant analysis has impeded clinical adoption in infection diagnosis. The recently released Oxford Nanopore MinION platform presents the ability to sequence DNA in real-time, opening immense potential to shorten the time from DNA to answers. However, there is still a lack of adequate bioinformatics software to take full advantage of this feature. Here, we present a bioinformatics pipeline for identification of pathogens and antibiotic resistance profile off the MinION sequencer in real-time. At the core of the pipeline, we developed three streaming algorithms for species typing, strain typing and antibiotic resistance profile identification. Using three Klebsiella pneumoniae samples, we demonstrate that our pipeline can identify bacterial species and strain information within 30 minutes of sequencing time, initial drug-resistance profiles within two hours, and complete resistance profiles within 12 hours. We also show that our pipeline can process XXX times the current throughput of the MinION, in preparation of future higher throughput platforms. We anticipate these devices and associated analysis methods will become useful clinical tools to guide appropriate therapy in time-critical clinical presentations such as bacteraemia and sepsis.

Keywords: sample; article; author

Content

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Sub-sub-sub heading for section Text for this sub-sub-sub-heading ...In this section we examine the growth rate of the mean of Z_0, Z_1 and Z_2. In addition, we examine a common modeling assumption and note the importance of considering the tails of the extinction time T_x in studies of escape dynamics. We will first consider the expected resistant population at vT_x for some $v > 0$, (and temporarily assume $\alpha = 0$)

$$E\big[Z_1(vT_x)\big] = E\bigg[\mu T_x \int_0^{v\wedge 1} Z_0(uT_x)\exp\big(\lambda_1 T_x(v-u)\big)\,du\bigg].$$

If we assume that sensitive cells follow a deterministic decay $Z_0(t) = xe^{\lambda_0 t}$ and approximate their extinction time as $T_x \approx -\frac{1}{\lambda_0}\log x$, then we can heuristically estimate the expected value as

$$\begin{aligned} E\big[Z_1(vT_x)\big] &= \frac{\mu}{r}\log x \int_0^{v\wedge 1} x^{1-u}x^{(\lambda_1/r)(v-u)}\,du \\ &= \frac{\mu}{r}x^{1-\lambda_1/\lambda_0 v}\log x \int_0^{v\wedge 1} x^{-u(1+\lambda_1/r)}\,du \\ &= \frac{\mu}{\lambda_1-\lambda_0}x^{1+\lambda_1/rv}\left(1-\exp\left[-(v\wedge 1)\left(1+\frac{\lambda_1}{r}\right)\log\right.\right. \end{aligned}$$

Thus we observe that this expected value is finite for all $v > 0$ (also see [1, 2, 3, 4, 5]).

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Competing interests
The authors declare that they have no competing interests.

Author's contributions
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Figures

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Tables

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