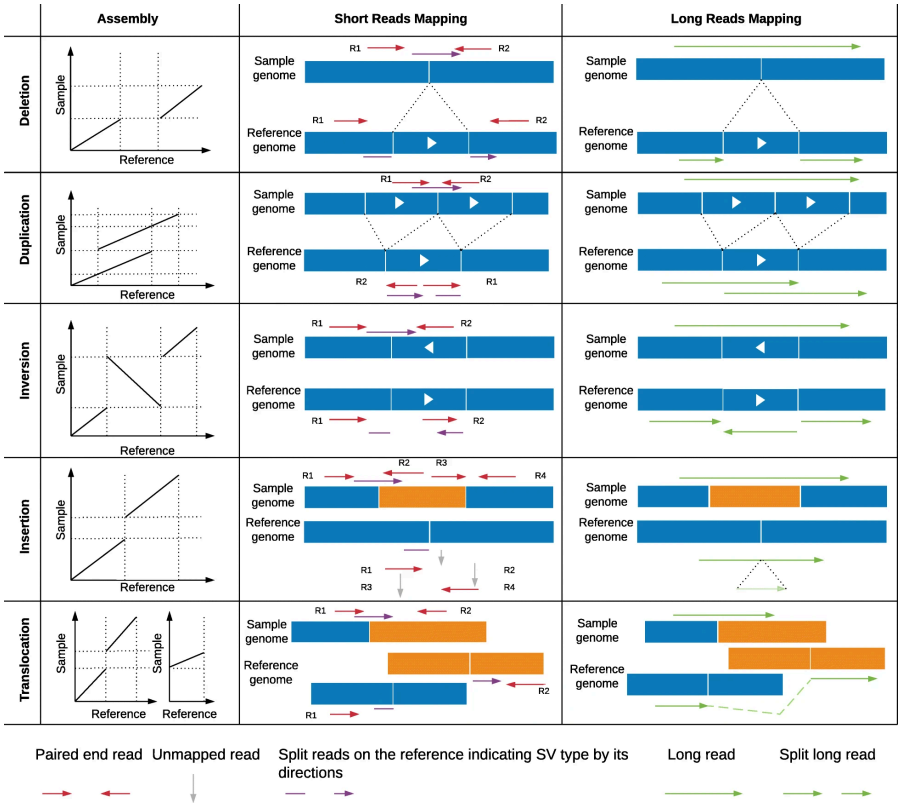
Long read structural variant calling:

- [Structural variant calling: the long and short of it]



- The term structural variant is loosely defined, but Mahmoud et al. considers it to be a genomic alteration ≥ 50bp.
- Can include CNVs (deletions and duplications), translocations, insertions, inversions, and translocations.
- Long reads are superior to short reads in capturing structural variants

Structural Variant Callers:

PBSV:

- github link
- Tool suite used for the structural variant calling analysis within PacBio's GUI (SMRT LINK)
- Best for:

> `pbsv` calls insertions, deletions, inversions, duplications, and translocations. Both single-sample calling and joint (multi-sample) calling are provided. `pbsv` is most effective for:
>
> - insertions 20 bp to 10 kb
> - deletions 20 bp to 100 kb
> - inversions 200 bp to 10 kb
> - duplications 20 bp to 10 kb
> - translocations between different chromosomes or further than 100kb apart on a single chromosome

- From Mahmoud et al. :
    - *"PacBio structural variant calling and analysis tools (PBSV) is a method developed by PacBio to detect SVs within the range of 20+ bp. Reads supporting a putative SV are used to generate a consensus, which is then re-aligned to the reference genome."*

Sniffles:

- **github link**
- From Mahmoud et al. :
    - *"Sniffles operates on a per read base, also capable of reporting very low-frequency SVs in the sample. This is particularly useful in cancer or in mosaic variation. Furthermore, Sniffles allows the detection of more complex or adjacent SVs such as inversions flanked by deletions or inverted tandem duplications. It implements a statistical framework to reduce the number of false-positive calls."*

VCFs from multiple variant callers → consensus sequences:

- How to interpret SV VCFs
- Simple combination of multiple somatic variant callers to increase accuracy
    - *“we found that the specific callers used is not critical and recommend a consensus strategy consisting of at least three callers, where variants found by n – 1 callers are accepted”*