Trends in Genetics

Time to go bigger: emerging patterns in macro-genetics

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Abstract:	The increasing availability of large-scale and high-resolution datasets in population genetics is moving the field toward a novel research agenda. We show how this shift toward macro-genetics should generate new perspectives and theories allowing describing, understanding and predicting patterns of genetic diversity at broad spatial, temporal and taxonomic scales.

Time to go bigger: emerging patterns in macro-genetics

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Abstract

The increasing availability of large-scale and high-resolution datasets in population genetics is moving the field toward a novel research agenda. We show how this shift toward macro-genetics should generate new perspectives and theories allowing describing, understanding and predicting patterns of genetic diversity at broad spatial, temporal and taxonomic scales.

Keywords: biodiversity, population genetics, genomics, patterns, large-scale, comparative studies.

Main text

Population genetics aims at exploring within-species genetic diversity over space, taxa and time, and at identifying the underlying evolutionary forces. In the early 1920's, technical limitations impeded the founding fathers of population genetics (Sewall Wright, John Haldane, Ronald Fischer) from quantifying their central focus, i.e. genetic diversity. The early foundations of the discipline were therefore purely theoretical, and poorly substantiated by natural observations. It is only some decades ago –with the development of molecular analysis techniques– that population genetics entered a new era allowing empirical testing of founding theories, and leading to the emergence of new theories (e.g. the neutral theory of molecular evolution [1]). More recently, high-throughput sequencing reinforced this empirical era with unprecedented abilities to gather improved genetic information over large numbers of markers, individuals, species and locations at relatively low costs.

These two major steps in population genetics are now making a large amount of detailed datasets available to scientists (Fig.1a), allowing a shift from local-scale studies (i.e. a single species in a single environment at a given period) to fascinating perspectives on the large-scale *spatial, temporal and taxonomic* distribution of genetic diversity in nature (e.g. [2]). Describing and understanding *general and repeatable patterns* of genetic diversity (i.e. "laws" *sensu* [3]) should provide invaluable ecological and evolutionary opportunities to fuel the development of new theories, and to set sustainable management strategies. We argue the time is ripe to move to a "macro-genetics" view of population genetics, echoing the recent shift of ecology to "macro-ecology", allowing pursuance of new ambitions in population genetics.

Three recently published papers [4–6] perfectly illustrate the scientific benefits of considering macro-scale genetic datasets through considering numerous taxa, large spatial extents or long time series. First, Romiguier *et al.* [4] used transcriptome sequencing to identify *taxonomic patterns* of genomic diversity in 76 animal species (covering eight different phyla), and to reveal the species traits underpinning genomic diversity. Why some species exhibit a high genetic diversity whereas others are genetically impoverished constitute one of the oldest riddles of population genetics. Theory predicts that long-lived species with high parental investment –contrary to species with short lifespans and high fecundity– often suffer from low population sizes, featured by impoverished genetic diversity. The authors confirmed this theory by demonstrating that animal species investing in propagule quality (i.e. K-like strategy) have lower genomic diversity than species investing in propagule quantity (i.e. r-like strategy). More specifically, they found striking correlations between genomic diversity, fecundity and propagule size (Fig. 1b). By identifying traits underlying genomic diversity across a broad range of taxa, this study not only resolved an old conundrum in population genetics; it also has the potential to inform species conservation in terms of trait-mediated extinction risks.

Second, Miraldo *et al.* [5] harnessed the potential of archived genetic databases to reveal *spatial patterns* of genetic diversity and to explore how humans impact these patterns. The authors relied on ~86,000 available georeferenced mitochondrial sequences from more than 4500 amphibian and mammal species worldwide, to provide the first global map of genetic diversity. This global mapping revealed clear latitudinal gradients (as observed traditionally for species diversity), with genetic diversity decreasing from the tropics to the poles (Fig. 1c). In addition, authors identified significant anthropogenic impacts on the genetic diversity of amphibians, pinpointing urgent biodiversity conservation challenges at the global scale. By its unprecedented spatial scale, this work identified hotspots of genetic diversity across the planet, and paved the way for novel avenues into both theoretical and applied evolution.

Third, Chen *et al.* [6] performed a 20-year field survey of an endangered bird species (*Aphelocoma coerulescens*) to describe *temporal patterns* of genomic diversity in a focal population. Through detailed temporal screening of changes in genome-wide diversity, they identified a rapid decline in the number of individuals immigrating from peripheral populations to the focal population, likely due to increased anthropogenic fragmentation of the surrounding landscape. They further demonstrated that immigrants played a vital role in maintaining low levels of inbreeding in the focal population (Fig. 1d). Inbreeding negatively influences traits related to the fitness of plants and animals, leading to inbreeding depression [7]. Accordingly, the authors showed that the reduction in the number of immigrants over time due to human activities was associated with strong inbreeding depression on several fitness-related traits, including reduced hatching success and survival rates. This study demonstrates the strength of long-term genetic surveys to illuminate the harmful effects of habitat fragmentation on the well-being of wild populations, and to uncover “early signals” of population decline that can be efficiently employed to preclude population extinctions.

Ongoing data generation and accumulation clearly is initiating a major shift towards unraveling broad-scale patterns of genetic diversity and their underlying processes, and hence to resolve open and integrative questions in evolutionary biology. This shift to a macro-genetics view of population genetics goes beyond comparative population genetics, by embracing all scales of variation -i.e. taxonomic, spatial and temporal scales-, which is a necessary step to better appraise how underlying processes interact across scales. To further exemplify this perspective, we highlight how this shift toward macro-genetics will improve long-term species conservation, provided that massive data generation is accompanied by parallel computational developments to reduce both data and systematic errors that may drastically slow down the achievements of these fascinating goals. First, understanding the role of genetic diversity in structuring ecological communities has been the focus of many studies, yet we still do not know the large-scale impacts of genetic diversity on species' assemblages to recommend management for high genetic diversity as a means of preserving ecosystem functioning [8]. Second, a more holistic perspective on population genetic patterns associated with species' interactions (e.g. host-parasite or plant-pollinator dynamics) could highlight the crucial role of "genetic synchronism" in rendering specialized ecological networks of interacting species more vulnerable to environmental changes [9]. Third, it is widely accepted that both non-adaptive and adaptive (i.e. driven by natural selection) components of genetic diversity govern the eco-evolutionary dynamics underlying long-term species' survival. However, we still question whether these distinct, yet not mutually exclusive, components follow similar temporal and spatial patterns and to what extent they contribute to the ability of species to cope with environmental changes [10]. We argue that the opportunities provided by recent sequencing approaches and decades of genetic diversity data accumulation should be exhaustively exploited to boost our understanding of the broad-scale processes driving macro-genetic diversity in light of sustainable conservation of ecosystems and their services.

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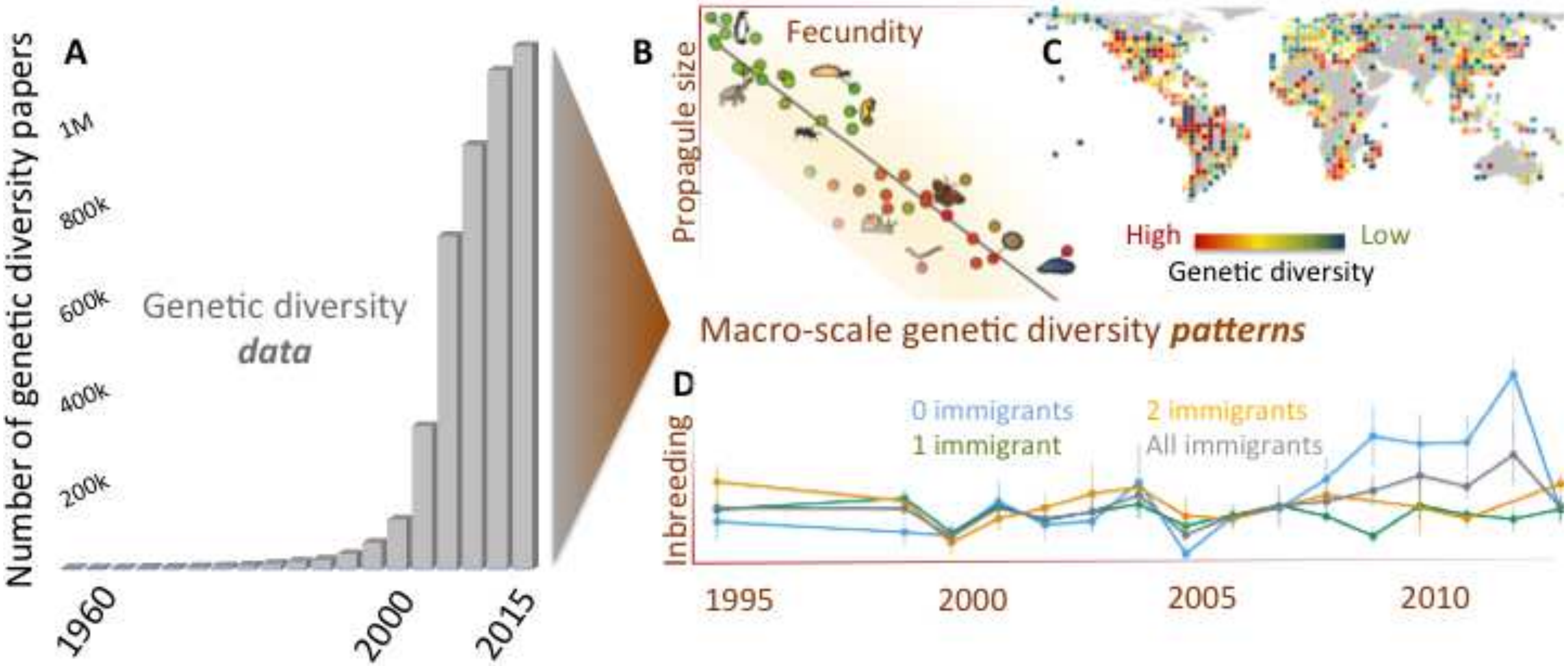
Figure legend

Figure 1. Genetic data accumulation is leading to macro-genetics. The development of next-generation sequencing techniques ((A), 2000's) and the accumulation of data are generating new scientific opportunities on the large-scale and universal *taxonomic* (B), *spatial* (C) and *temporal* (D) patterns of genetic diversity. In (B): Genetic diversity of species varies along the propagule size-fecundity continuum [4]. In (C): *G*enetic diversity of mammals and amphibians increases in the tropics [5]. In (D): Changes over time in the inbreeding coefficient of nestlings from a bird population depend on the number of immigrant parents for each nestling [6]. [Note: copyrights for the panels B-D of the figure will be requested to the publishers upon acceptance]


A
Number of genetic diversity papers
1M
800k
600k
400k
200k
1960
2000
2015
Genetic diversity
data
B
Propagule size
Fecundity
C
High
Low
Genetic diversity
Macro-scale genetic diversity *patterns*
D
Inbreeding
0 immigrants
1 immigrant
2 immigrants
All immigrants
1995
2000
2005
2010

Cover Letter

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Dear Editor,

Please consider this proposal for a MS entitled "Time to go bigger: emerging patterns in macro-genetics" by Simon Blanchet, Jérôme G. Prunier and Hanne De Kort that we would like to submit for publication as a "*Spotlights*" in ***Trends in Genetics***.

We build on three recently published papers (Chen et al. *Curr Biol* 2016; Miraldo et al. *Science* 2016; Romiguier et al. *Nature* 2014) to show that population genetics is currently on the verge of a major shift featured by data generation and analyses at unprecedentedly broad and integrative scales. We argue that this is moving the field toward a novel research agenda (encompassed in the term "macro-genetics"), consisting in analyzing and understanding patterns of within-species genetics diversity at broad taxonomic, spatial and temporal scales.

A major revolution in population genetics occurred sixty years ago when technological advances permitted to empirically test the mathematical theories founded in the early 1920's by Sewall Wright, John Haldane and Ronald Fischer. This resulted in thousands of studies assessing spatial and temporal variation in within-species genetic diversity in humans, plants and animals. We argue that both the accumulation of datasets in the last decades, and the ongoing rise of high-throughput sequencing technologies are laying the groundwork for a new major step permitting unrevealing and understanding *patterns of genetic diversity across large taxonomic, spatial and temporal* scales, as exemplified by the combination of three papers we highlight here. Exploring *large-scale and general patterns* of genetic diversity will offer new opportunities for answering fascinating and long-standing questions related to the processes underlying species evolution, paving the way for new theoretical foundations and improved management practices.

We believe ***Trends in Genetics*** is the most appropriate medium to convey our influential message to a large scientific audience, but also to governmental and non-governmental agencies in charge of managing and conserving biological resources. For these reasons, we believe that our MS is appropriate for publication in ***Trends in Genetics***.

This MS has been read and applauded by several experts in the field including Mark Beaumont (Univesity of Bristol, UK), Lounès Chikhi (CNRS and Instituto Gulbenkian de Ciência, Portugal), Hervé Philippe (CNRS, France), Virginie Stevens (CNRS, France) and Olivier Rey (University of Perpignan, France).

As potential reviewers we may propose: Christophe Eizaguirre (population genomics, c.eizaguirre@qmul.ac.uk); Louis Bernatchez (conservation genetics and genomics, Louis.Bernatchez@bio.ulaval.ca; Joost Raymaekers (populations genomics, joost.raeymaekers@ntnu.no); Matthew Fitzpatrick (ecological genomics, mfitzpatrick@umces.edu); Aaron Shafer (large scale genomics, aaronshafer@trentu.ca).

Sincerely yours,

Simon Blanchet, Jérôme Prunier and Hanne De Kort.