

Step 1: Synthesize 500,000 29-mer oligos + attachment group (-SH, amine; NHS).

1. Synthesizer = 50,000 oligos/day 500,000 oligos in 10 days
2. Bar-code = 19-mer; "Primer" = 10-mer

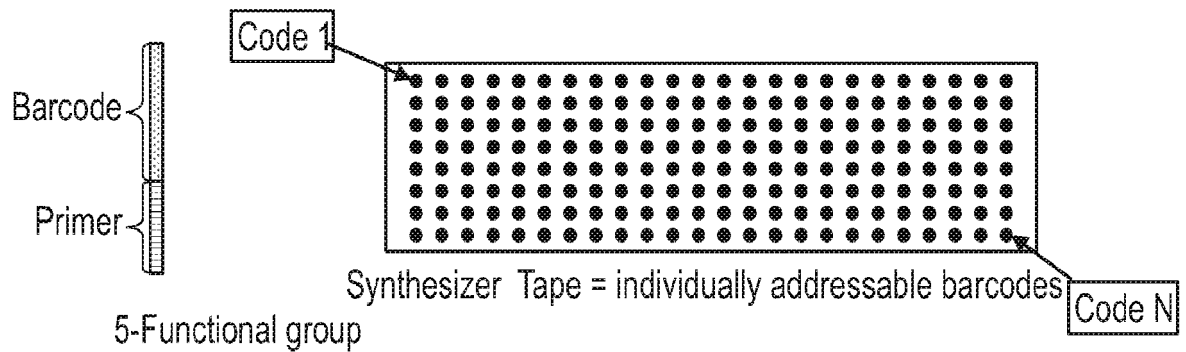


Fig. 1A

Step 2: Ligate overhang primer with monotemplate sequence in individual wells

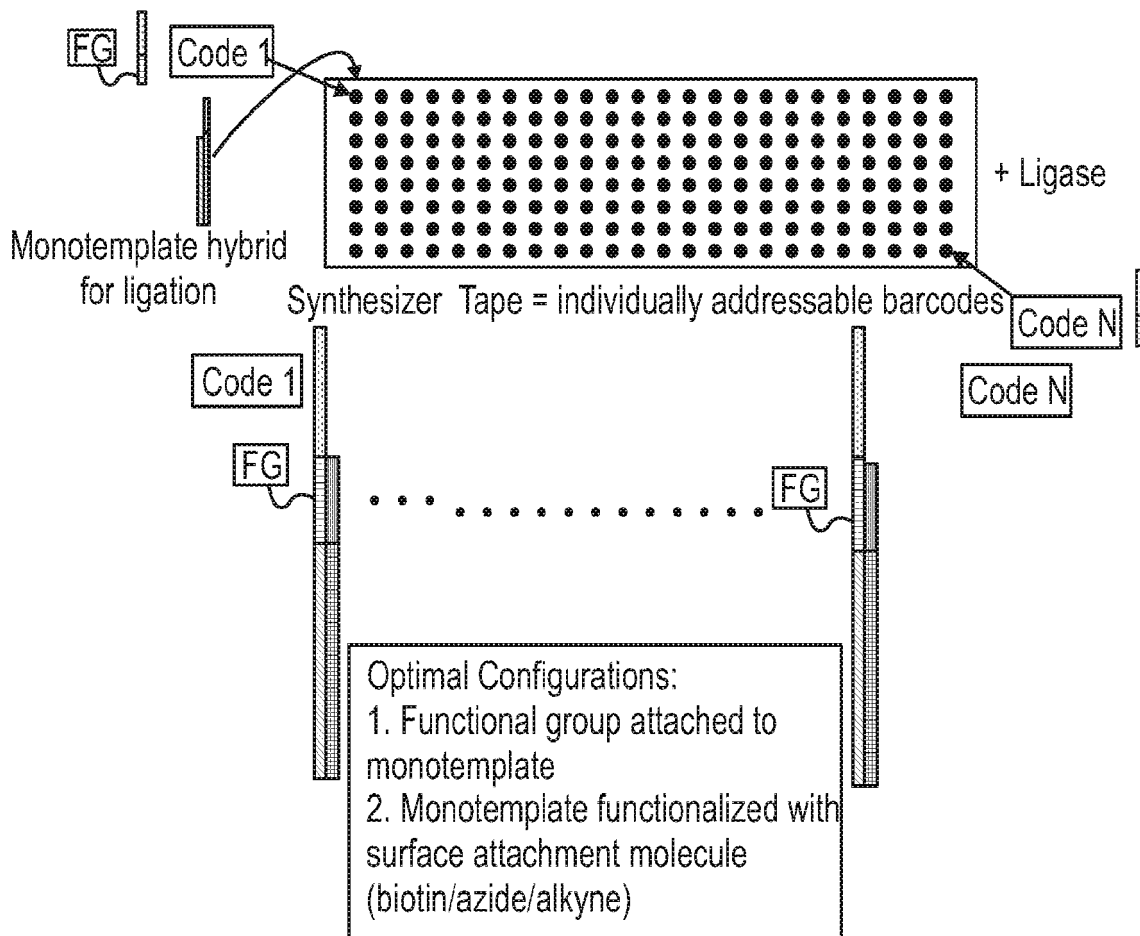


Fig. 1B

Step 3: Robotically add compounds with reactive group (RG) to individual wells with functionalized codes.

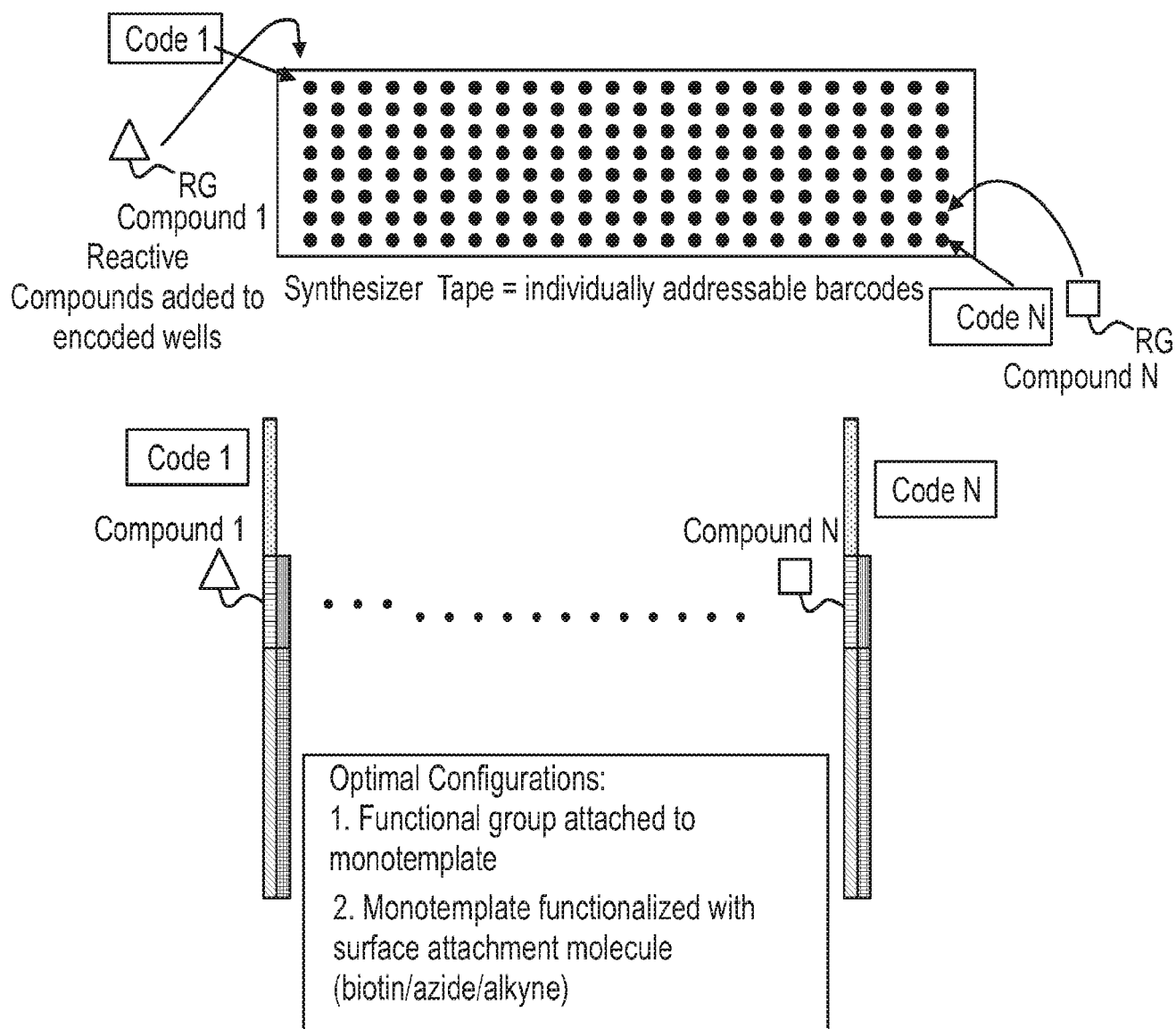


Fig. 1C

Step 4: Immobilize compounds via hybridization or surface functional group to Single Molecule surface (or Pizam flow cell surface).

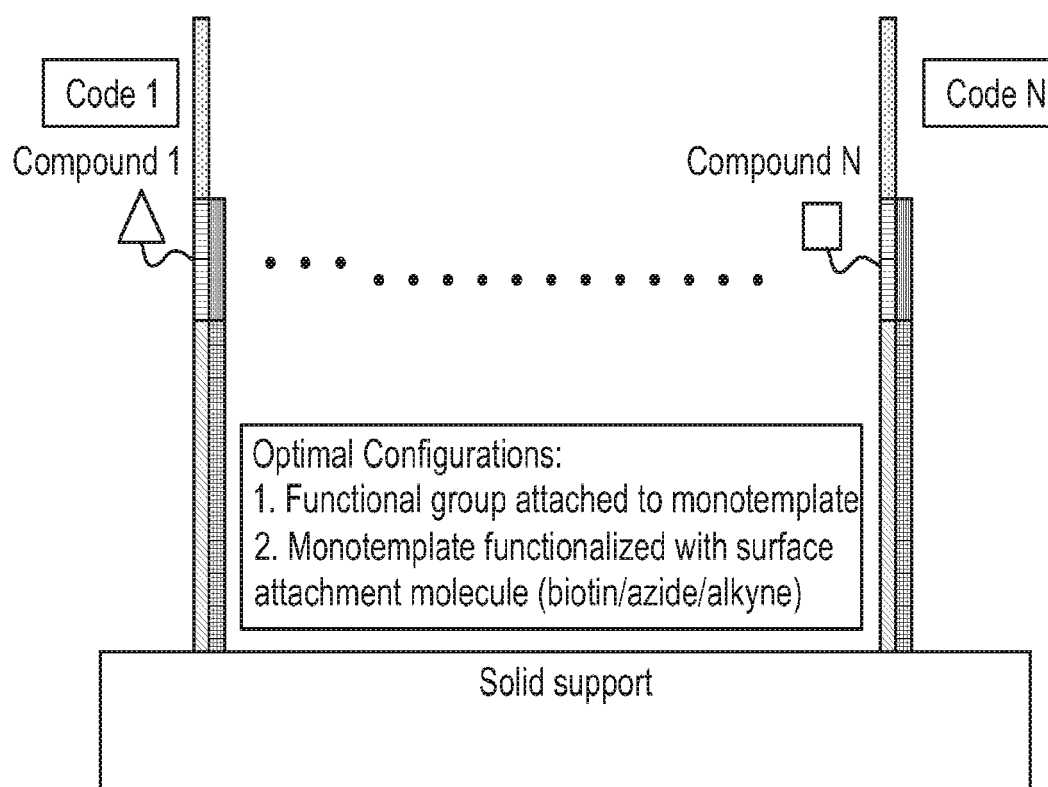


Fig. 1D

Step 5: Flow in target molecules and record real-time images of binding kinetics to compounds.

Multi-labeled Target

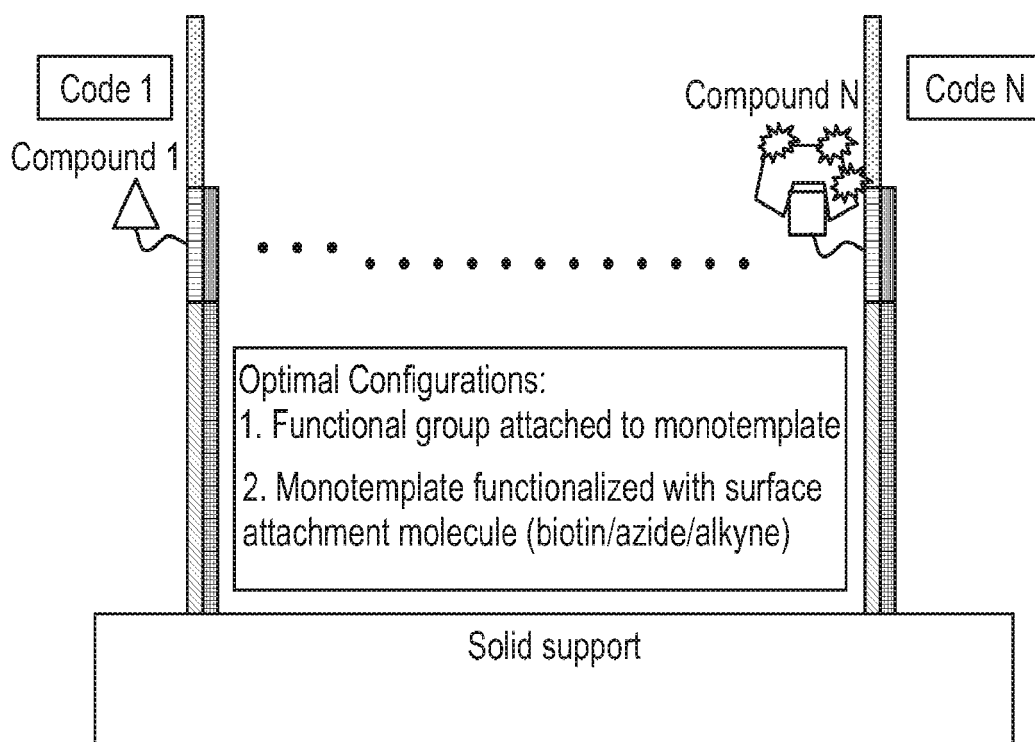
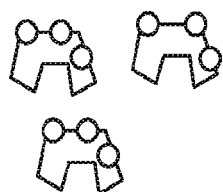


Fig. 1E

Step 6: Sequence encoded molecules to identify "leads" or "hits".

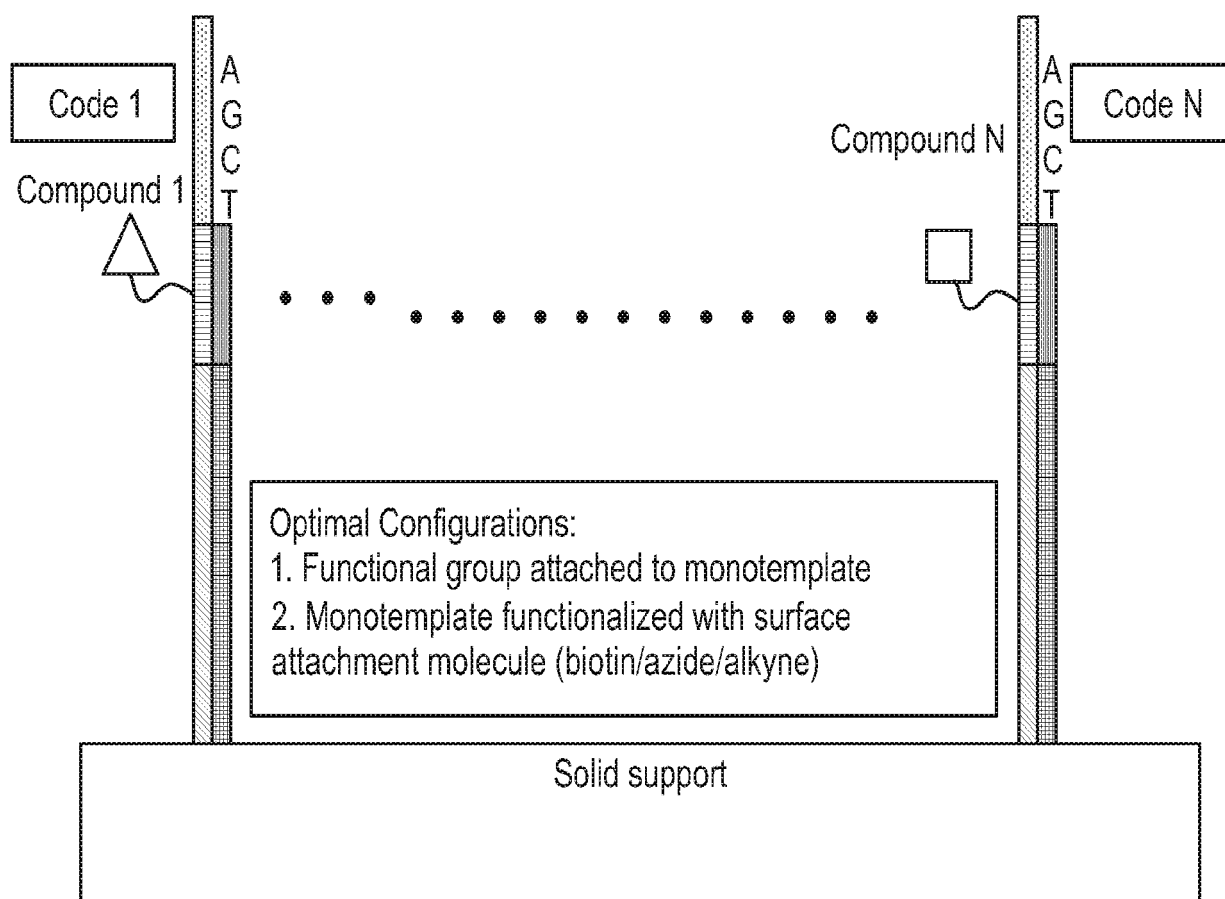


Fig. 1F

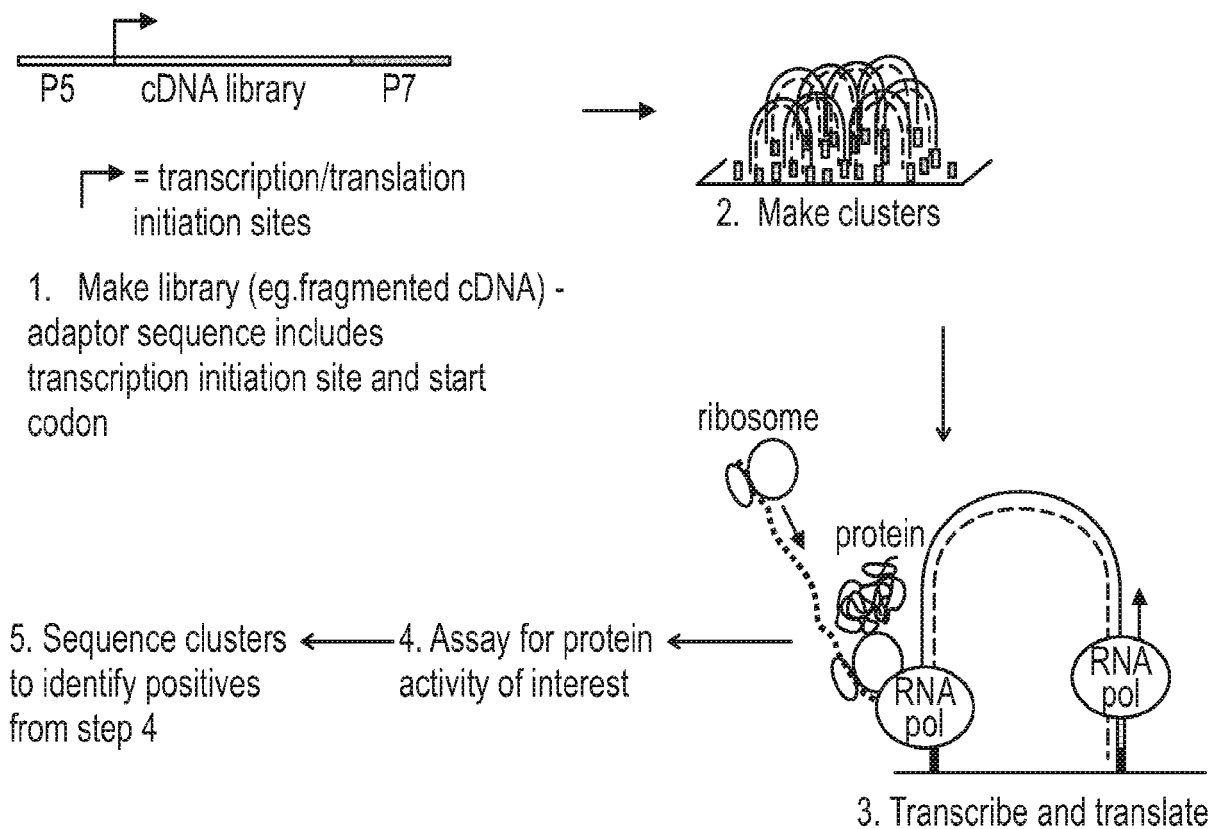
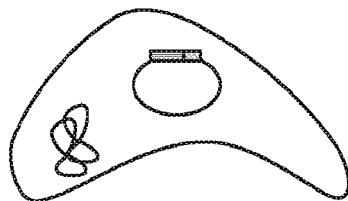
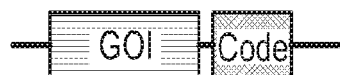


Fig. 2

1. Create bacterial library with mRNA transcripts + index
(index: 10bp = 10^6 codes; 20 bp = 10^{12} codes)



2. Lyse Bacteria - collect mRNA transcripts



3. 1/2 sample → Sequencing determine indices for mutations.
Mutation Y_1 = Code X_1
Mutation Y_2 = Code X_2
Mutation Y_N = Code X_N
4. 1/2 sample → on flow cell translation/assay

Fig. 3A

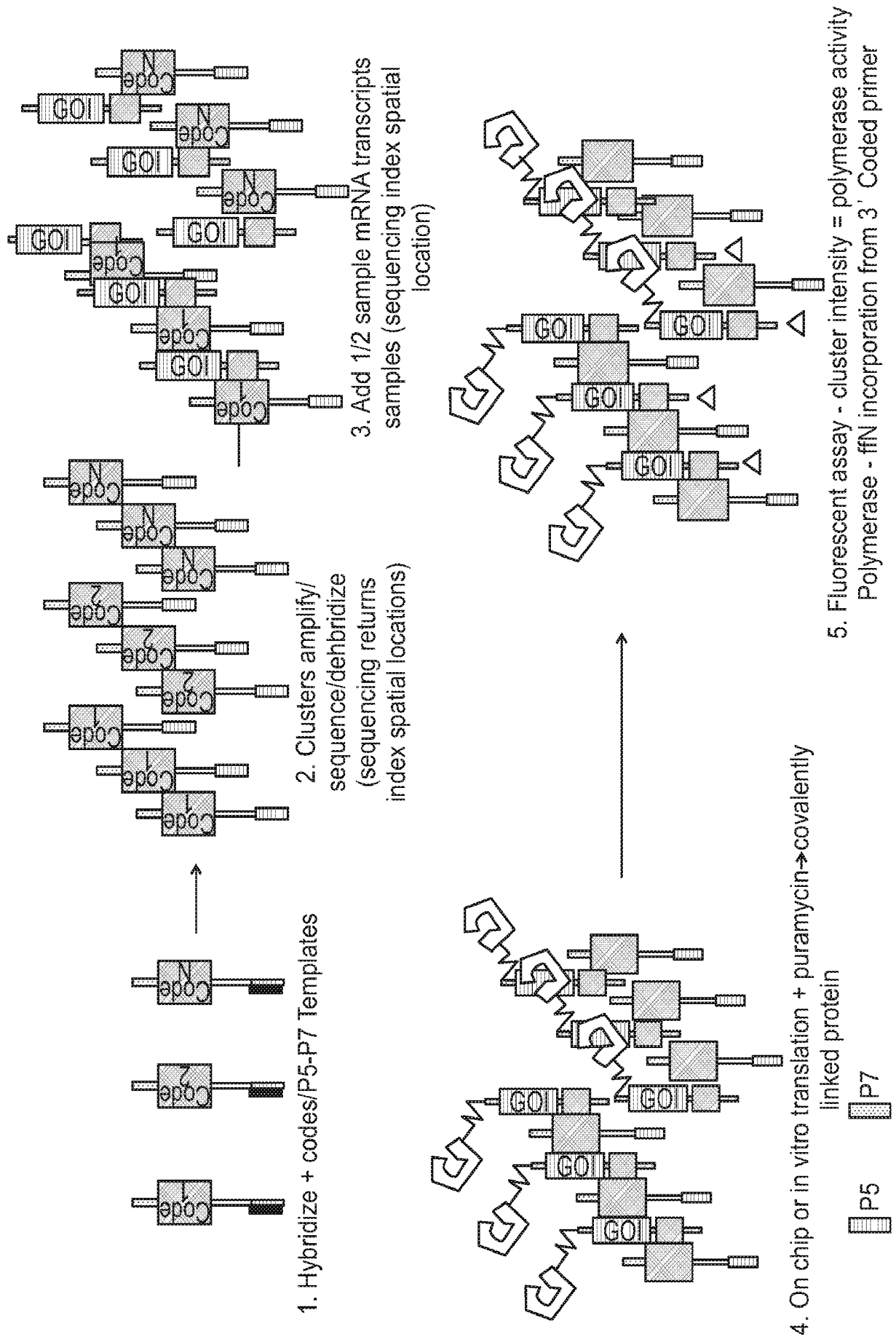


Fig. 3B

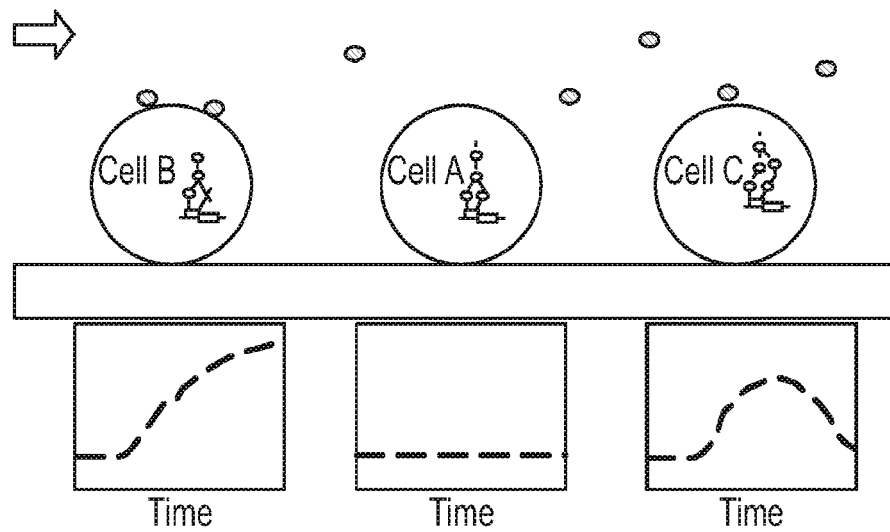


Fig. 4

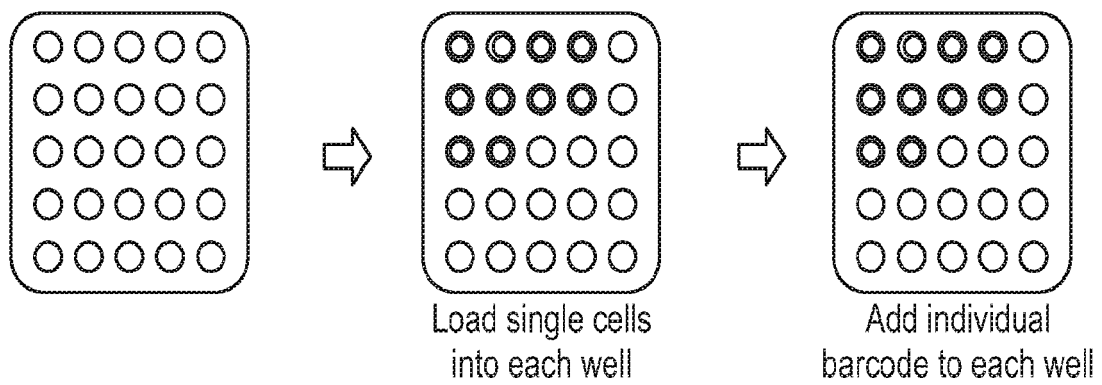


Fig. 5

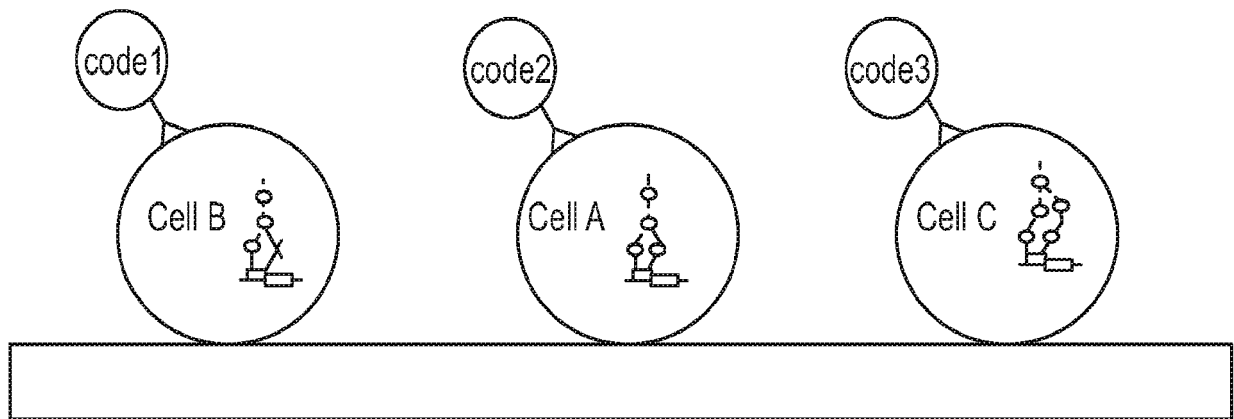


Fig. 6

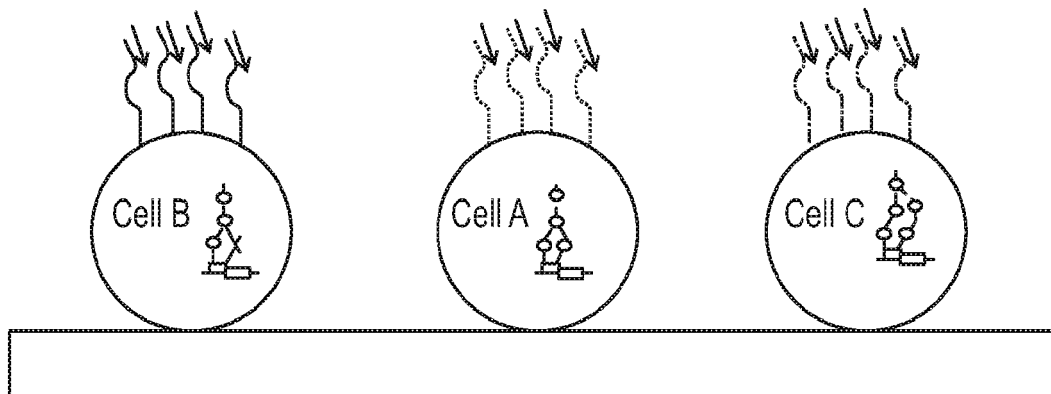


Fig. 7

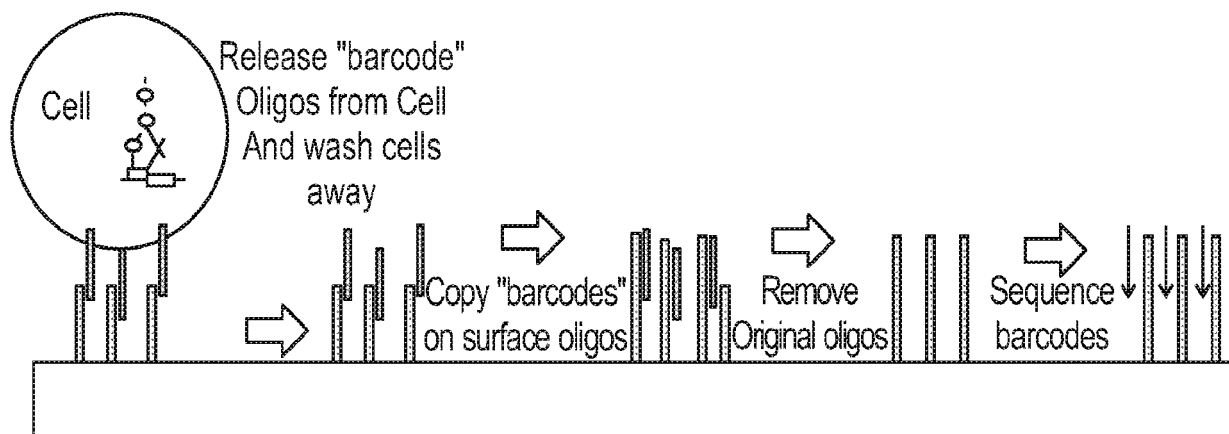


Fig. 8

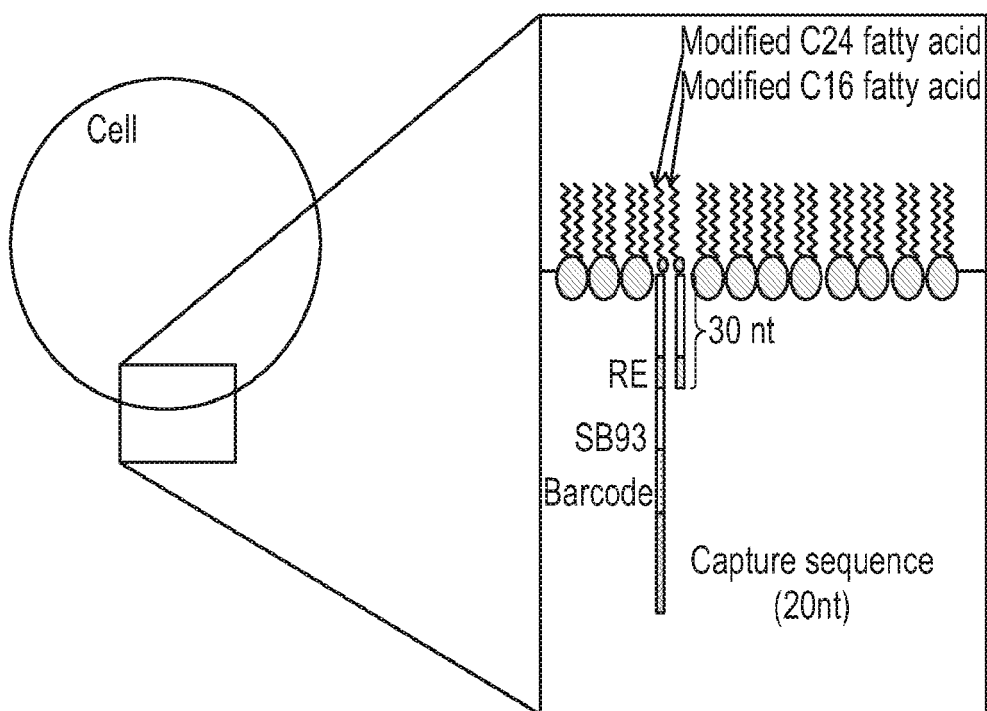


Fig. 9

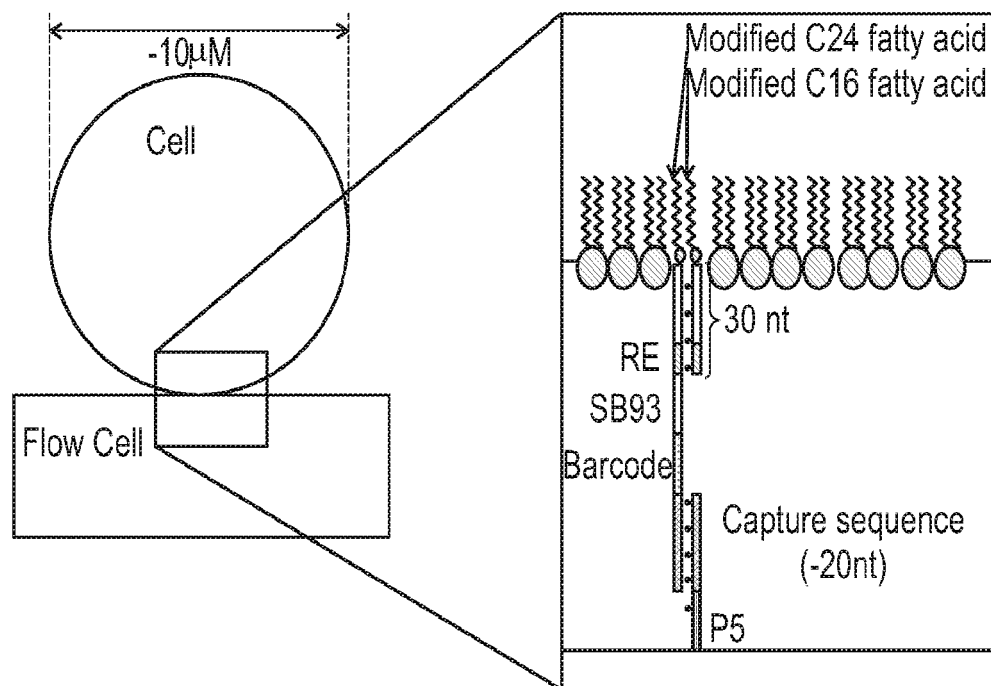


Fig. 10

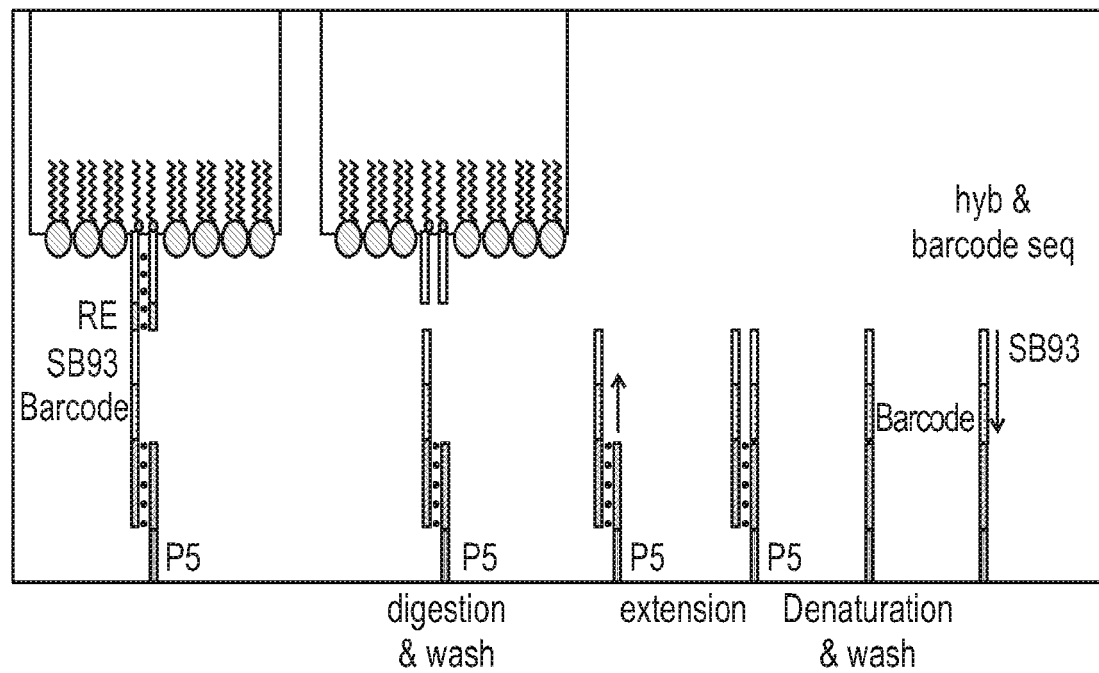


Fig. 11

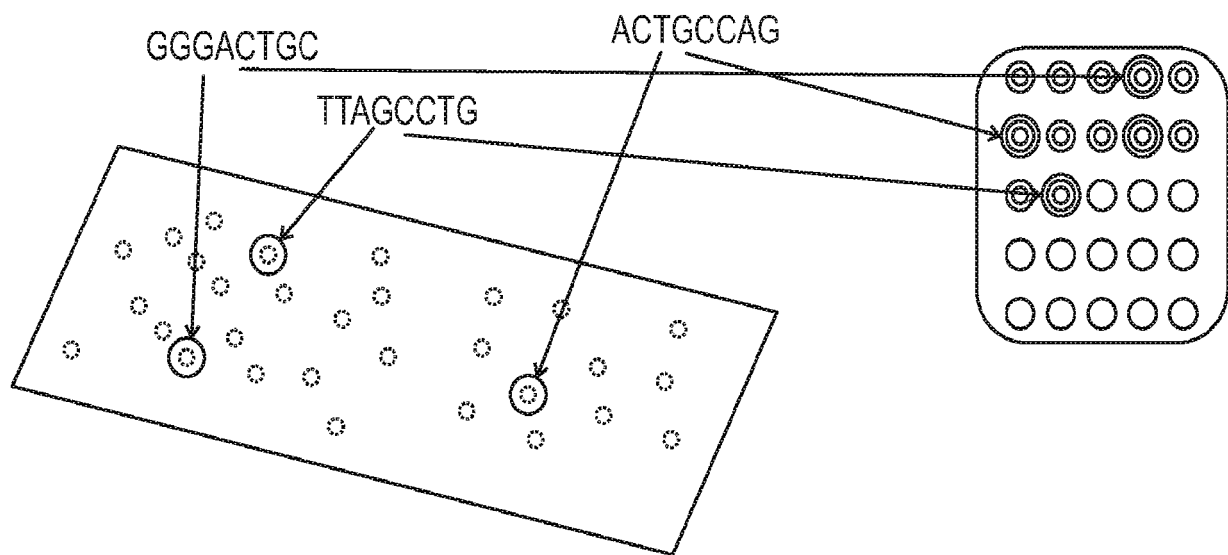


Fig. 12