The present invention relates to a method for assembly of nucleic acid sequence data comprising nucleic acid fragment reads into (a) contiguous nucleotide sequence segment(s) comprising the steps of: (a) obtaining a plurality of nucleic acid sequence data from a plurality of nucleic acid fragment reads; (b) aligning said plurality of nucleic acid sequence data to a reference sequence; (c) detecting one or more gaps or regions of non assembly or non matching with the reference sequence in the alignment output of step (b); (d) performing de novo sequence assembly of nucleic acid sequence data mapping to said gaps or regions of non assembly; and (e) combining the alignment output of step (b) and the assembly output of step (d) in order to obtain (a) contiguous nucleotide sequence segment(s). In addition a corresponding program element or computer program for assembly of nucleic acid sequence data and a sequence assembly system for transforming nucleic acid sequence data comprising nucleic acid fragment reads into (a) contiguous nucleotide sequence segment(s) is provided.