In their review article, Stritt and Gagneux provide a thorough and well-written analysis of the literature on the evolution of the Mycobacterium tuberculosis complex (MTBC), a monomorphic bacteria. This bacterial species complex exhibits a large genome size, high GC content and low level of genetic diversity, those genomic features occur in the context of a slow growth rate and clonaliy (i.e. lack of HGT)°. The authors highlight the challenges presented by the extreme clonality of the MTBC and other monomorphic bacterial populations, to investigate the evolution of their genetic characteristics. They provide a comprehensive overview of the literature investigating the basic evolutionary processes (i.e. recombination, mutation rates, genetic drift and selection) occurring in MTBC populations.
The paper is actually divided into four sections corresponding to each of these processes and how they have been evidenced and sometimes quantified in MTBC. In each part, the authors raise several questions. The authors review experimental and empirical studies of the MTBC complex that have attempted to answer these questions. They provide clear and sometimes detailed explanations of the models/hypotheses that have been put forwrad to explain the evolution of these monomorphic bacteria, and then discuss the limitations of these models. Doing so they underline that some studies are may be "too" narrative, without clear hypothesis testing. The authors highlight a key area for future investigations: simulation studies and propose an existing tool to conduct such studies.
The paper is somehow unusual in its form even for a review paper (with a discussion proposing a protocols an an analytical tool for going forward), but it is not a problem as it is the purpose of journals/platform such as PCI to have papers that do not follow "preformatted" guidelines.
Overall, Stritt and Gagneux have produced a well-written and comprehensive review of the literature on the evolution of monomorphic bacteria, with a focus on the MTBC. Altogether, it provides a valuable resource for researchers studying the evolution of monomorphic bacterial populations and underlines weaknesses in the analytical tools used .
I have nevertheless, a few suggestions to improve the manuscript and may be make it useful for a larger audience.

**Two general comments.**

First, for a review paper, there is in my opinion a lack of synthetic view on the main hypotheses found in the literature on how these genomes evolve, the predictions derived from these hypotheses (and how or whether these predictions have been thoroughly tested). Overall I gathered that: lack of HGT but intra-chromosomal recombination has been demonstrated (inferred from experimental evidence and population genomic investigation on MTBC); rates of evolution have been measured and are rather slow but actually very variable according studies and many studies could suffer from methodological studies; strong genetic drift is often referred to but difficult to measure (with Dn/ds quantification or estimation of Ne); positive selection (on resistance genes) is recurrently evidenced.
Can the authors come up with a table summarizing studies that have put forward clear hypotheses and predictions or attempted to quantitatively estimate each factor (may be for each section)? For instance:
-lack of HGT: list of studies with experimental evidence, list of studies with empirical evidence (pop genomic studies), which dataset they have worked on and what they have concluded.
-low rate of evolution: a table summarizing studies that have measured this rate with which method (experimental work, Beast estimates) and on which dataset. (I guess figure 3 does the job but it should come earlier in the paragraph)
-strong genetic drift: prediction (low Ne, overabundant nonsynonymous polymorphism), list of studies estimating dn/ds to estimate genetic drift in MTBC, measuring Ne using Bayesian skylineplots (again dataset used, methods and their conclusions…)
And etc.. for positive selection.

May be the literature is too all over the place to make such a table…It's a suggestion to shorten the paper : a lot of what is specified in the text could then be summarized in the table and the text would be more about the methodological issues of the approaches presented.

Another general comment I have is that, the article is focused primarily on the MTBC, and for now it is difficult to see what is applicable to other monomorphic bacterial populations or other microorganisms. It would have been helpful to provide more discussion on how this review may be generalized to other systems. Many of the characteristics of MTBC populations (low GC contents, strong genetic drift, lack of HGT) reminded me of intracellular bacterial symbionts. Can the authors in the discussion widen their scope and argue how what we learn from MTBC population genetics is informative for other model species (which study also suffers from narratives that are not always put to the test)? Could they specify which of their recommendation (e.g. question the use of Bayesian skyline plots for estimating Ne) applies to "all"/ "most" bacterial population studies.

Specific comments

- Throughout the manuscript, it is not always easy to follow what are generalities (for population genomics study of bacteria, populations genomics in general) or specific to the study system. Make sure that it is clear when the study you are citing is focused on MTBC.
- Figue 2 is a nice summary of some genetic characteristics of MTBC, but it is difficult to understand how and on which data they have been built from, please give some sort of mat and meth, at least in a sup mat, with a link to a dataset.
- The paper is long, and sometimes gives too many details on very general matters that are interesting, well written, but can be a bit confusing as it distracts from the main messages. : May be go through the paper and see how you can shorten non-essential paragraphs. For instance line 51 to 64 is a general paragraph on bacterial phylogenies which is not very useful in the rest of the paper (I don't think the authors come back to how "linked selection" has affected inferences on evolutionary processes explaining MTBC evolution).

  Less important but still , line 129: the authors mention that lack of HGT could be an adaptation to parasitism but do not further review a study that have investigated this hypothesis in MTBC..it's a bit "off track" in this paragraph.

  The definition of genetic drift from line 339 is a bit long (delete last sentence of the §), shorten the intro on genetic drift. I believe this review is intended to readers who are already familiar with population genetics concepts.

  The § from line 629, on dN/dS measure and its caveats is also very general, it should either be deleted or come earlier, when dN/ds are mentioned in the context of estimating genetic drift.

Very specific comments:

- P12: Define genome erosion: genome size diminution or low coding density?
- Line 432: you mean "positive selection at synonymous sites"?
- Line 719 "sputum": I guess you meant some?