



# The Journal of Molecular Evolution Turns 50

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Molecular evolution as a distinct discipline began to take shape in the 1960s as insights from biochemistry and population genetics combined with the emerging field of molecular biology, which offered new tools for comparing biomolecules and their sequences across evolutionary distance. Two early achievements, the establishment of molecular clocks and the subsequent development of the neutral theory, laid the foundation for molecular evolution (Suárez-Díaz 2016). Following on these accomplishments, the Journal of Molecular Evolution was founded and its first issue was published 50 years ago this month (see Liberles 2019). In this special issue, we celebrate the history of this journal and the field that it chronicled over the last half century.

Just as molecular evolution emerged from the techniques and insights of molecular biology, biological chemistry, and population genetics, the field has kept pace through monumental changes in the life sciences, as advances in molecular biology have brought about the new paradigms of genomics, bioinformatics, and systems biology. In the last 50 years, molecular evolution has given us a clearer understanding of evolutionary history, evolutionary processes, and the diversity of the biosphere. As the first journal dedicated to molecular evolution, the Journal of Molecular Evolution has published many seminal articles throughout the field's history.

In this special 50th anniversary issue, we highlight some of the most important studies that were published over the journal's history. This sampling of topics reflects the choices

of individual editors and is necessarily non-exhaustive. We invited current members of the editorial board to each choose an article from the journal archive that has had a substantial impact on their respective discipline and write a perspective piece summarizing the article, its scientific context, the subsequent research that it motivated since its publication, and their perspective on future directions in that area. We present 10 such articles in this issue, which span a broad range of topics within molecular evolution.

- The structures of cytochrome c and the rates of molecular evolution (Dickerson 1971)
- Coenzymes as fossils of an earlier metabolic state (White 1976)
- Evolutionary trees from DNA sequences: A maximum likelihood approach (Felsenstein 1981)
- Dating of the human-ape splitting by a molecular clock of mitochondrial DNA (HKY85) (Hasegawa et al. 1985)
- Plant mitochondrial DNA evolves rapidly in structure, but slowly in sequence (Palmer and Herbon 1988)
- Probabilistic reconstruction of ancestral protein sequences (Koshi and Goldstein 1996)
- Relationships Between Genomic G + C Content, RNA Secondary Structures, and Optimal Growth Temperature in Prokaryotes (Galtier and Lobry 1997)
- Exploring Nonnatural Evolutionary Pathways by Saturation Mutagenesis: Rapid Improvement of Protein Function (Miyazaki and Arnold 1999)
- On the Origin of Metabolic Pathways (Lazcano and Miller 1999)
- On the Possibility of Constructive Neutral Evolution (Stoltzfus 1999)

These articles highlight many of the historical strengths of the journal. With its founding editor, Emile Zuckerkandl, there was an early emphasis on methods for better understanding molecular evolutionary history and processes (Lehman 2013; Liberles 2019). Dr. Zuckerkandl is most well known for his development of molecular clocks along with his postdoctoral supervisor, Linus Pauling, himself a

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founding editorial board member. Early seminal articles published in the journal expand on the topic of molecular clocks (Hasegawa et al. 1985 (commentary by Zardoya 2021)) as well as the related subjects of neutral evolution in the idea of constructive neutralism (Stoltzfus 1999) and evolutionary rates (Dickerson 1971 (commentary by Alvarez-Ponce 2021); Palmer and Herbon 1988 (commentary by Christensen 2021)).

As the first journal dedicated to the study of molecular evolution, the journal also published major advances in phylogenetic methods (Felsenstein 1981 (commentary by Posada and Crandall 2021); Hasegawa et al. 1985 (commentary by Zardoya 2021)) that draw upon model-based substitution processes and evolutionary rates. This was used by Felsenstein, for example, in the development of maximum likelihood methods on top of a new evolutionary rate model (Felsenstein 1981 (commentary by Posada and Crandall 2021)). Further, substitution models can be used for ancestral sequence reconstruction. One of the first algorithms for maximum likelihood ancestral protein sequence reconstruction was published in the journal (Koshi and Goldstein 1996 (commentary by Selberg et al. 2021)).

The journal also maintained a focus on chemical and biochemical evolution, leading to its publication of seminal studies on evolutionary mechanisms (Galtier and Lobry 1997 (commentary by Meyer 2021) including constructive neutralism (Stoltzfus 1999 (commentary by Muñoz-Gómez et al. 2021)), and the interplay between evolutionary processes, biophysical processes, and experimental tools (Miyazaki and Arnold 1999 (commentary by Voskarides, 2021)). With the inclusion of chemical evolution in its purview, the Journal of Molecular Evolution has also retained a tradition in publishing key studies about the origin and early evolution of life (White 1976 (commentary by Goldman and Kacar 2021); Lazcano and Miller 1999 (commentary by Becerra 2021)), a subfield at the interface of biology and chemistry.

Of course, all of these early articles predate the incredible paradigm shift that all life sciences have undergone over the last two decades thanks to genomics, bioinformatics, computational biology, and systems biology. As the field of molecular evolution expanded to integrate high throughput biological data with an understanding of the processes that generate them, so too has the scope of the journal (Liberles et al. 2020). Since the field of molecular evolution began roughly six decades ago, this deeper understanding of molecular-level evolutionary mechanisms and processes, along with the tools to measure them, have become indispensable parts of all biomedical and life sciences.

While the articles in this 50th anniversary edition celebrate a selection of the past achievements published in the journal, they also describe the subsequent research that they have motivated since its publication and the future research

that they are likely to inspire. As documented here, molecular evolution has had a storied history. It will also undoubtedly have a far reaching and consequential future, where it now more than ever lies at the center of modern biology.

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