a

Prepare genomic DNA sample
Randomly fragment genomic DNA and ligate adapters to both ends of the fragments.

Attach DNA to surface
Bind single-stranded fragments randomly to the inside surface of the flow cell channels.

Bridge amplification
Add unlabeled nucleotides and enzyme to initiate solid-phase bridge amplification.

Denature the double stranded molecules

b

First chemistry cycle: determine first base
To initiate the first sequencing cycle, add all four labeled reversible terminators, primers, and DNA polymerase enzyme to the flow cell.

Image of first chemistry cycle
After laser excitation, capture the image of emitted fluorescence from each cluster on the flow cell. Record the identity of the first base for each cluster.

Before initiating the next chemistry cycle
The blocked 3' terminus and the fluorophore from each incorporated base are removed.

GCTGA...

Sequence read over multiple chemistry cycles
Repeat cycles of sequencing to determine the sequence of bases in a given fragment a single base at a time.