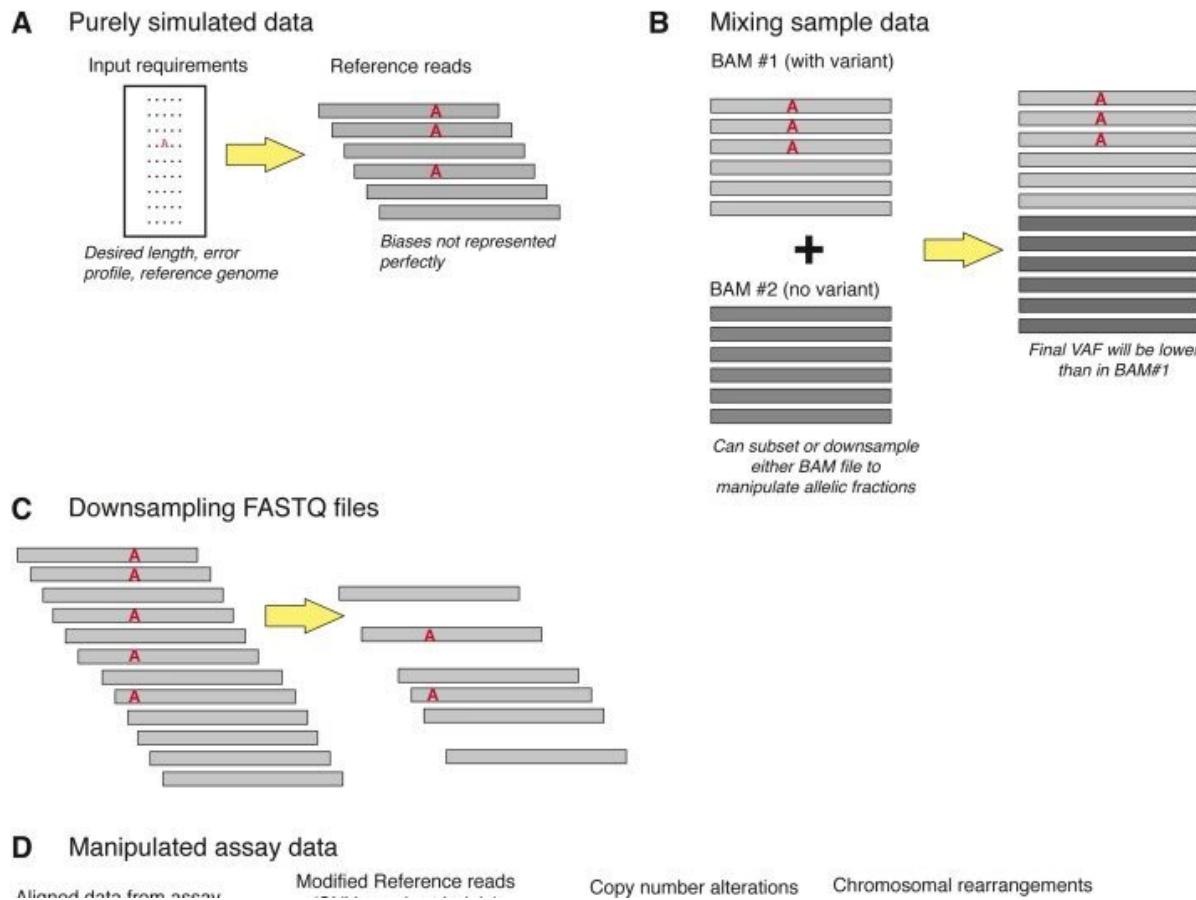


Recommendations for in silico approaches for validating next-generation molecular sequencing analysis pipelines

October 18 2022



Types of in silico data. (A) Purely simulated data can simulate almost any type of variant but cannot mimic all types of sequencing biases. (B) Mixing sample data combines real data from more than one sample to represent particular VAFs. (C) Downsampling FASTQ files can be used to test the effect of lower coverage on variant calling performance. (D) Manipulated assay data is one of

the most common types of in silico data generated by clinical laboratories, because it uses real data from the laboratory, which is modified to introduce variants, such as SNVs, copy number alterations, and chromosomal rearrangements. (E) Data reanalysis can be used to help validate bioinformatics pipeline changes with existing data. Credit: *The Journal of Molecular Diagnostics* (2022). DOI: 10.1016/j.jmoldx.2022.09.007

The Association for Molecular Pathology (AMP), a global, molecular diagnostic professional society, today published consensus recommendations for the use of in silico approaches for validating Next-Generation Sequencing (NGS) data analysis pipelines.

The manuscript, "Recommendations for the Use of In Silico Approaches for Next Generation Sequencing Bioinformatic Pipeline Validation: A Joint Report of the Association for Molecular Pathology, Association for Pathology Informatics, and College of American Pathologists," was released online ahead of publication in *The Journal of Molecular Diagnostics*.

"As more laboratories around the country use in silico data to simulate variants to help validate the performance of clinical NGS data analysis pipelines, clinical laboratory professionals may need an aid for understanding both the value these methods bring and the important nuances and limitations of these approaches," said Justin Zook, Ph.D., Co-Chair of the AMP In Silico Pipeline Validation Working Group and Co-Leader of the Biomarker and Genomic Sciences Group at the National Institute of Standards and Technology.

"AMP convened a panel of subject matter experts from AMP, Association for Pathology Informatics, and College of American Pathologists to explore the advantages and disadvantages of these various

types of in silico data. This new JMD report summarizes our key findings and provides useful recommendations to help clinical laboratory professionals select the most appropriate format for their specific purpose."

AMP devotes significant resources to developing evidence-based and consensus-driven practice guidelines to help establish essential elements of high-quality test design, such as analytical and clinical validity. The In Silico Pipeline Validation Working Group led the collective effort to review the available published literature and analyze the different types of in silico data and how they can be used in the clinical molecular diagnostic laboratory.

The new report also presents survey data on current use cases and highlights potential future applications. The team offered the following expert consensus opinion general recommendations based on these findings.

Consensus Recommendations

1. The laboratory may use in silico data files to supplement NGS analytical validation, particularly to assess analytical sensitivity or false negative rates for specific variants; however, in silico [data files](#) cannot supplant the use of physical samples (e.g., patient samples).
2. The laboratory should understand the functional limitations of the type(s) of in silico data being utilized.
3. The laboratory should understand the limitations of most in silico data for assessing performance in particular genome contexts and variant types susceptible to systematic sequencing and mapping errors.
4. The laboratory may consider using in silico samples for minor updates to clinical bioinformatics software pipelines.

5. Commercial vendors and internal pipeline developers should include options in their analysis pipelines to facilitate easier in silico data file import and analysis by clinical laboratories.

"AMP is committed to collaborating with the broader clinical laboratory community to help identify areas of opportunity to continuously improve clinical practice, molecular diagnostic testing, and patient care," said Eric J. Duncavage, MD, Co-Chair of the AMP In Silico Pipeline Validation Working Group and Professor of Pathology and Immunology at the Washington University School of Medicine in St. Louis.

"This new joint report reviews, analyzes, and presents the latest data to help guide clinical laboratory professionals on when and how to use these important supplementary in silico data approaches. We intend to review and update these consensus recommendations as new data and other in silico methods become available."

More information: Eric J. Duncavage et al, Recommendations for the Use of In silico Approaches for Next Generation Sequencing Bioinformatic Pipeline Validation: A Joint Report of the Association for Molecular Pathology, Association for Pathology Informatics, and College of American Pathologists, *The Journal of Molecular Diagnostics* (2022). [DOI: 10.1016/j.jmoldx.2022.09.007](https://doi.org/10.1016/j.jmoldx.2022.09.007)

Provided by Association for Molecular Pathology

Citation: Recommendations for in silico approaches for validating next-generation molecular sequencing analysis pipelines (2022, October 18) retrieved 8 May 2024 from <https://medicalxpress.com/news/2022-10-silico-approaches-validating-next-generation-molecular.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.