CRISPR-Analytics (CRISPR-A): a platform for precise analytics and simulations for gene editing

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Synbio

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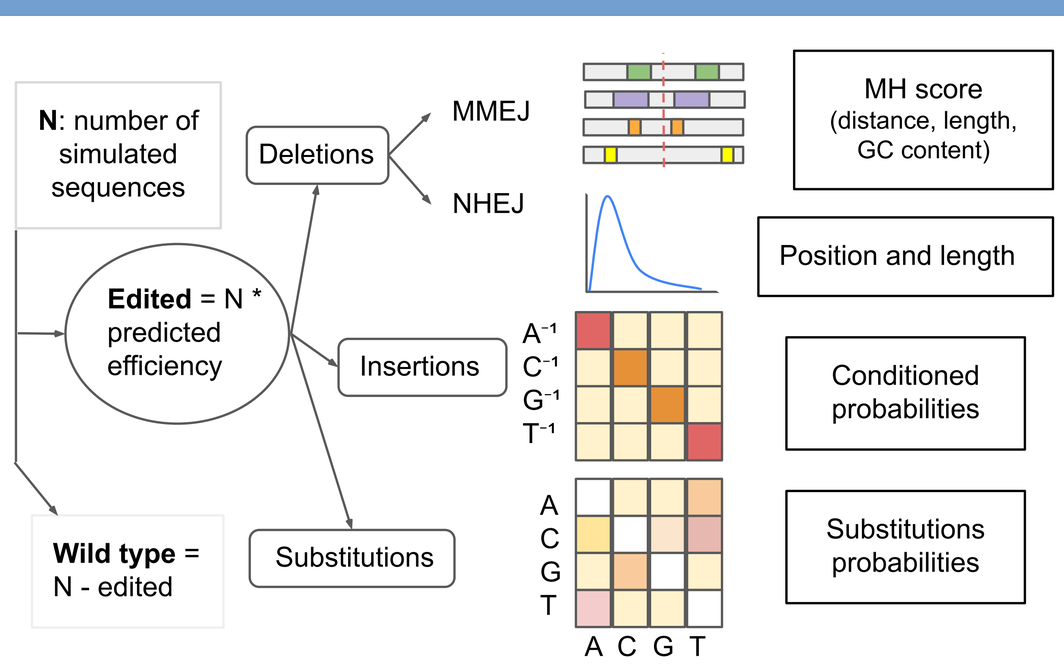
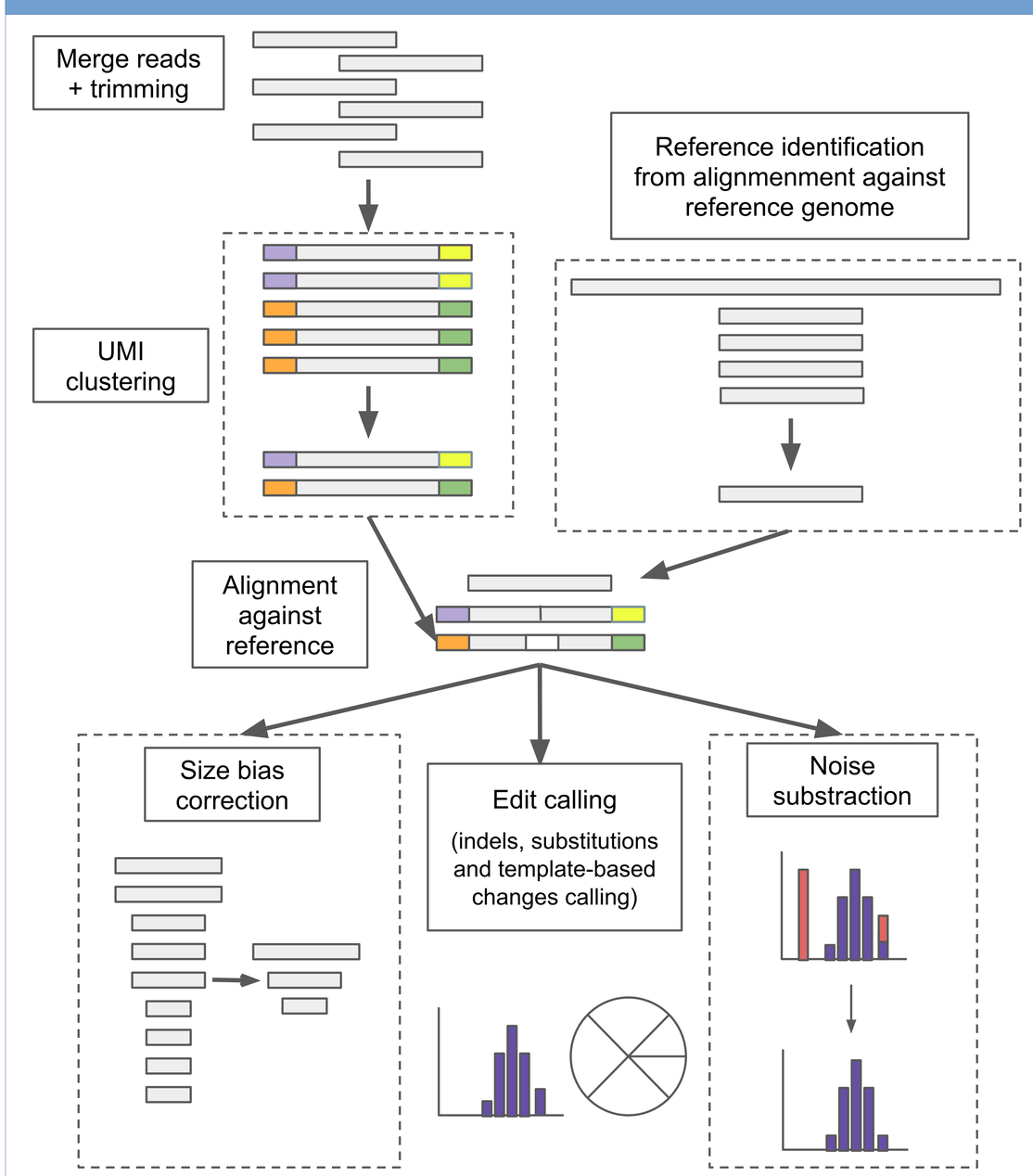
We have developed CRISPR-Analytics, CRISPR-A, a comprehensive and versatile genome editing **web application** tool, and a **nextflow pipeline** to give support to **gene editing** experimental design and analysis. This tool is ideal for analyzing highly sensitive cases such as clinical samples or experiments with low editing efficiencies. CRISPR-A is ideal to support multiple kinds of experiments such as double-stranded DNA break-based engineering, base editing (BE), primer editing (PE), and homology-directed repair (HDR).

SIMULATIONS PIPELINE



Simulation is based on the **fitting** of multiple parameters that describe the distribution of edits and its characteristics and proportions. Once the number of edited sequences is determined by the **protospacer predicted efficiency**, other **probability distributions** are applied to decide the number of each kind of edits (NHEJ deletions, MMEJ deletions, insertions and substitutions).

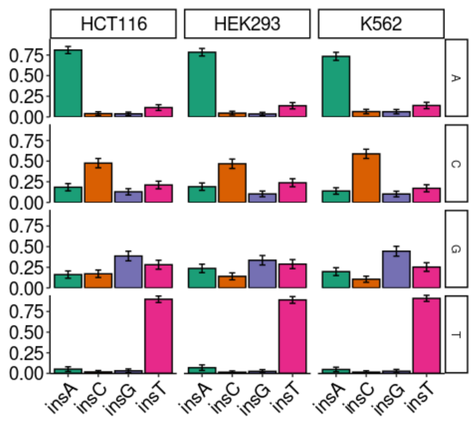
ANALYSIS PIPELINE

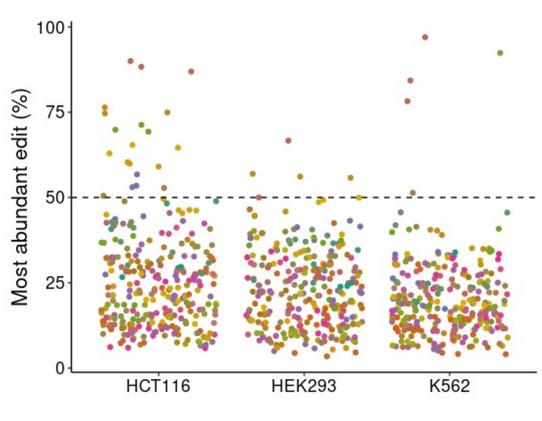


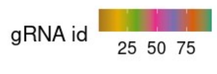
The analysis algorithm is composed of three mandatory steps:
1) reads **pre-processing** for quality assessment,
2) reads **alignment** against reference amplicon, and
3) **edit calling.**

In dashed line boxes, all processes that are optional: **UMI** clustering, reference discovery, size **bias correction**, and **noise subtraction** based in an empirical model from negative control samples.

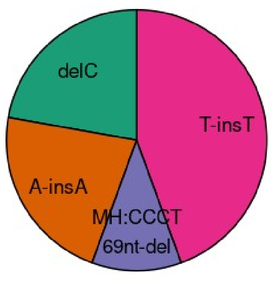
CASE EXAMPLE



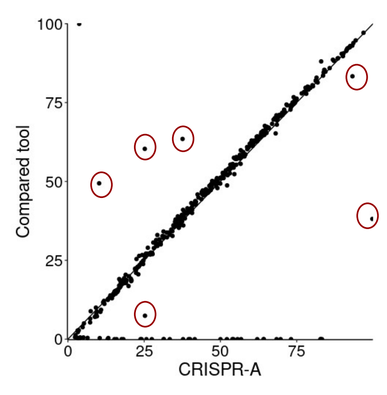


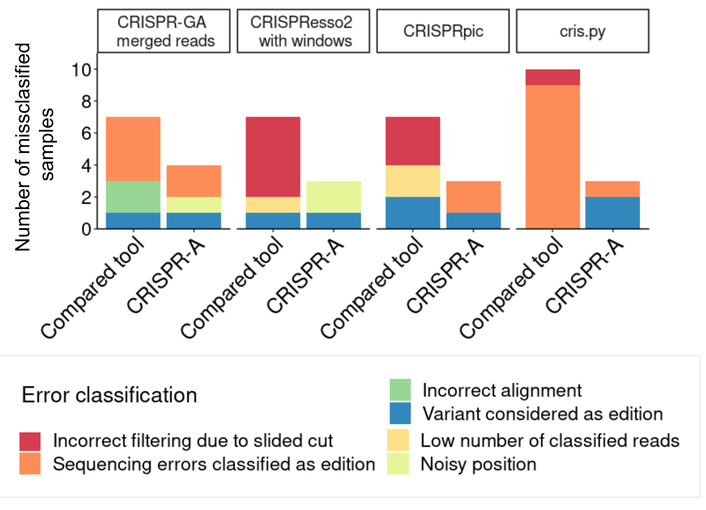


HCT116, HEK293 and K562 edited in 96 different targets. Percentages of **inserted nucleotides** in function of the free nucleotide at 3' in three different cell lines (top left). In the plot in the right side, we have represented tha **variants diversity** by samples; calculated through the percentage of the most abundant variant among all kinds of edits. In the pie chart (bottom) we can see the **nature of the variants with higher abundance**. All these variants that are above the 50% (dashed line in top-right plot).



BENCHMARCKING





Error characteritzation from the most discrepant values in t-cell edited samples (978 samples). CRISPR-A results are compared with the results of other tools for more distant results (red circles). Errors are classified in function of their source.

Reference:

Sanvicente-García, M., García-Valiente, A., Jouide, S., Jaraba-Wallace, J., Bautista, E., Escobosa, M., ... & Güell, M. (2022). CRISPR-Analytics (CRISPR-A): a platform for precise analytics and simulations for gene editing. bioRxiv.

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Funding:

European Commission | Horizon 2020 European Union funding for Research & Innovation