

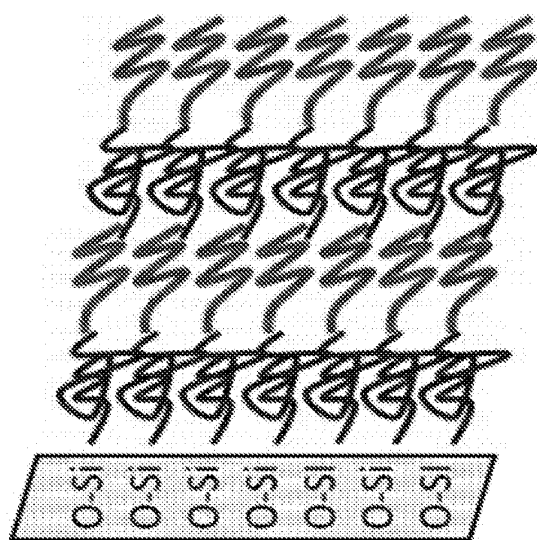


FIG. 1

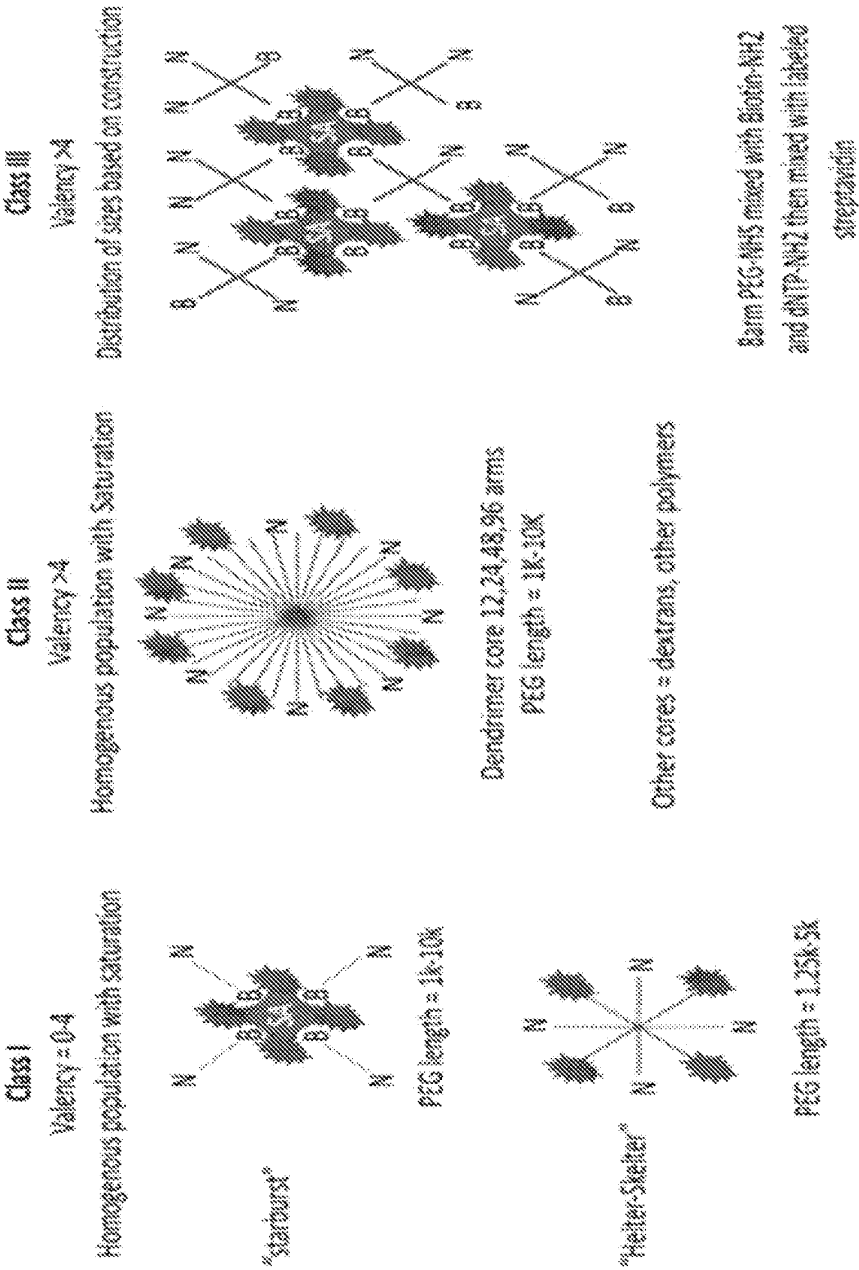


FIG. 2

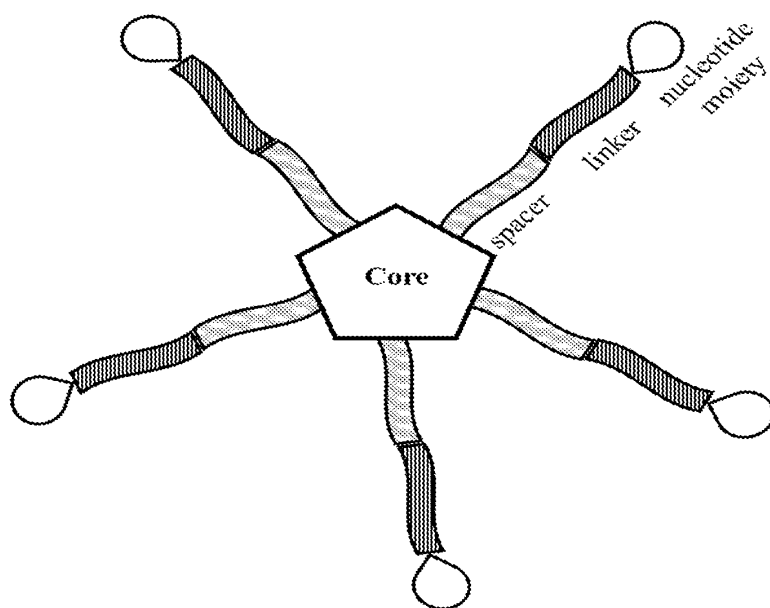


FIG. 3

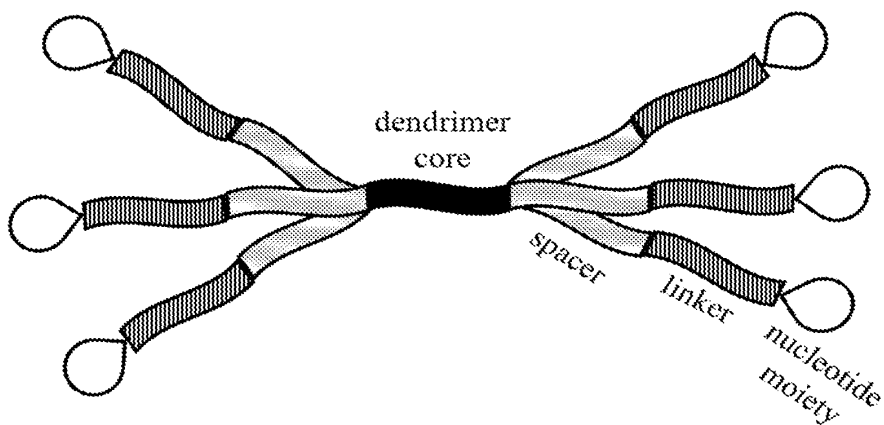


FIG. 4

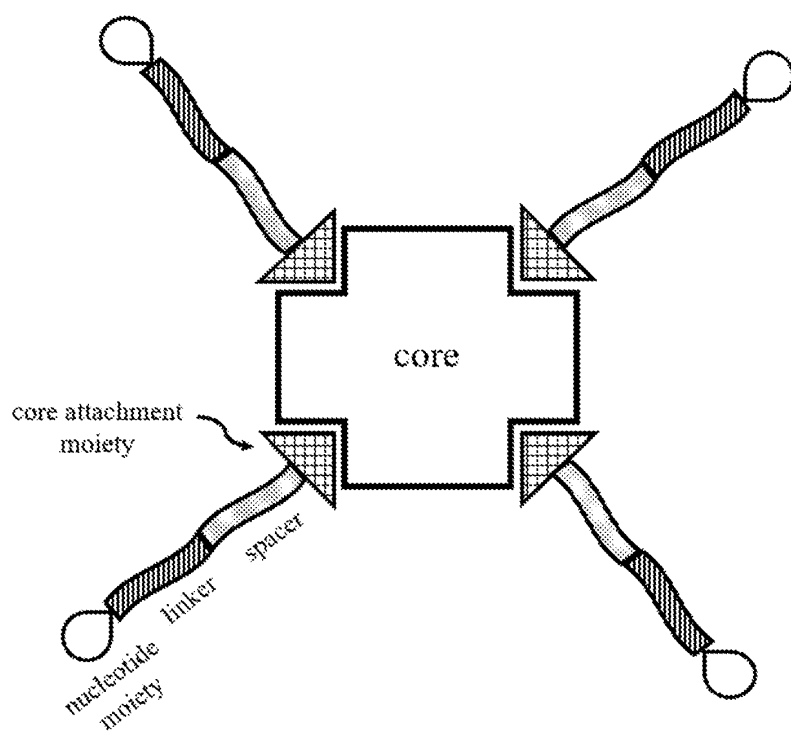


FIG. 5

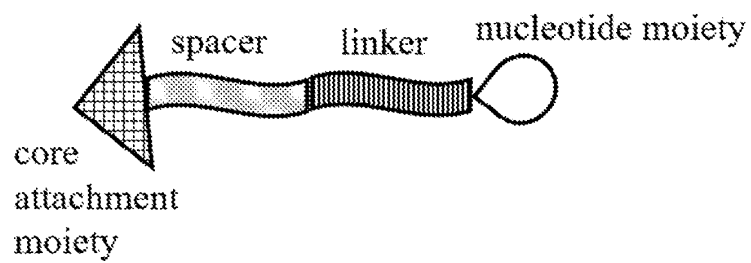
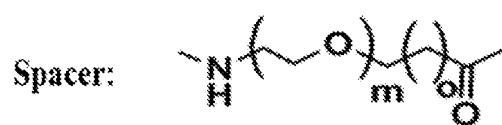
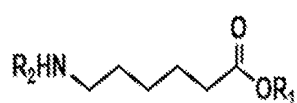


FIG. 6

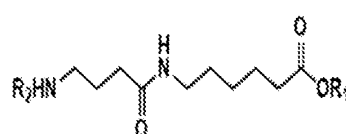


Linkers:

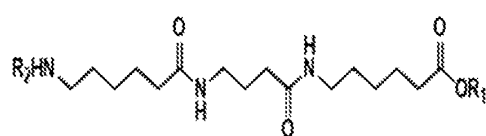
11 atom Linker:



16 atom Linker:



23 atom Linker:



N3 Linker:

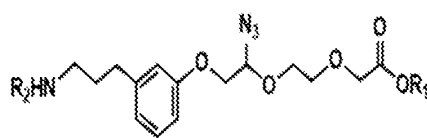


FIG. 7

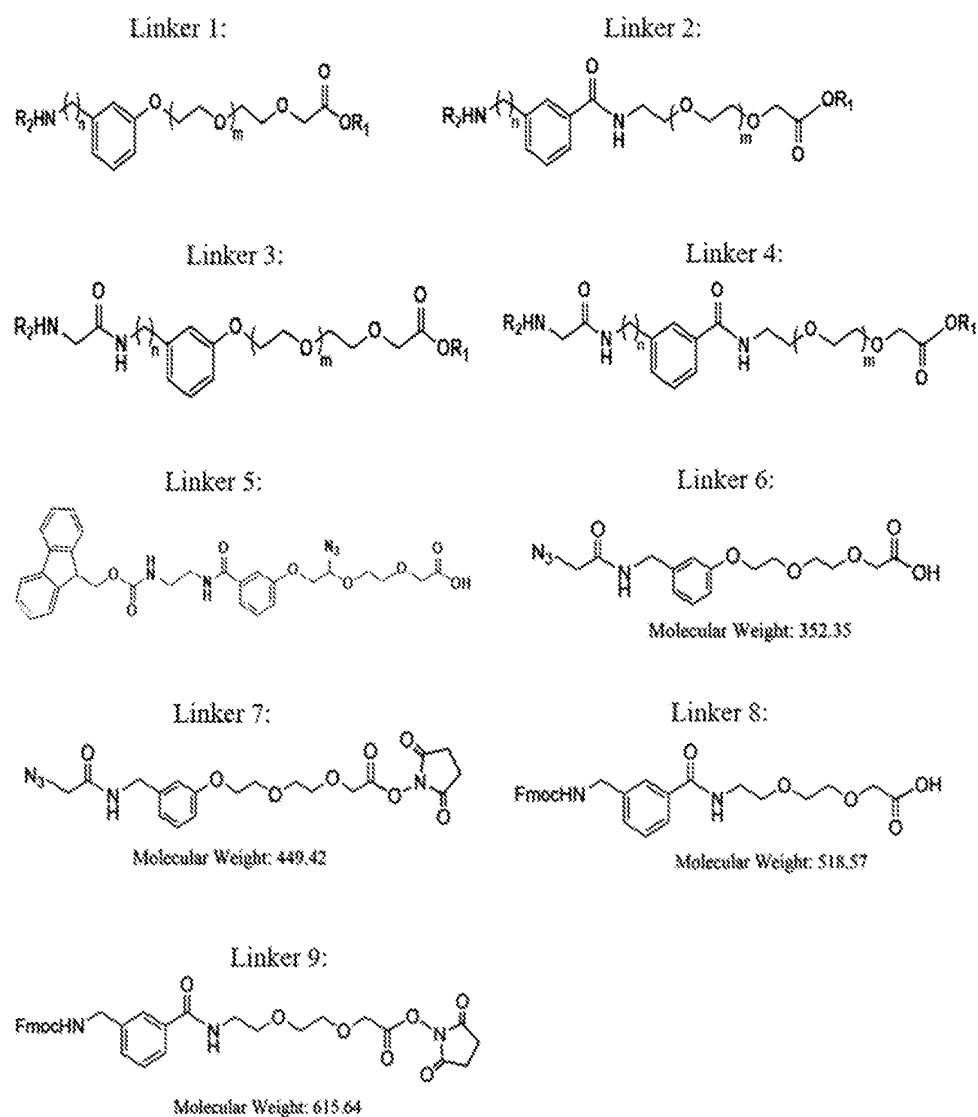
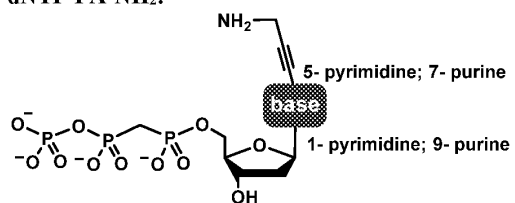
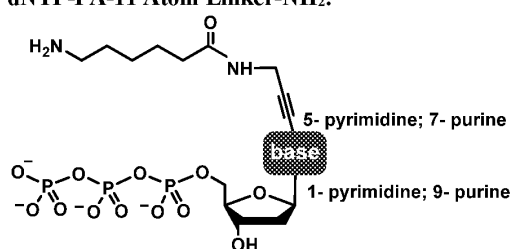


FIG. 8

dNTP-PA-NH<sub>2</sub>:



dNTP-PA-11 Atom Linker-NH<sub>2</sub>:



dNTP-PA-16 Atom Linker-NH<sub>2</sub>:

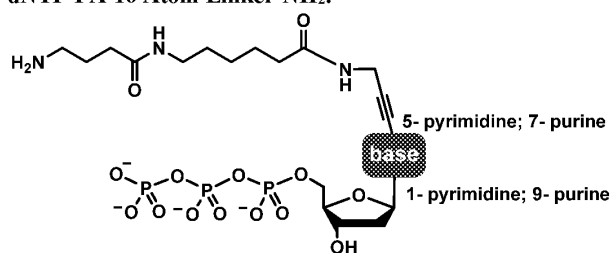


FIG. 9

NC(=O)CCCCCNC(=O)CCCCCNC(=O)CCCCCNC(=O)C#CC1=CC=NC=C2C(=C1)N=CN=C2[C@@H]3O[C@H](COP(=O)([O-])OP(=O)([O-])OP(=O)([O-])O)[C@H](O)[C@@H](O)[C@H]3O

5- pyrimidine; 7- purine  
base  
1- pyrimidine; 9- purine

FIG. 10

5- pyrimidine; 7- purine

base

1- pyrimidine; 9- purine

The chemical structure shows a nucleoside analog. It consists of a sugar moiety (1-pyrimidine; 9-purine) linked via a phosphate group to a flexible linker (5-pyrimidine; 7-purine). The linker is composed of a benzene ring connected to a polyether chain (-(CH<sub>2</sub>)<sub>n</sub>-O-(CH<sub>2</sub>)<sub>m</sub>-O-). The sugar moiety is a pyrimidine or purine base attached to a ribose or deoxyribose sugar. The phosphate group is a triphosphate group (O<sup>-</sup>-P(=O)(O<sup>-</sup>)<sub>2</sub>-O-P(=O)(O<sup>-</sup>)<sub>2</sub>-O-P(=O)(O<sup>-</sup>)<sub>2</sub>-O-).

Chemical structure of a nucleoside derivative with a poly(amide ether) side chain. The structure shows a nucleoside core (sugar, phosphate, and base) where the base is labeled "base" and the sugar is labeled "1- pyrimidine; 9- purine". The side chain consists of a poly(amide ether) segment with a repeating unit of  $n$  and a terminal unit of  $m$ . The side chain is attached to the base via a triazole linkage. The labels "5- pyrimidine; 7- purine" and "1- pyrimidine; 9- purine" are also present.

FIG. 11

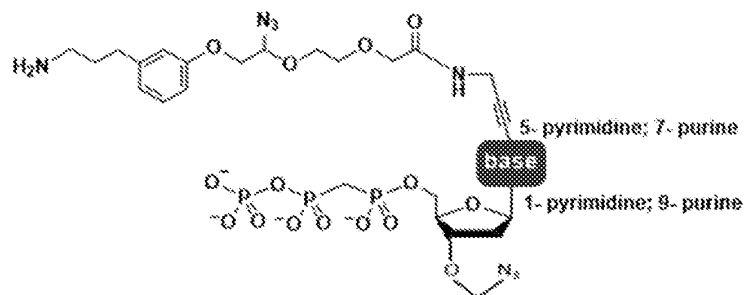
dNTP-PA-N3 Linker-NH<sub>2</sub>:

FIG. 12

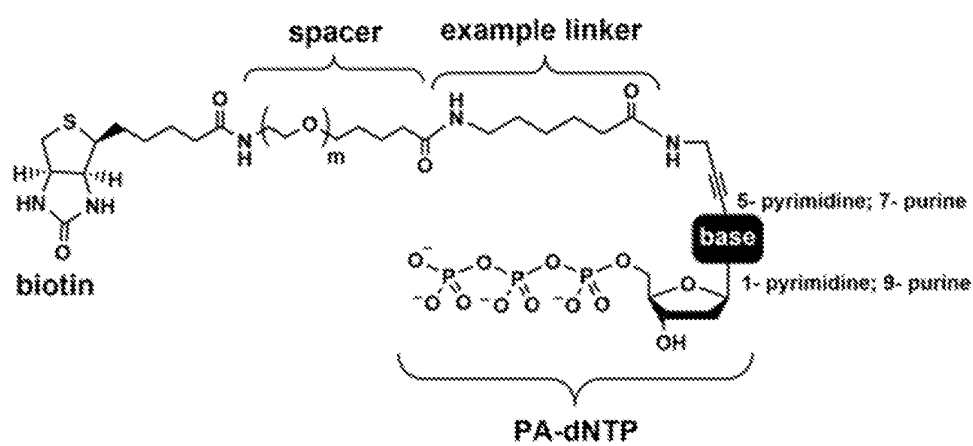


FIG. 13

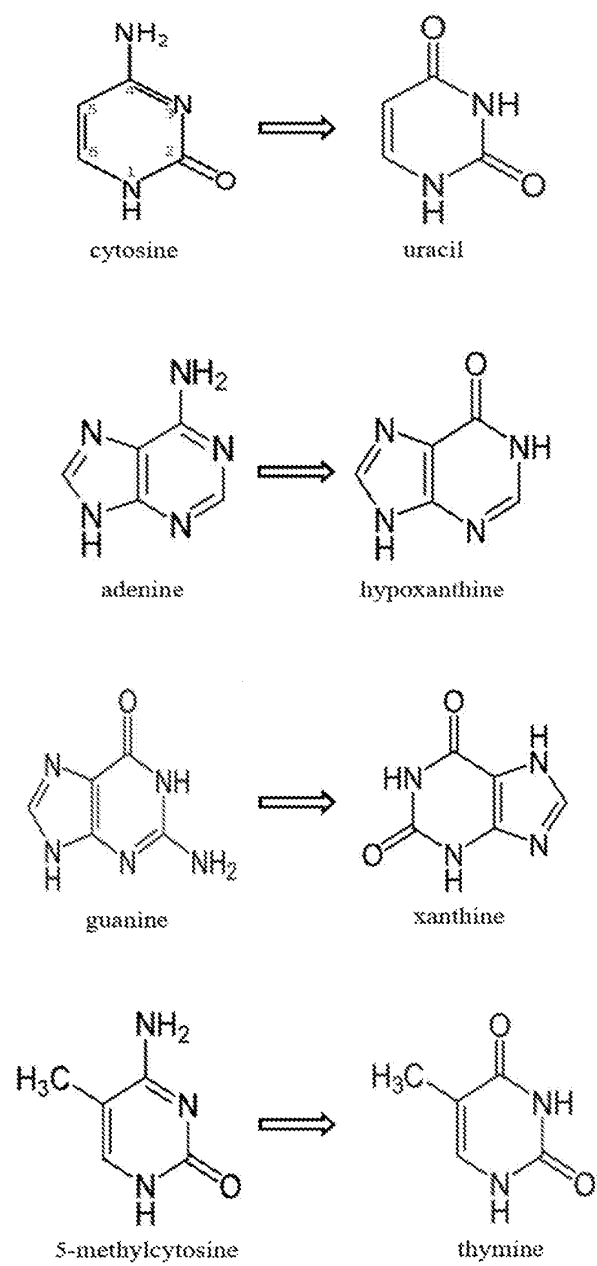


FIG. 14

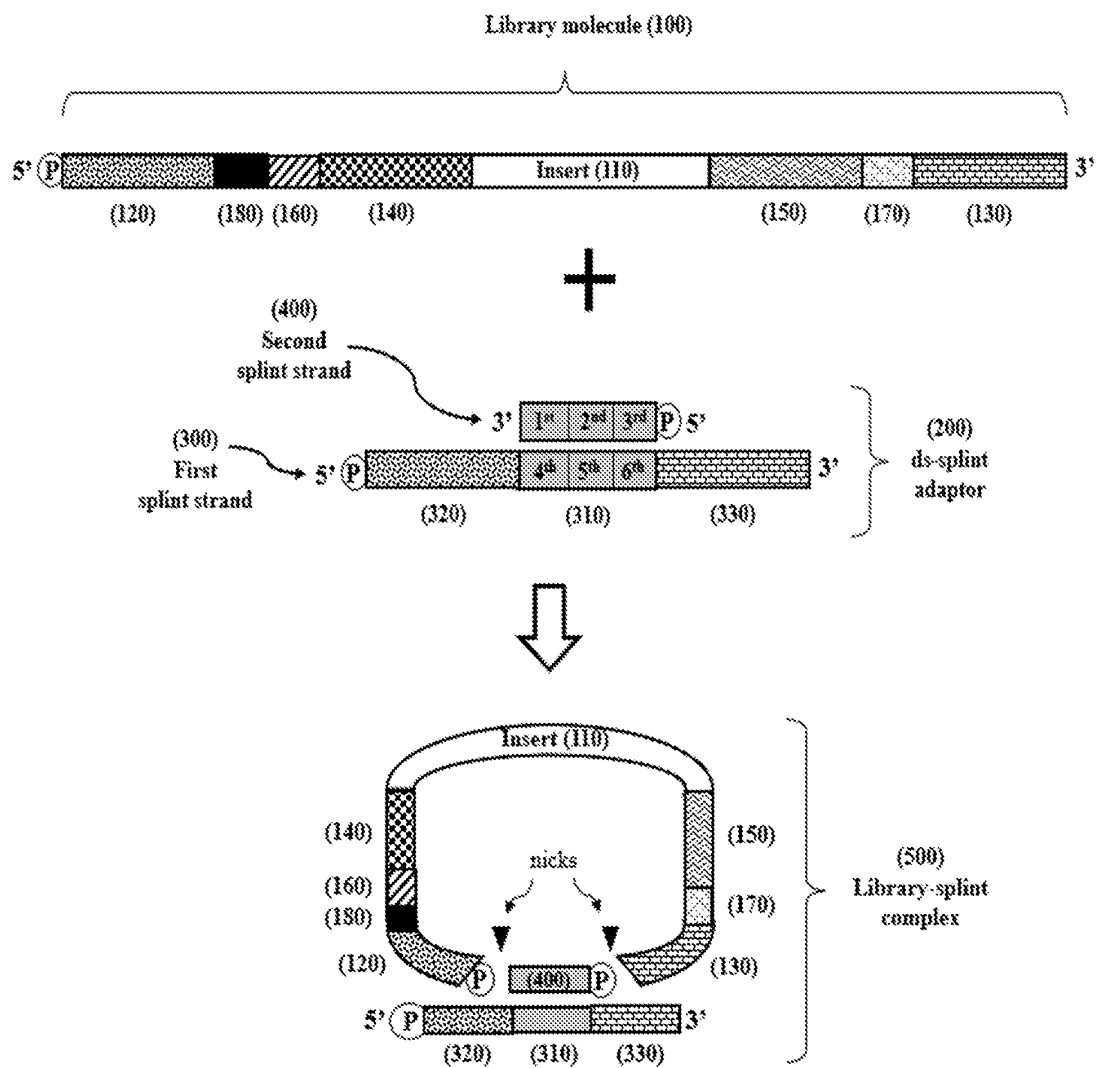


FIG. 15

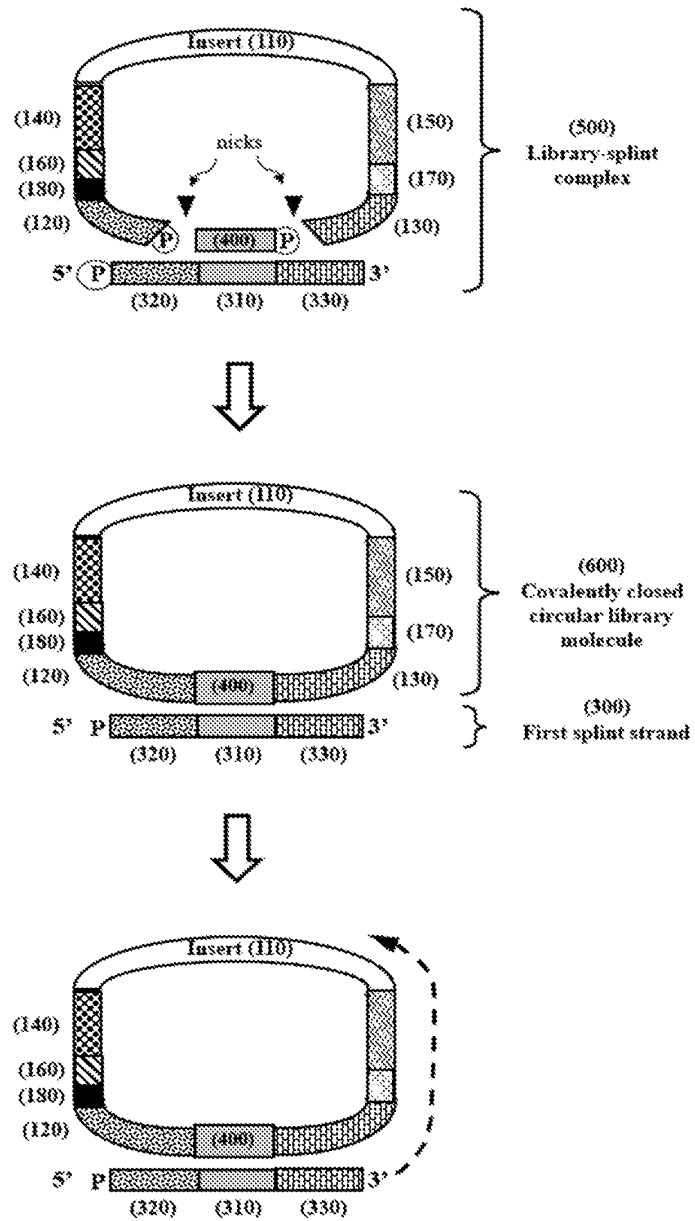


FIG. 16

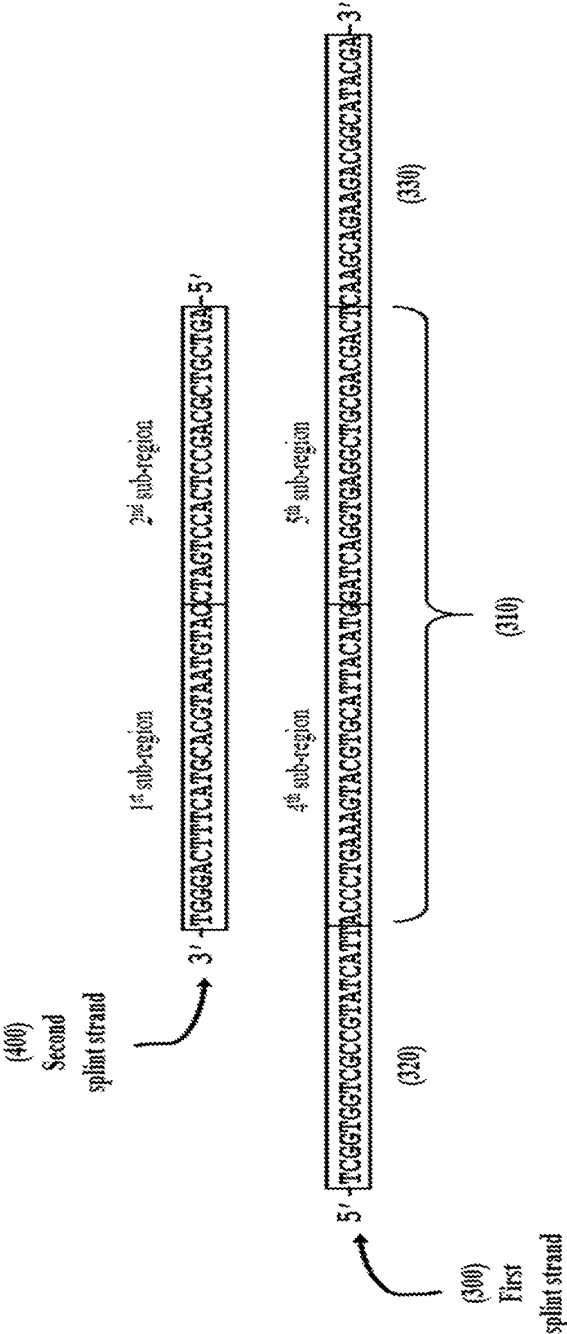


FIG. 17

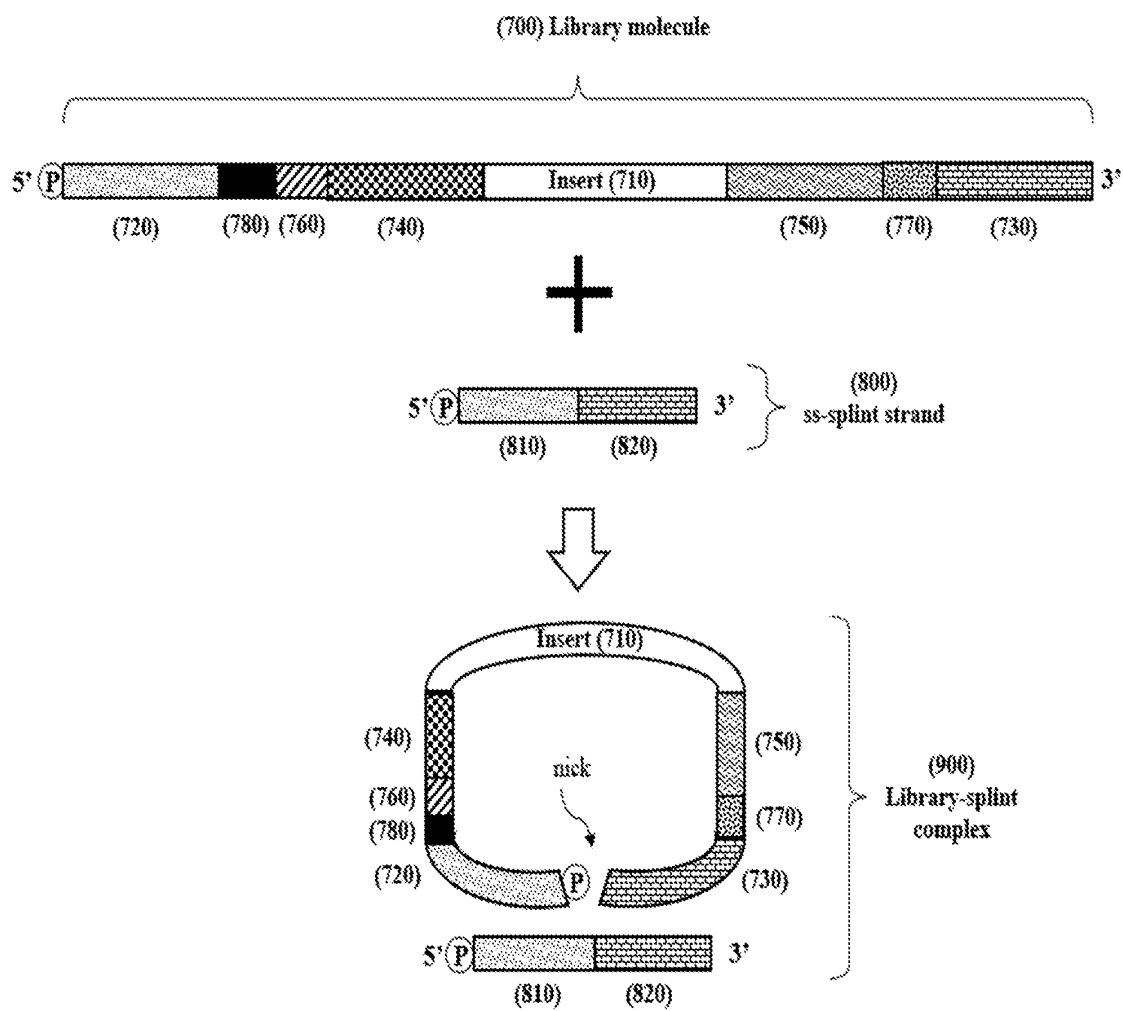


FIG. 18

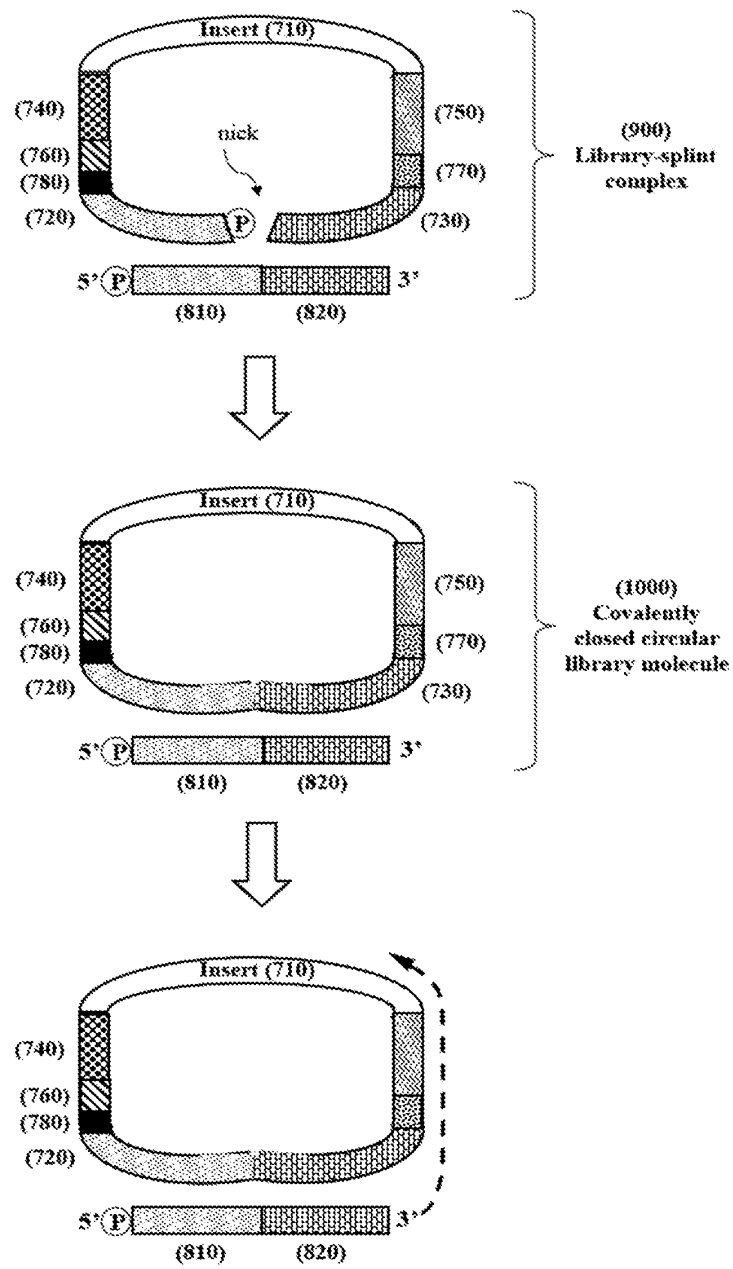


FIG. 19



FIG. 20

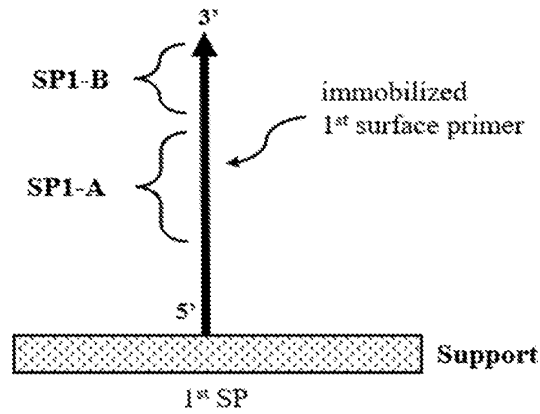
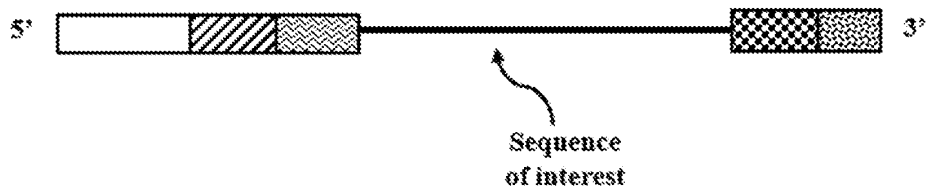


FIG. 21



-  = 2<sup>nd</sup> portion of a 1<sup>st</sup> surface primer binding site (SP1-B')
-  = reverse seq'g primer binding site
-  = forward seq'g primer binding site
-  = soluble amplification primer binding site
-  = 1<sup>st</sup> portion of a 1<sup>st</sup> surface primer binding site (SP1-A')

FIG. 22

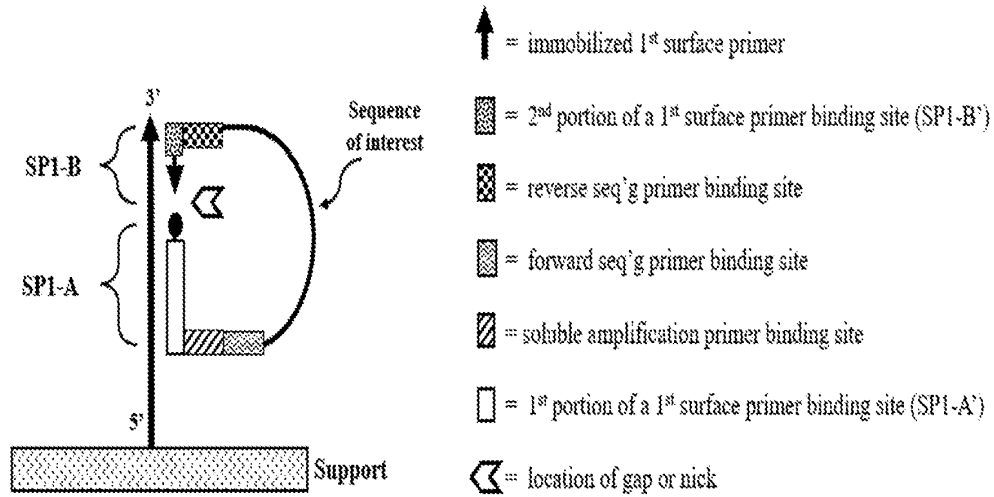


FIG. 23

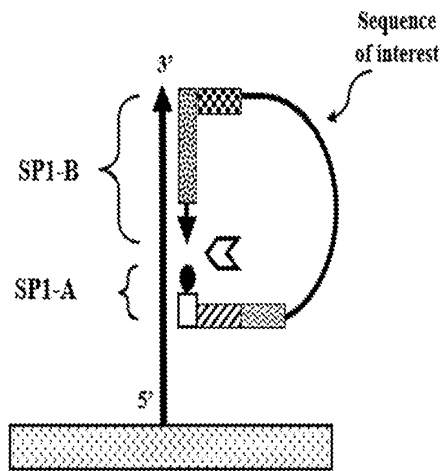


FIG. 24

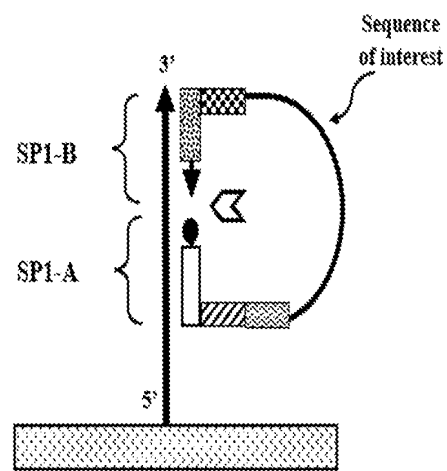


FIG. 25

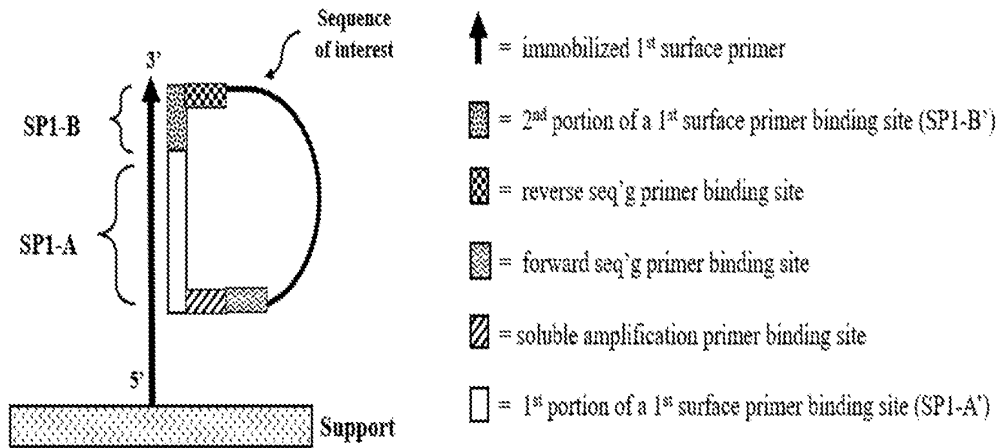


FIG. 26

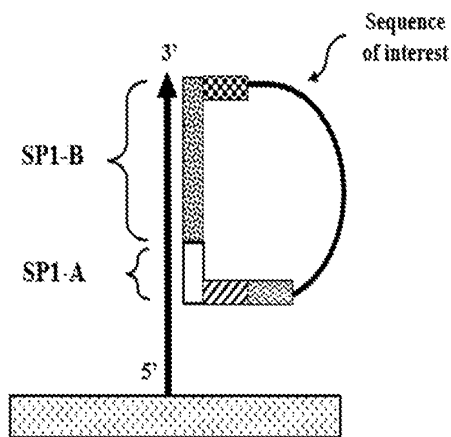


FIG. 27

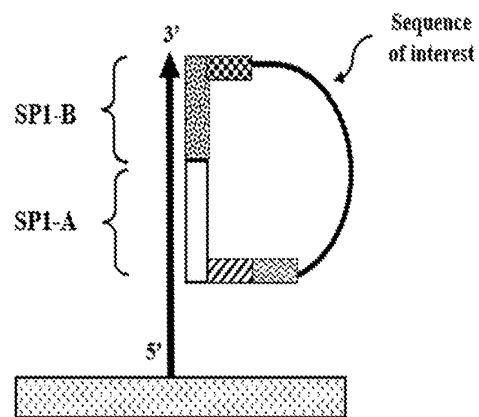


FIG. 28

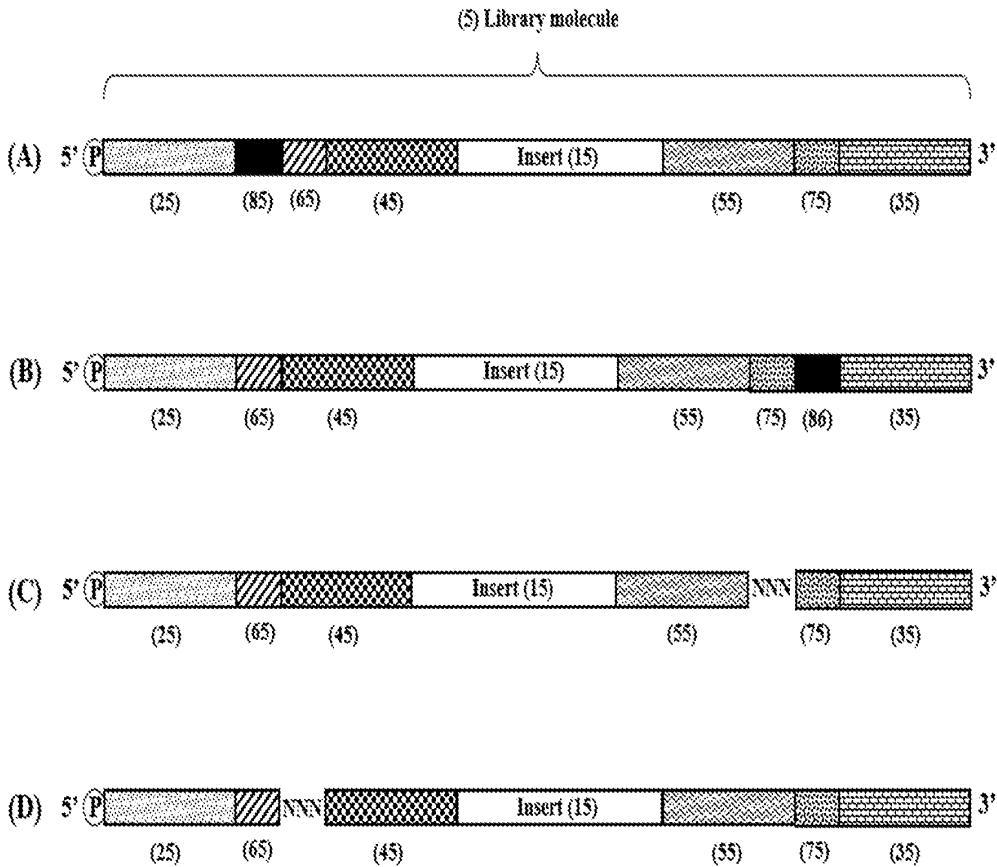


FIG. 29

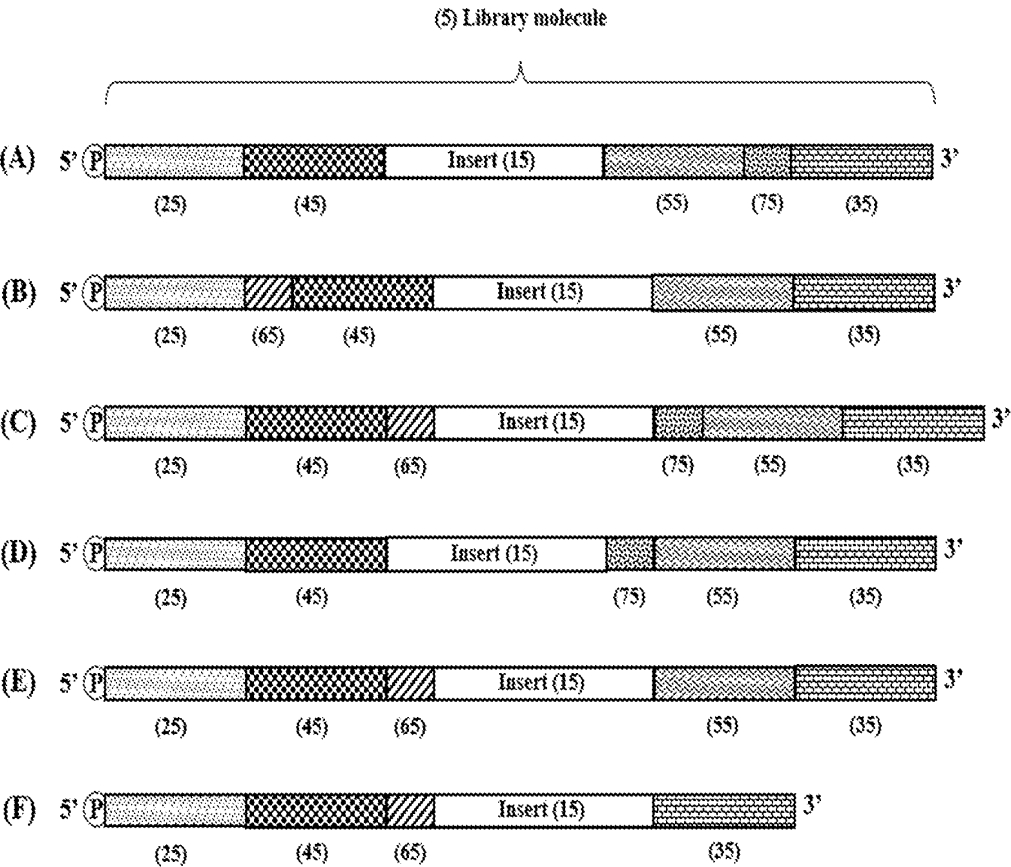


FIG. 30

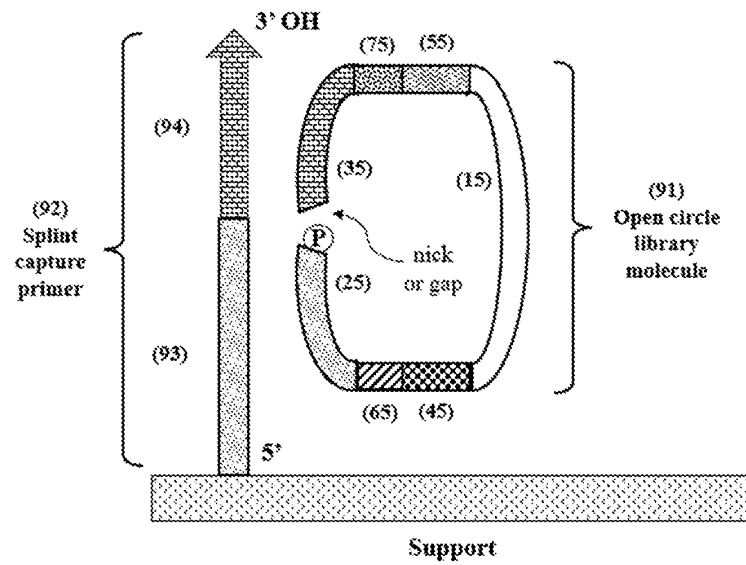


FIG. 31A

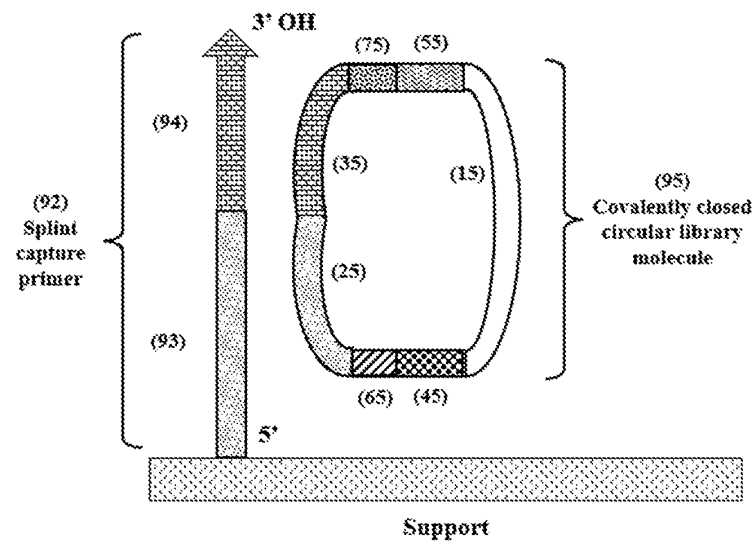


FIG. 31B



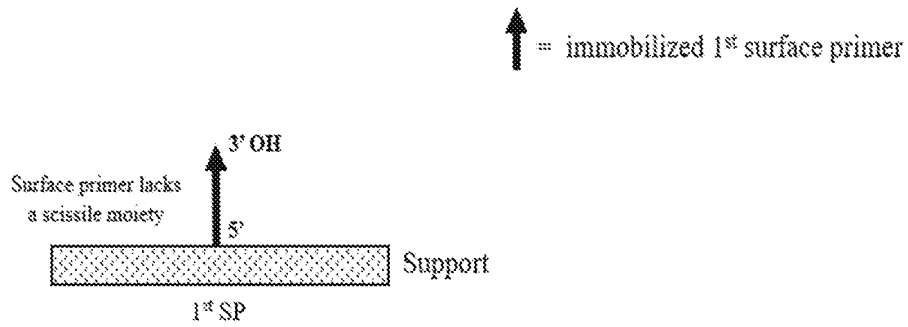


FIG. 33

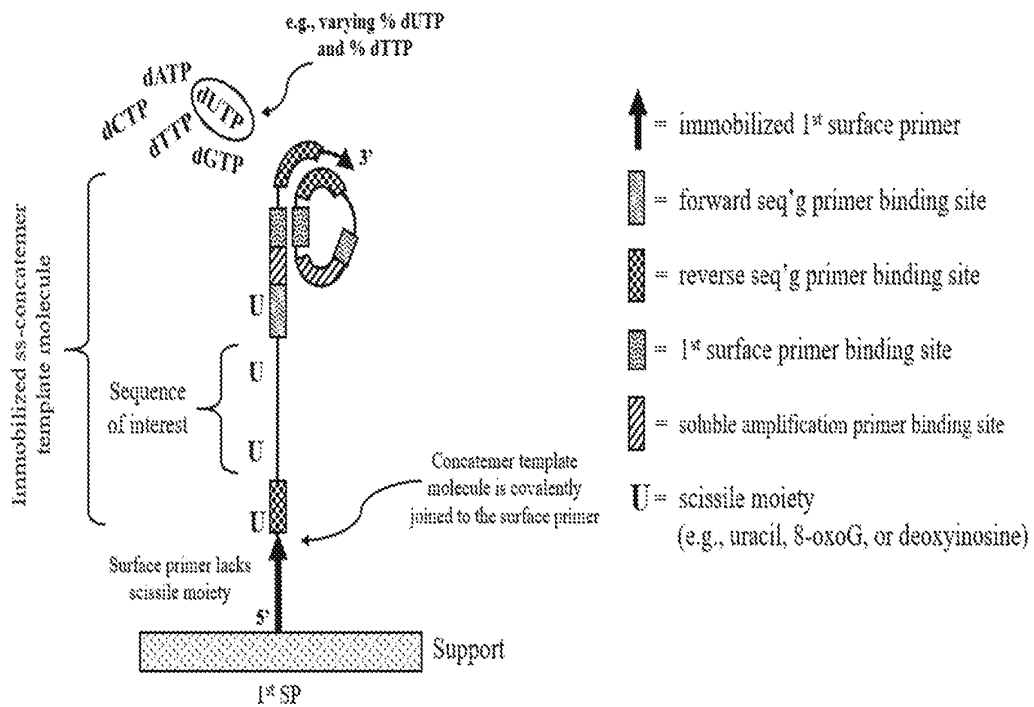


FIG. 34

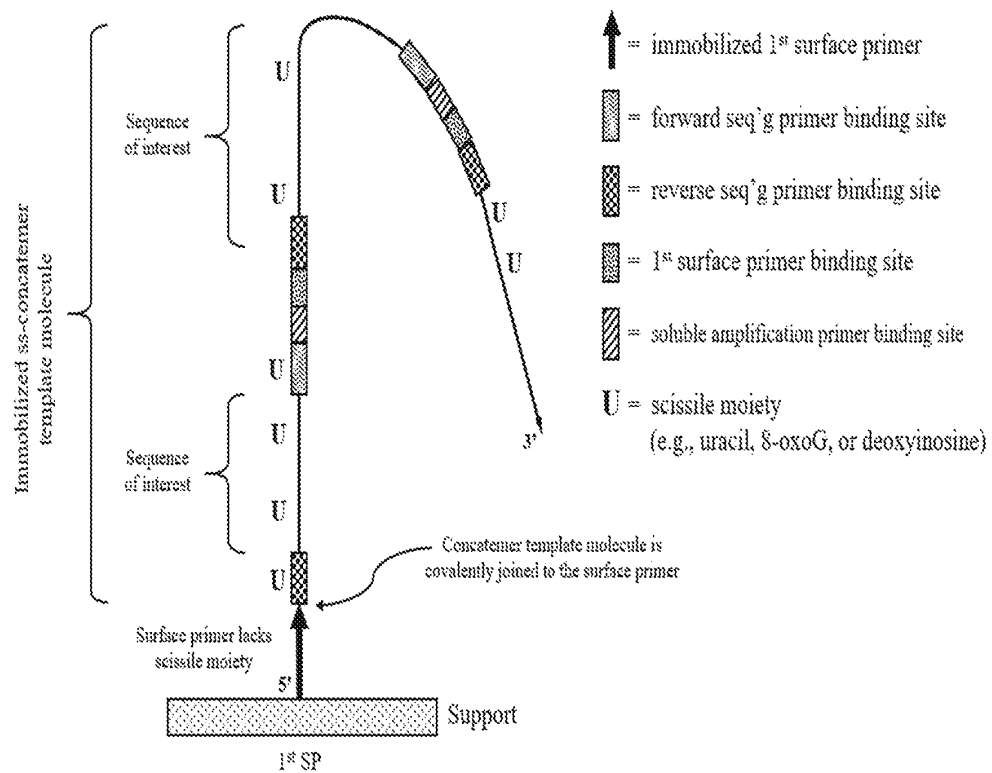


FIG. 35

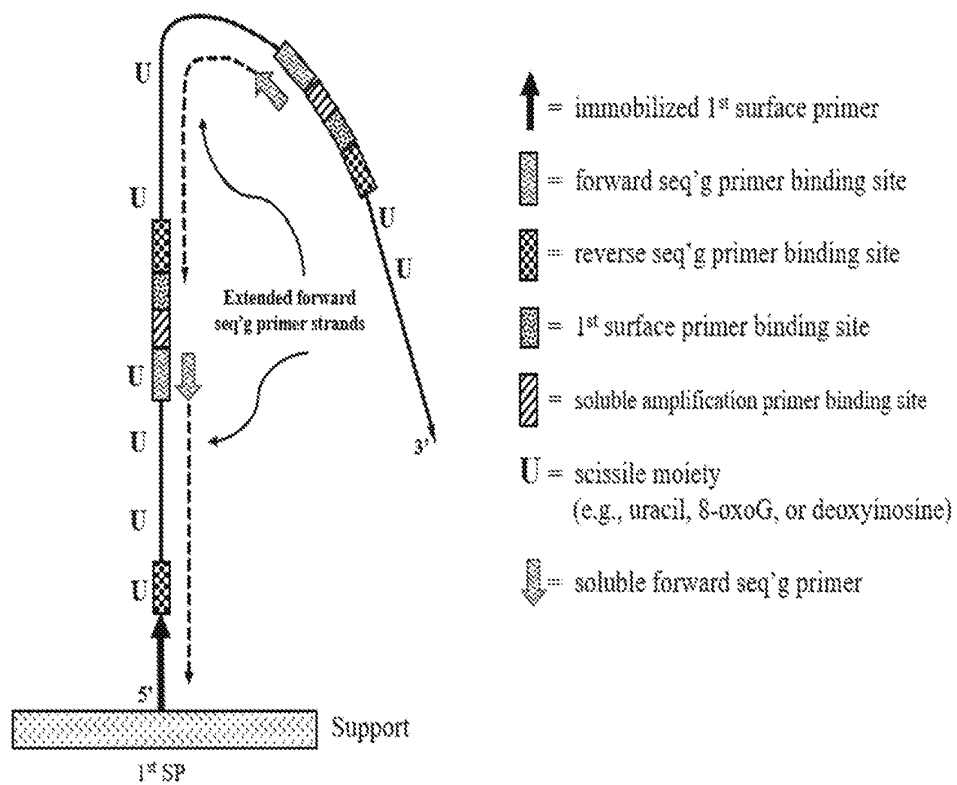


FIG. 36

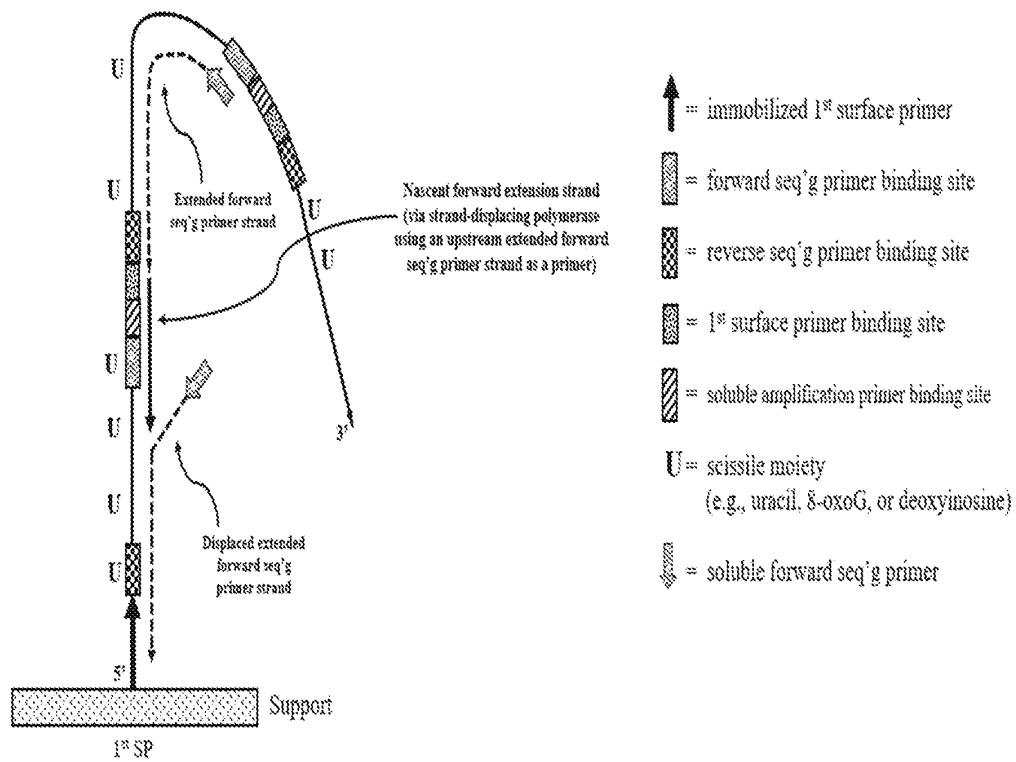


FIG. 37

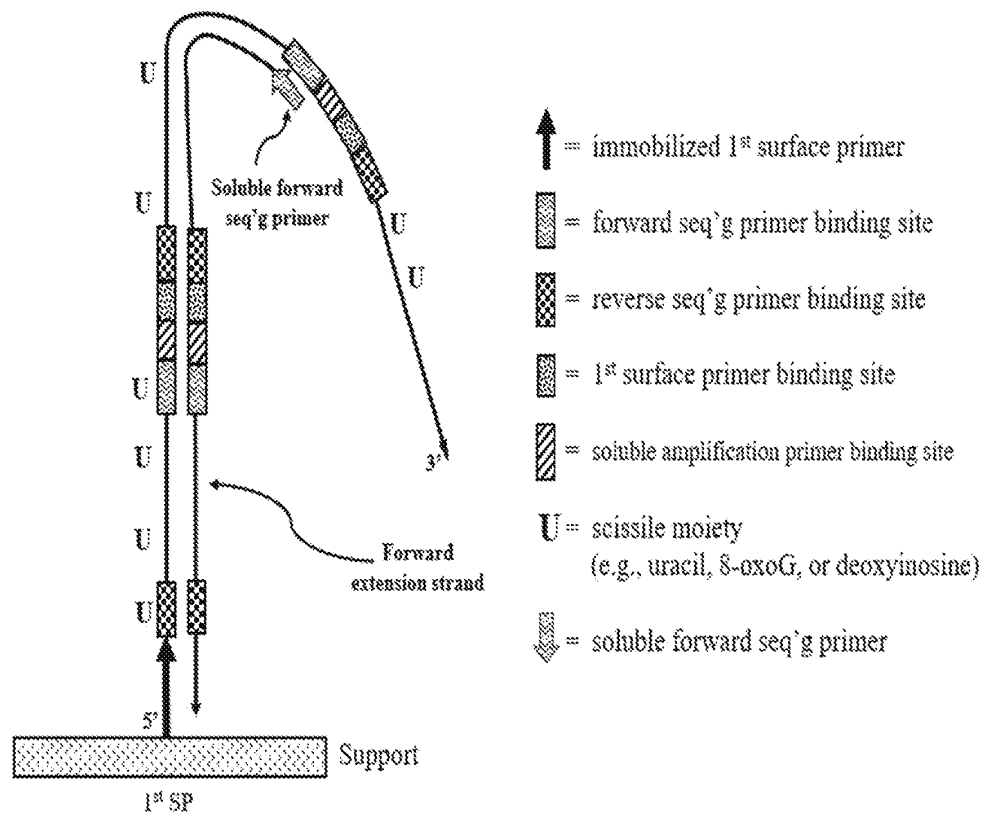


FIG. 38

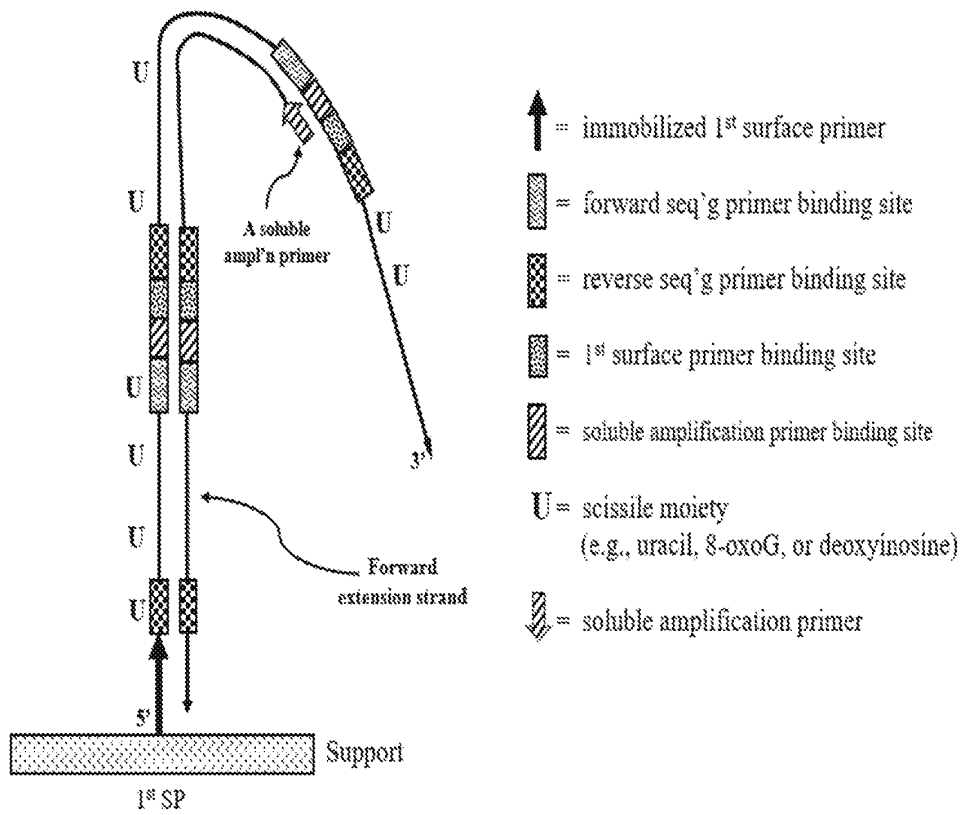


FIG. 39

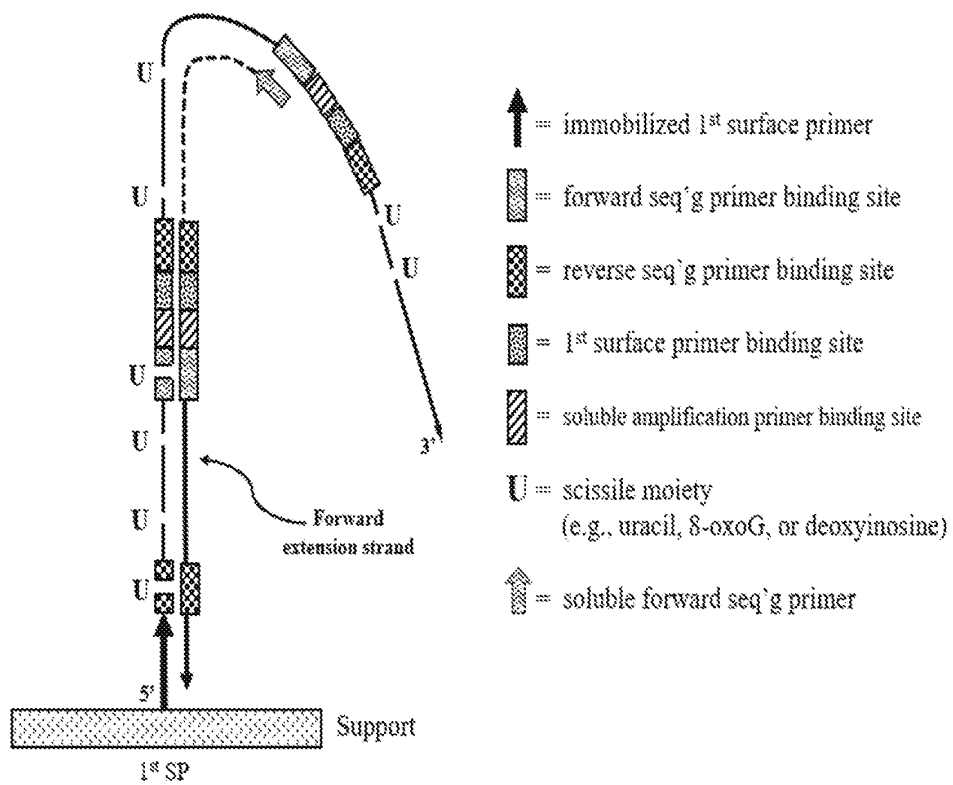


FIG. 40

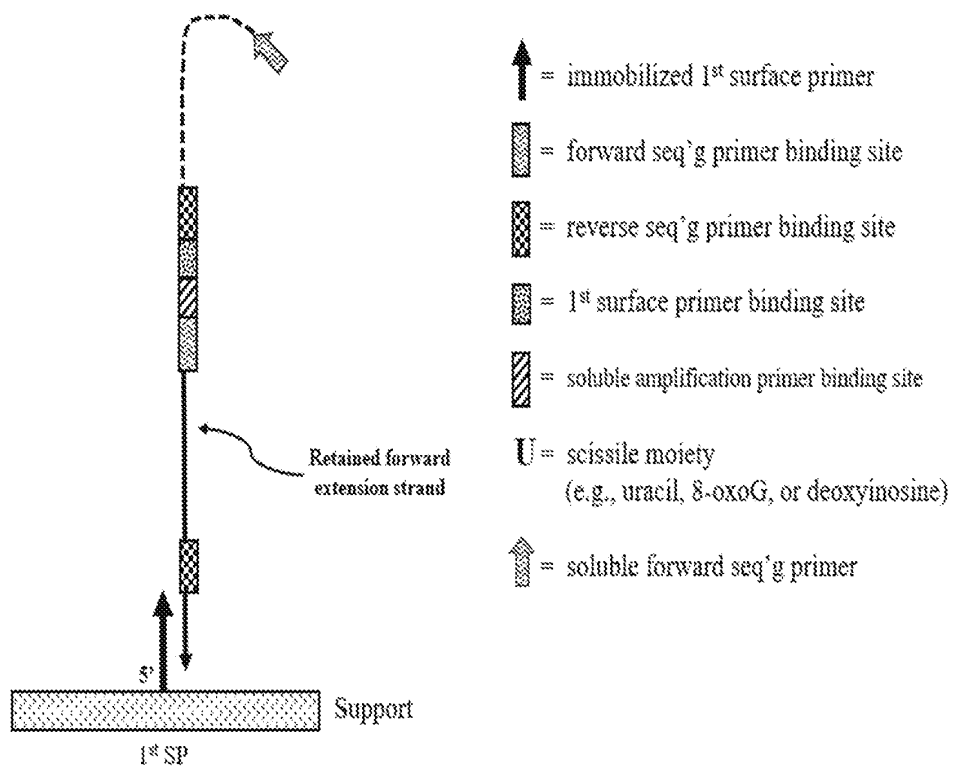


FIG. 41

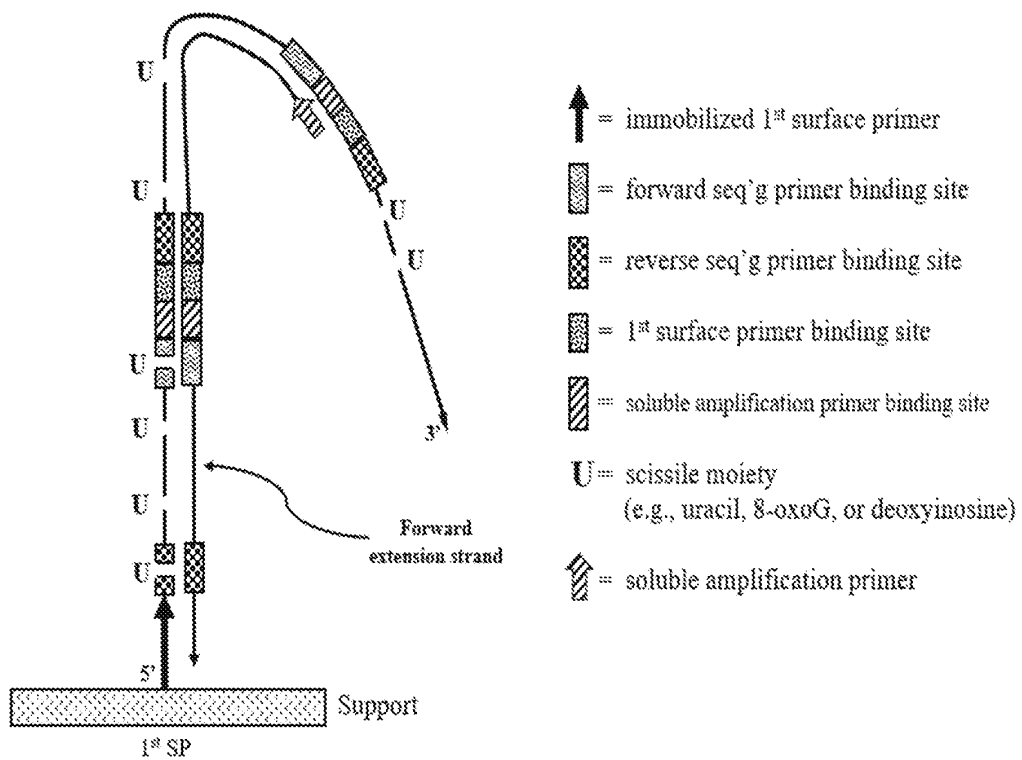


FIG. 42

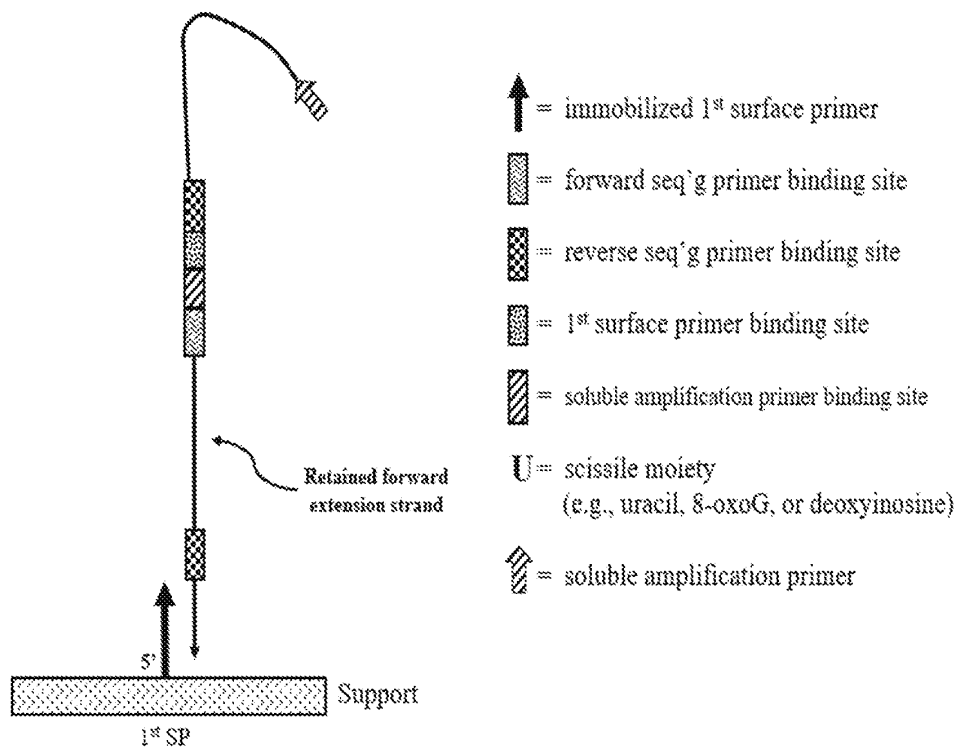


FIG. 43

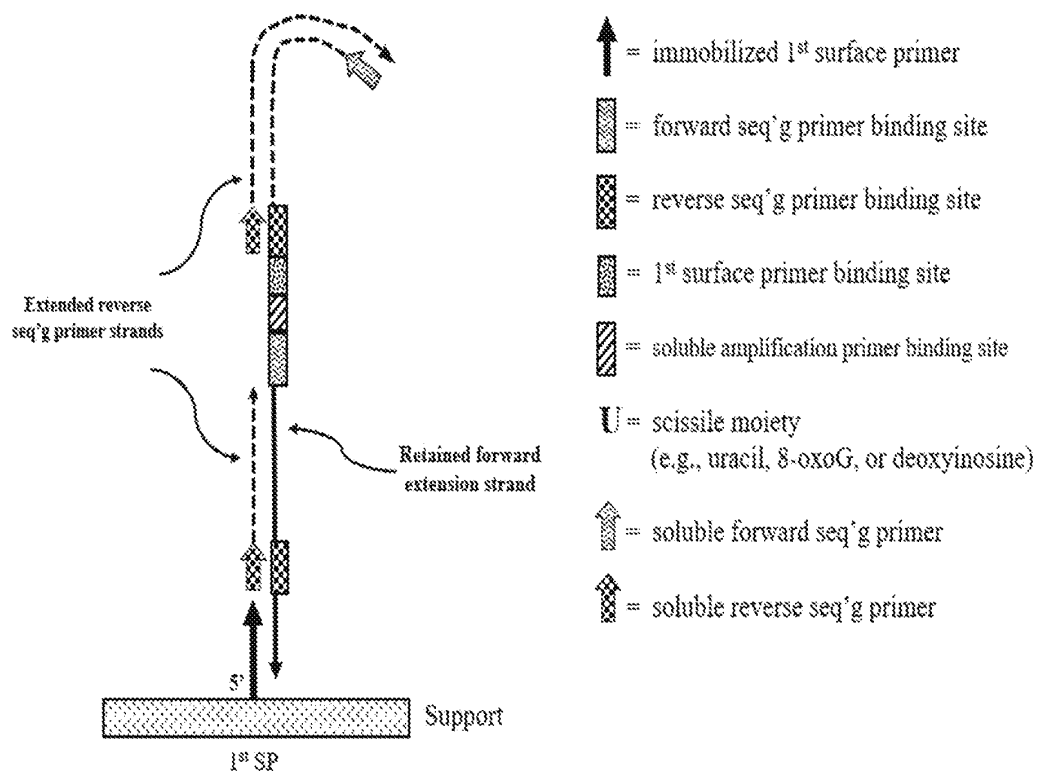


FIG. 44

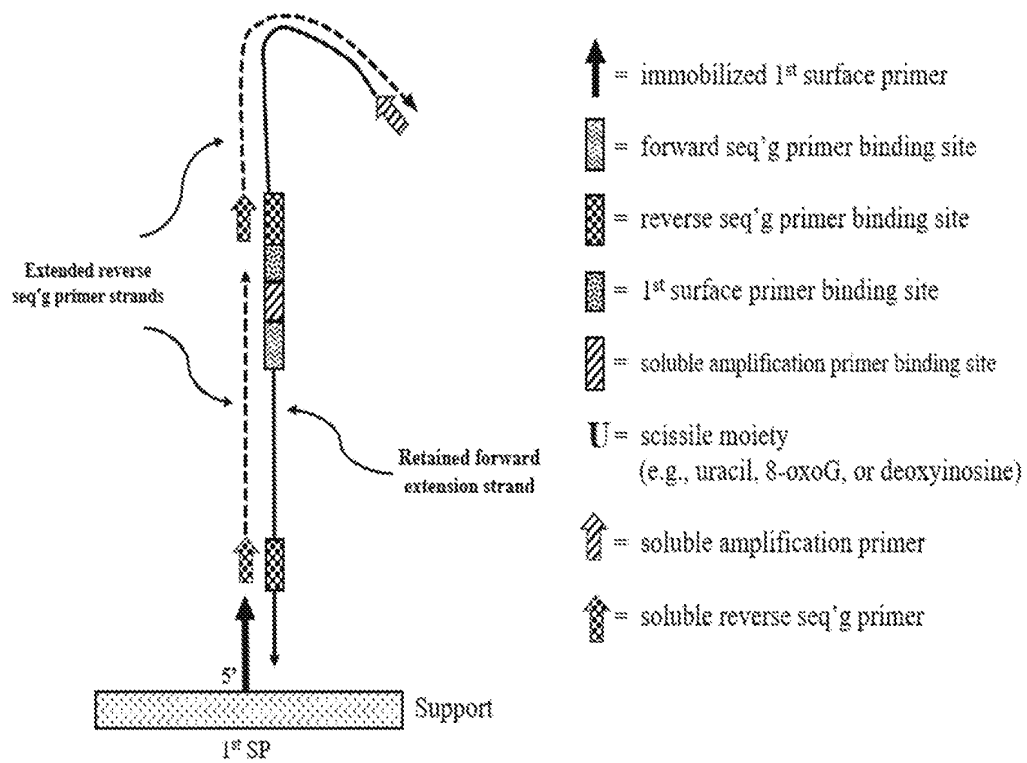


FIG. 45

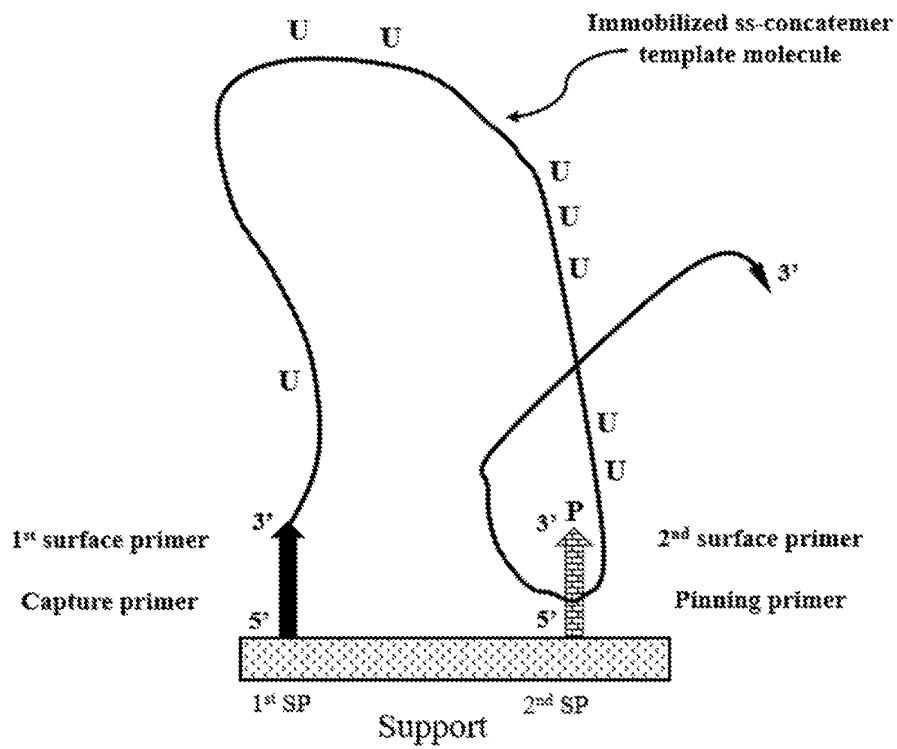


FIG. 46

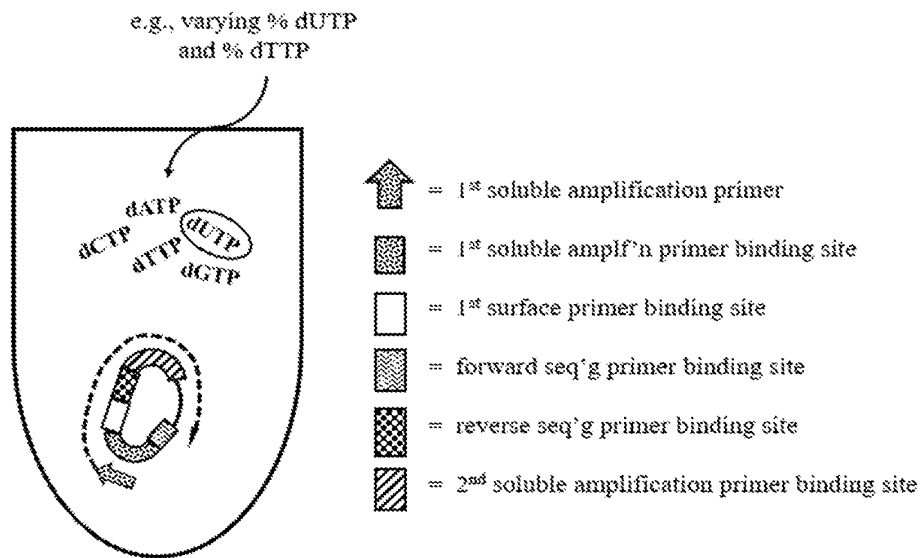


FIG. 47A

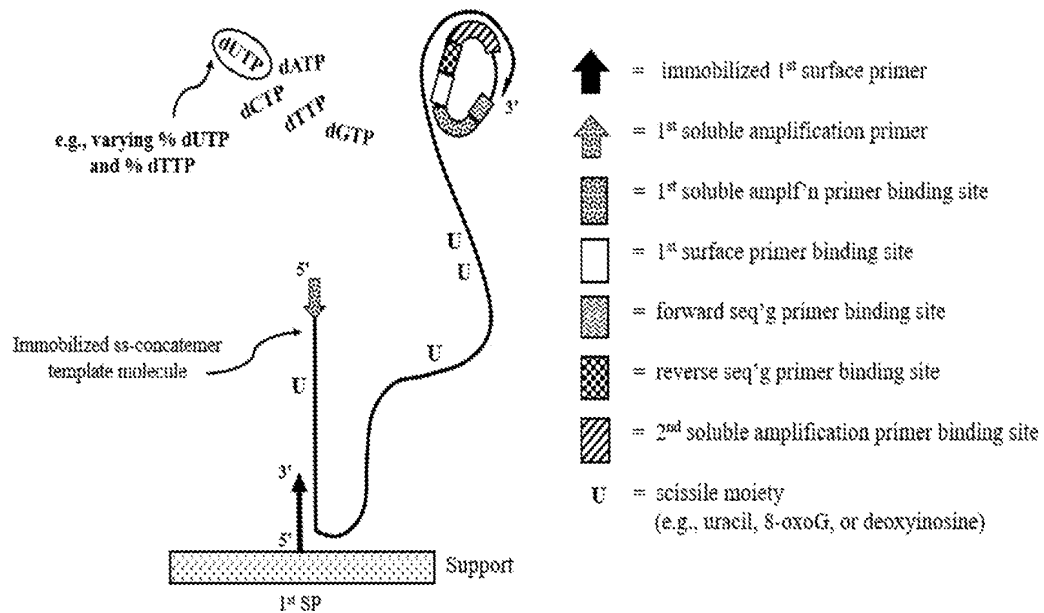


FIG. 47B

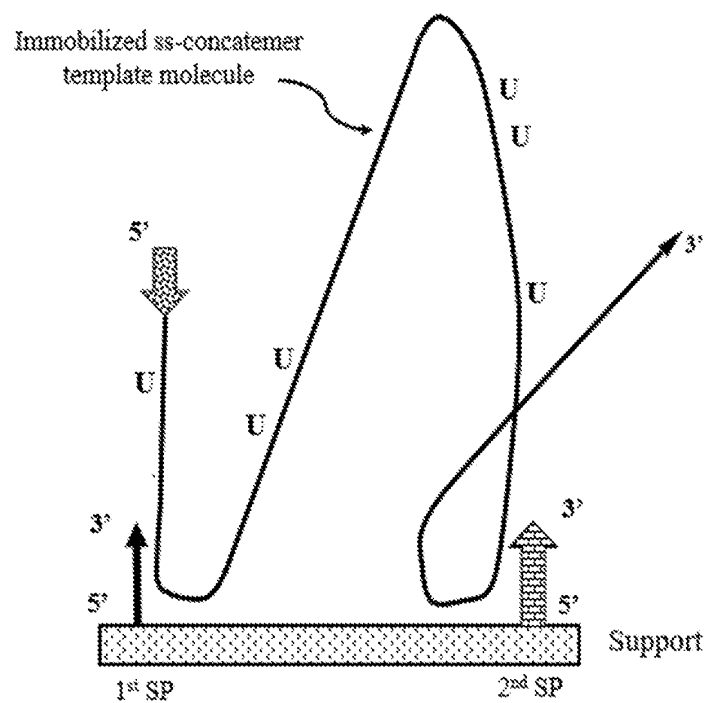


FIG. 47C

**Wild type DNA polymerase from Thermococci archaeon**  
**GenBank accession RLF 89458.1; isolate B13\_G1 (SEQ ID NO:13)**

MILDTDYITENGKPVIRIFKKEKGEFKIEYDRNFEPYIYALLEDDIESIEDIKKITGERHG  
KKVRIIRVEKVKKKFLGEPiEVWKLVEHPQDVPAIRDAIRSHPAVREIFEYDIPFAKRY  
LIDKGLVPMEGGEELKLLAFDIETFYHEGDEFAEGEILMISYADESGAKVITWKKIDLPI  
VEVVSTEREAIKRFLQVLREKDPDVLLTYNGDNFDFAYIKKRCEKLGLKFTIGRDGSEPK  
IQRMGDRFAVEVKGRiHLDLYPVVRHTIRLPTYTLEAVYEAVFGKKKEKVYAEIIEAEAWK  
SEEGLRVAQYSMEDARATYELGREFFPMEVELAKLIGQSVWDVSRSSSTGNLVEWYLLRV  
AYERNELAPNKPGEYQRRMRSSYIGGYVKEPEKGLWESIAYLDFRSLYPSIIIVTHNVS  
PDTLEKECKNYDVAPIVGYRFCKDFKGFIPSILEDLIETRQKVKKMKATIDPIEKKMLD  
YRQRAKILANSYYGYQGYPKARWYSKECAESVTAWGRHYIETTIKEAEKFGFKVLYADT  
DGFFATIPNEKPETIKSKAKKFLKHINEKLPGMLELEYEGFYLRGFFVTKKKYALIDEDG  
HITTRGLEVVRRDWSEIAKETQAKVLEVILREGSIEKAAGIVKKVVEDLANYPVPEKLI  
IHEQITRELKDYKATGPHVAIAKRLQARGIKVKPGTIISYVVLKGSKKISDRVILFDEYD  
SSRHKYDPDYYIHNQVLPVLRILEAFGYKEKDLEYQRMKQTGLGAWLKMGGK

**FIG. 48**

**Wild type DNA polymerase from Thermococci archaeon**  
**GenBank accession RLF 78286.1; isolate B89\_G9 (SEQ ID NO:14)**

MILDTDYITENGKPVIRIFKKEKGEFKIEYDRNFEPYIYALLEDDIESIEDIKKITGERHG  
KKVRIIRVEKVKKKFLGEPiEVWKLVEHPQDVPAIRDAIRSHPAVREIFEYDIPFAKRY  
LIDKGLVPMEGGEELKLLAFDIETFYHEGDEFAEGEILMISYADESGAKVITWKKIDLPI  
VEVVSTEREAIKRFLQVLREKDPDVLLTYNGDNFDFAYIKKRCEKLGLKFTIGREGSEPK  
IQRMGDRFAVEVKGRiHLDLYPVVRHTIRLPTYTLEAVYEAVFGKKKEKVYAEIIEAEAWK  
SEEGLRVAQYSMEDARATYELGREFFPMEVELAKLIGQSVWDVSRSSSTGNLVEWYLLRV  
AYERNELAPNKPGEYQRRMRSSYIGGYVKEPEKGLWESIAYLDFRSLYPSIIIVTHNVS  
PDTLEKECKNYDVAPIVGYRFCKDFKGFIPSILEDLIETRQKVKKMKATIDPIEKKMLD  
YRQRAKILANSYYGYQGYPKARWYSKECAESVTAWGRHYIETTIKEAEKFGFKVLYADT  
DGFFATIPNEKPETIKSKAKKFLKHINEKLPGMLELEYEGFYLRGFFVTKKKYALIDEDG  
HITTRGLEVVRRDWSEIAKETQAKVLEVILREGSIEKAAGIVKKVVEDLANYPVPEKLI  
IHEQITRELKDYKATGPHVAIAKRLQARGIKVKPGTIISYVVLKGSKKISDRVILFDEYD  
SSRHKYDPDYYIHNQVLPVLRILEAFGYKEKDLEYQRMKQTGLGAWLKMGGK

**FIG. 49**

**Wild type DNA polymerase from Euryarchaeota archaeon**  
**GenBank accession NOZ 58130; isolate M\_MaxBin.100 (SEQ ID NO:15)**

MPRILKGFLIDADYETVEGRALIRLFLRGEEGSFVVYDDSFSPYFYALPGDEPERVKERI  
LASGAAEAIQKVEIEEKRLFGTTPRVALRITVSHPQDVPRIRERIRRVEGVDLILEHDILF  
VRRYLIDRGIKPLTWLRLEVEERDGRALLRGVEQLEEEPPELRVAAVDIEVYNPKGAPRS  
SKDEIIMISVATSDGVEKVLTWREVQGLEQVEVLQDEKEMLLRFAELIKEGDYDVIVGYN  
TDSFDFPYIRDRLKKLGISLPLGRLDAALEVSRRGALPEARIRGRAHVDLYPIVRRHVKL  
NSYVLESVVEELLGIKKEKLDGERLFTYWDEGGEKRALLARYALEDARVTLALAEEKFLPL  
YCELSTIVGQSLNDVARMTSGQLVEWLLMRYATPRGELIPNHPAGEEYAAARATYAGGY  
VREPKRGLVEHIAVDFDRSLYPSIIVSHNIDPSTLIVGNCEENRAPELEYCFSLEREGFI  
PAILKELIRRAEIKRELKRSEGDRRRTLSFAEKALKILANSFYGYMGYPRARWYRRECA  
ESVAAFARMYIKQVMRIAEFEFKLEVYGD TDSL FVVI PPEKRELAQKFLQKVNESMPGI  
IELEFEGFYRRGLFVTKKRYALLSEDGKMVVGKLEFVRDWAPIARETQKEVLRILLEEA  
DPEKAARLVRDVIERIRQRRVSLEDITITYTQLTKRIKSYKSLEPHVAAQKLKERGREVA  
PGMIIGYIITKGTKGISQRATPVEFARLEDYDPEYYIDNQILPAIQRIFEAIGYTRDYLK  
EGITQTSLSRWF

**FIG. 50**

**Wild type DNA polymerase from Euryarchaeota archaeon**  
**GenBank accession RMF 90817.1; isolate J060 (SEQ ID NO:16)**

MARDLLLDIDYVTVDEKAQVRLFLKDKILFDPGFQPYFYVLAHDGAVEERLRDFGAVEAV  
QRRMLGREMRFFKLILSHPSEVPKIREEVRSIEGVEGIFEHDILFARRYLIDKGLTPLNY  
AEYRAEQGFLKGISSAGEGPESLRVMAFDIETYNPKGAPRAEKDPVIMLSLSTNTGLRRL  
LTYKSGEGLDFVELVEDEKALLHRFKELVNEEGVEVLVGYNSDQFDLPYLVARAKALGVE  
LPLGQDGSQPQIRKGRGLVESVVKGRPHVDLYPIVRRNVRLSSYVLENNVKEVLGREKEK  
IPHDAMCGYWDRGGRELQRFMAYSMEDADVTLELAERFLPLYIELSRVVGLPLHDVART  
AGQLVEWLLIREAFARGEVVPNKGSGREYLARSEDYAGGYVMEPVKGIVENIVVDFRS  
LYPSIIVTHNIDPATLRPGRGENSPPELDYHFTTEEGFIPSVLKRVLERRLSAKRRMKE  
ARDPGEKRMLDISQRALKI IANSFYGYMGYPRARWYKKECAESVTSFARMYTKKVMAIAE  
EEYGFKVVYGD TDSL FIVVQPEEKERAMSFMEDVNRRLPGTVELEYDGFYPRGIFITKKR  
YALIDEKGNIVVGKLETVRRDWTRLSRDTQQKVL SVILREGDPKKAADIVKDTINRLKER  
RVDLEDITITYTQLTKGIGRYKNVGPHVKAAQKAIDRGREVNPGMAIGYI I KKGRLISDR  
AEPVEDATIEDYDVYYIENQVLPPVARIMEVLGYSKEHLKEEMVQGS LQRWF

**FIG. 51**

**Wild type DNA polymerase from Hadesarchaea archaeon**  
**GenBank accession MBC 7218772.1; isolate MAG-18 (SEQ ID NO:17)**

MRGLLFDDVDIAEEEEERNVRLFVKVASETVVAIDPQFEEYFYVVADHPAKTSKLIKIEL  
DEGGRPIRPKSVEMVRRTLLGNEVEAIRVSFHQPRDAAKLRHKIRELPGVKEIYEFDIPP  
ARRYLIDRGLTPMAGIEFSGSIEVRDGVKTVVMDGPPKPAPVEETRLNIMSFDIEVYNPT  
GSVRPDKDPIIMISLADNRGLRKVITWKNFDKKPEYVEVVGSEREMIKKFVELVKERD  
ILLGYNTDLFDLPYIRSRAQLRVKLDLGRDGSELVVRKRRFATASKIRGRVHVDVFAMV  
DFLATIGSIRLIHYSLADVYRHYAGREKPDFEFSEMINAWERGGDAGRFLFLEYSMSDADA  
TLEVGSSELLPLFLGLTRVVGQTLFDVQRMTPGQLVEWLLVAEHAHRIGELVPPRPVGEEFE  
ERAEGTFTGAYVMEPVKGLHEDLVVDFRSLYPSIIIVTHNIDPSTLNCRDCKPGEREQVP  
GLSYYFCKRRKGFI PAVLERVIEERTKLKAEKKIGRETREYRALDARQWAMKIVANSFY  
GMLGYPRARWYSKQCAESVTSFGRHYIHRTIEMAREFGLEVYGD TDSLHCKLNGK TREE  
AMVFLRKVNESLPGIMELELEGFYPRGIFITKKRYAMVDDEGRMVVKGLEFVVRDWAAIA  
KKTQEEVLRAILRDGSPKKAEEIIRKTT RDVYEGRVNLEDLI IYTQLKMPIESYKAIGPH  
VVAAKRLRELGHEIEPGMMIAYIEVKGPSISDRAVPVEDFEGKEYDPDYVVGHQILPAV  
MRIMEVLGYSEEDLKFEREKQIGLDRFMK

**FIG. 52**

**Wild type DNA polymerase from Thermococcus sp. 2319x1**  
**GenBank accession WP 175059460.1 (SEQ ID NO:18)**

MILDTDYITKDGKPIIRIFKKENGFEKIELDPHFQPYIYALLKDDSAIEEIKAIKGERHG  
KTVRVLDVAVKVRKKFLGREVEVWKLIFEHPQDVPAMRDKIKEHPAVIDIYEYDIPFAKRY  
LIDKGLIPMEGDEELKLLAFDIETFYHEGDEFGKGEIIMISYADEEEARVITWKNIDL  
PYVDVVSNEREMIKRFVQVVKEKDPDVIITYNGDNFDLPYLIKRAEKLGI RLVLGRD  
KENPEPKIQRMGDSFAVEIKGRIHFDLFPVVRRTINLPTYTLEAVYEAVLGKTKSKL  
GAEEIAAIWETEESMKKLAQYSMEDARATYELGKEFFPMEAEALAKLIGQSVWDVSR  
SSTGNLVEWYLLRVAYARNELAPNKPDEEEYKRRLRTTYLGGYVKEPEKGLWENI  
IYLDFRSLYPSIIIVTHNVSPDTLEKEGCENYDIAPIVGYKFCKDFPGFIPSILGDL  
IAMRQEIKKMKATIDPIEKKMLDYRQRAVKLLANSYYGYMGYPKARWYSKECAESV  
TAWGRHYIEMTIKEIEEKFGFKVL YADTDGFYATIPGEKPEIIKKKAREFLNYIN  
SKLPGLLELEYEGFYLRGFFVTKKRYAVI DEEGRITTRGLEVVRRDWSEIAKETQAK  
VLEAILKDGSVEKAVEIVRDVVEKIAKYRVPLEKLVIHEQITRDLKDYKAIGPHVSI  
AKRLATRGIKVKPGTIISYLVKGGGRISDRVILLTEYDPEKHKYDPDYIENQVLP  
AVLRILEAFGYRKEDLRYQSSKQTGLDAWLKR

**FIG. 53**

**Wild type DNA polymerase from *Candidatus Hadarchaeum yellowstonense***  
**GenBank accession KUO 42443.1; isolate YNP\_45 (SEQ ID NO:19)**

MLLDVDYAEKEEKPSIRLFVKTGSEVLVAIDPDFEYFYVVS DHPAKASKLIEKVEVEED  
GVSIRPKGVEIVKRTFLGNEVEAIKVSFYQAKDSSKLRHKIRELPGVREIYEFDIPPAR  
YLIDRGLTPMAGVEFDGRIEERQGIKTIVILDSPPRPAQVEEPKLNIMSFIDIEVYNPTGSV  
RPDKDPIIMISLADNNGLRKVI TWKNFERSQEYVEVVG SEREMIKRFVDLVKERDVIDLL  
GYNTDLFDLPYIRSRAQLKVKLDLGRDGSELVVRKRRFATASKIRGRIHVDVFAMVDFL  
ATIGSIKLIHYS LADVYRHLLGKEKPDFEFTMVDAWEKGGDAGRKFLEYSMSDADATLE  
VGLELLPLFLGLTRVVGQTLFDVQRMTPGQLVEWLLVAEAHRIGELVPGRPVGEEYEERM  
EETFVGAYVMEPVKGLHENLVVDFDRSLYPSIIIVTHNIDPSTLNCKDCKPGEREQVPGLE  
YYFCRRRKGFIPATLQRIIEERMKLKAE LKKLVRGTK EYRALDARQWAMKIVANSFYGML  
GYPRARWYSKECAESVTSFGRHYIHKTIDMAREFGLEVVGDTDSLHCKLNGKTREEALA  
FLKKVNDSLPGIMELELEGFYPRGIFITKKRYAMIDDEGRMVVKGLEFVRDWAIAAKKT  
QEEVLKAILRDGSPEKAAEII RKTTRDVYEGRVNLEDLI IYTQLKMPIESYKAIGPHVVA  
AKRLRELGHIEIPGMMIAYVEVKGPGSISERAVPVEDFKGREYDPDYYVGHQVLPVAMRI  
MEVLGYREIDLKFERQRQVGLDRFMK

**FIG. 54**

**Wild type DNA polymerase from *Euryarchaeota archaeon***  
**GenBank accession NOZ 77387.1; isolate M\_MaxBin.027 (SEQ ID NO:20)**

MDGFLLDVYKTVDEKPVVRLFLRDVIALDPSFRPYVYVACDDPRAVAGEIKDLELDGRR  
PVTGVEEMERGLLGRPRRFLKVYLGHPPQVPRVRDLLRRLPGVSAVLEDDILFSRRYLID  
KGLVPTAWVELQGRVEGSEFWVEEVRAEGPLPRLKVMSFDIETYNPKGAPRGDQDPIIM  
VSMATSGGLRKVL SWKAPTAGLEFVETLEDEAAVLRRFEELVRQEDPDILVGYN TDNFDF  
PYLNQRLKALGIELALGRDGSPHKTSTRMG MSETRMAGRPHMDLYPIVRRSLRLPSYVLE  
DVVAEVLGEEKEKVPGERMGEIWDKGGEELDRFFRYSLEDAEVTLRIGEKYLPLYIELSR  
LVGQSIHDVARMTAGQLVEWYLMREAFARGEVIPERPGGREFARRAGDTYEGGYVREPRK  
GLLEKVFDFRSLYPSVIVTHNIDPSTIRPGPGENQPPGIDYHFTTEKEGFIPALLKRLVA  
RRAELKEEMKKARDPGERKMLDVQQQALKILANSFYGYMGYPRARWYRKECAESVTAFAR  
DYIKKMEVAEKEFGLEVVGDTDSLFI LVPGGKKERAF AFLEEVNRRLPGTIELEYEGF  
YRRGIFVTKKRYALIDEKDRIIVKGLEFVRDWAPIARDTQEKVLKALLKDASPEEAVRI  
VRKAMDDIRARRVSLEDLTIIYTQLTKK

**FIG. 55**

**Wild type DNA polymerase from *Geobacillus stearothermophilus* (Bst polymerase)  
GenBank accession AAB52611.1 (SEQ ID NO:21)**

MKKKLVLIDGNSVAYRAFFALPLLHNDKGIHTNAVYGFMTMLNKLAEEQPTHLLVAFDA  
GKTTFRHETFQEYKGGRRQQTPELSEQFPLLRELLKAYRIPAYELDHYEADDIIGTLAAR  
AEQEGFEVKIISGDRDLTQLASRHVTVDITKKGITDIEPYTPETVREKYGLTPEQIVDLK  
GLMGDKSDNIPGVPGIGECTAVKLLKQFGTVENVLASIDEVKGEKLEKENLRQHRDLALLS  
KQLASICRDAPVELSLDDIVYEGQDREKVIALFKELGFQS FLEKMAAPAAEGEKPLEEME  
FAIVDVI TEEMLADKAALVVEVMEENYHDAPIVGIALVNEHGRFFMRPETALADSQFLAW  
LADETKKKSMFDAKRAVVALKWKGIELRGVAFDLLLLAAYLLNPAQDAGDIAAVAKMKQYE  
AVRSDEAVYGKGVKRS LPDEQTLAEHLVRKAAAIWALEQPFMDLRLNNEQDQLLT KLEQP  
LAAILAEMEFTGVNVDTKRLEQMGSELAEQRLAIEQRIYELAGQEFNINSPKQLGVILFE  
KLQLPVLKKTGTGYSTSADVLEKLAPHHEIVENILHYRQLGKLQSTYIEGLLKVVPRPDG  
KVHTMFNQALTQTGR LSSAEPNLQNIPIRLEEGRKIRQAFVPSEPDWLI FAADYSQIELR  
VLAHIADDDNLI EAFQRDLDIHTKTAMDI FHVSEEEVTANMRRQAKAVNFGIVYGISDYG  
LAQNLNITRKEAAEFIERYFASFPGVKQY MENIVQEAKQKGYVTLLHRRRYLPDITSRN  
FNVRSFAERTAMNTPIQGSAA DIKKAMIDLAARLKEEQ LQARLLLQVHDELILEAPKEE  
IERLCELVP EVMEQAVTLRVPLKVDYHYGPTWYDAK

**FIG. 56**

**9°N polymerase (SEQ ID NO:22)**

MILDTDYITENGKPVIRVFKKENGEFKIEYDRTFEPYFYALLKDDSAIEDVKKVTAKRHG  
TVVKVKRAEKVQKKFLGRPIEVWKLYFNHPQDVPAIRDRI RAHPAVVDIYEYDIPFAKRY  
LIDKGLIP **A**EGDEELTMLAFDIETLYHEGEEFGTGPILMISYADGSEARVITWKKIDL PY  
VDVVSTEKEMIKRFLRVVREKDPDVLI TYNGDNFDFAYLKKRCEELGIKFTLGRDGSEPK  
IQRMGDRFAVEVKGRIFDLYPVIRRTINLPTYTLEAVYEAVFGKPKEKVYAE EIAQAW E  
SGEGLERVARYSMEDAKV TYELGREFFPMEAQLSRLIGQSLWDVSRSTGNLVEWFLLRK  
AYKRNELAPNKPDERELARRRGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP  
DTLNREGCKEYDVAPEVGHKFKCDFPGFIP SLLGDLLEERQKIKRKM KATVDPLEKKLLD  
YRQRAIKILANSFYGYGYAKARWYCKECAESVTAWGREYIEMVIRELEEKFGFKVLYAD  
TDGLHATIPGADAETVKKKAKEFLKYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE  
GKITTRGLEIVRRDWSEIAKETQARVLEAILKHGDVEEAVRIVKEVTEKLSKYEVPP EKL  
VIHEQITRDLRDYKATGPHVAVAKRLAARGVKIRPGTVISYIVLKGSGRIGDRAIPADEF  
DPTKHRYDAEYYIENQVLP AVERILKAFGYRKEDLRYQKTKQVGLGAWLKVKGKK

**FIG. 57**

**<sup>9</sup>N polymerase****UniProtKB - Q56366 (DPOL\_THES9) (SEQ ID NO:23)**

MILDTDYITENGKPVIRVFKKENGEFKIEYDRTFEPYFYALLKDDSAIEDVKKVTAKRHG  
TVVKVKRAEKVQKKFLGRPIEVWKLYFNHPQDVPAIRDRIRAHPAVVDIYEYDIPFAKRY  
LIDKGLIPMEGDEELTMLAFDIETLYHEGEEFGTGPILMISYADGSEARVITWKKIDL  
PYVDVVSTEEKEMIKRFLRVVREKDPDVLITYNGDNFDFAYLKKRCEELGIKFTLGRDGSEPK  
IQRMGDRFAVEVKGRIFHFDLYPVIRRTINLPTYTLEAVYEAVFGKPKEKVYAEIEAQAW  
ESGEGLERVARYSMEDAKVTYELGREFFPMEAQLSRLIGQSLWDVSRSTGNLVEWFLLRK  
AYKRNELAPNKPDERELARRRGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP  
DTLNREGCKEYDVAPEVGHKFCKDFPGFIPSLLDLLEERQKIKRKMATVDPLEKKLLD  
YRQRAIKILANSFYGGYGYAKARWYCKECAESVTAWGREYIEMVIRELEEKFGFKVLYAD  
TDGLHATIPGADAETVKKKAKEFLKYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE  
GKITTRGLEIVRRDWSEIAKETQARVLEAILKHGDVEEAVRIVKEVTEKLSKYEVPPEKL  
VIHEQITRDLRDYKATGPHVAVAKRLAARGVKIRPGTVISYIVLKGSGRIGDRAIPADEF  
DPTKHRYDAEYYIENQVLPAPERILKAFGYRKEDLRYQKTKQVGLGAWLKVKGKK

**FIG. 58****Therminator polymerase (SEQ ID NO:24)**

MILDTDYITENGKPVIRVFKKENGEFKIEYDRTFEPYFYALLKDDSAIEDVKKVTAKRHG  
TVVKVKRAEKVQKKFLGRPIEVWKLYFNHPQDVPAIRDRIRAHPAVVDIYEYDIPFAKRY  
LIDKGLIPMEGDEELTMLAFATLYHEGEEFGTGPILMISYADGSEARVITWKKIDL  
PYVDVVSTEEKEMIKRFLRVVREKDPDVLITYNGDNFDFAYLKKRCEELGIKFTLGRDGSEPK  
IQRMGDRFAVEVKGRIFHFDLYPVIRRTINLPTYTLEAVYEAVFGKPKEKVYAEIEAQAW  
ESGEGLERVARYSMEDAKVTYELGREFFPMEAQLSRLIGQSLWDVSRSTGNLVEWFLLRK  
AYKRNELAPNKPDERELARRRGYAGGYVKEPERGLWDNIVYLDFRSLYPSIIITHNVSP  
DTLNREGCKEYDVAPEVGHKFCKDFPGFIPSLLDLLEERQKIKRKMATVDPLEKKLLD  
YRQRLIKILANSFYGGYGYAKARWYCKECAESVTAWGREYIEMVIRELEEKFGFKVLYAD  
TDGLHATIPGADAETVKKKAKEFLKYINPKLPGLLELEYEGFYVRGFFVTKKKYAVIDEE  
GKITTRGLEIVRRDWSEIAKETQARVLEAILKHGDVEEAVRIVKEVTEKLSKYEVPPEKL  
VIHEQITRDLRDYKATGPHVAVAKRLAARGVKIRPGTVISYIVLKGSGRIGDRAIPADEF  
DPTKHRYDAEYYIENQVLPAPERILKAFGYRKEDLRYQKTKQVGLGAWLKVKGKK

**FIG. 59**

**Vent polymerase UniProtKB - P30317 (DPOL\_THELI) (SEQ ID NO:25)**

MILDTDYITKDGPKIIRIFKKENGFEFKIELDPHFQPYIYALLKDDSAIEEIKAIKGERHG  
KTVRVLDVAVKVRKKFLGREVEVWKLIFEHPQDVPAMRGKIREHPAVVDIYEYDIPFAKRY  
LIDKGLIPMEGDEELKLLAFDIETFYHEGDEFGKGEIIMISYADEEEARVITWKNIDLPI  
VDVVSNEREMIKRFVQVVKEKDPDVIIITYNGDNFDLPYLIKRAEKLGVRLVLGRDKEHPE  
PKIQRMGDSFAVEIKGRIHFDLFPVVRTINLPTYTLEAVYEAVLGKTKSKLGAEIEAAI  
WETEESMKKLAQYSMEDARATYELGKEFFPMEAEALAKLIGQSVWDVSRSTGNLVEWYLL  
RVAYARNELAPNKPDEEEYKRRLRTTYLGGYVKEPEKGLWENIIYLDFRSLYPSIIVTHN  
VSPDTLEKEGCKNYDVAPIVGYRFCKDFPGFIPSI LGDLIAMRQDIKKMKSTIDPIEKK  
MLDYRQRAIKLLANSILPNEWLP I IENGEIKFVKIGEFINSYMEKQKENVKTVVENTEVLE  
VNNLFAFSFNKKIKESEVKKVKALIRHKYKGKAYEIQLSGRKINITAGHSLFTVRNGEI  
KEVSGDGIKEGDLIVAPKKIKLNEKGV SINIPELISDLSEEETADIVMTISAKGRKNFFK  
GMLRTL RWMFGEENRRIRTFNRYLFHLEKLGLIKLLPRGYEVTDWERLKKYKQLYEKL  
SVKYNNGNKREYLVMFNEIKDFISYFPQKELEEWKIGTLNGFRTNCILKVEDDFGKLLGY  
VSEGYAGA QKNKTGGISYSVKLYNEDPNVLESMKNVAEKFFGKVRVDRNCVSI SKMAYL  
VMKCLCGALAENKRIPSVILTSPEPVRSFLEAYFTGDGDIHPSKRFR LSTKSELLANQL  
VFLNLSLGISSVKIGFDSGVYRVYINEDLQFPQTSREKNTYYSNLIPKEILRDVFGKEFQ  
KNMTFKKFKELVDSGKLNREKAKLLEFFINGDIVLDRVKS VKEKDYEGYVYDLSVEDNEN  
FLVGFGLLYAHNSYYGYMGYPKARWYSKECAESVTAWGRHYIEMTIREIEEKFGFKVLYA  
DSVSGESEIIIRQNGKIRFVKIKDLFSKVDYSIGEKEYCILEGVEALT DDDGKLVWKPV  
PYVMRHRANKRMFRIWLTNSWYIDVTEDHSLIGYLNTSKTKTAKKIGERLKEVKPFELGK  
AVKSLICPNAPLKDENTKTSEIAVKFWELVGLIVGDGNWGGDSRWA EYYLGLSTGKDAEE  
IKQKLEPLKTYGVISNYYPKNEKGDFNILAKSLVKFMKRHF KDEKGRRKIPEFMYELPV  
TYIEAFLRGLFSADGTVTIRKGVPEIRLTNIDADFLREVRKLLWIVGISNSIFAETTPNR  
YNGVSTGTYSKHLRIKNKWRFAERIGFLIERKQKRLLEHLKSARVKRNTIDFGFDLVHV  
KVEEIPYEGYVYDIEVEETHRFFANNILVHNTDGFYATIPGEKPELIK KAKEFLNYINS  
KLPGLLELEYEGFYLRGFFVTKKRYAVIDEEGRITTRGLEVVRRDWSEIAKETQAKVLEA  
ILKEGSVEKAVEVVRDVVEKIAKYRVPLEKLV IHEQITRDLKDYKAIGPHVAIAKRLAAR  
GIKVKPGTIIISYIVLKSGKISDRVILLTEYDPRKHKYDPDYYIENQVLPAVLRILEAFG  
YRKEDLRYQSSKQTGLDAWLKR

**FIG. 60**

**Deep Vent polymerase UniProtKB - Q51334 (DPOL\_PYRSD) (SEQ ID NO:26)**

MILDADYITEDGKPIIRIFKKENGFEKVEYDRNFRPYIYALLKDDSQIDEVRKITAERHG  
 KIVRIIDA EKVRKKFLGRPIEVWRLYFEHPQDVPAIRDKIREHSAVIDIFEYDIPFAKRY  
 LIDKGLIPMEGDEELKLLAFDIETLYHEGEEFAKGPIIMISYADEEEEAKVITWKKIDL PY  
 VEVSSSEREMIKRFLKVIREKDPDVIITYNGDSFDLPYLVKRAEKLGIKLPGRDGSEPK  
 MQRIGDMTAVEIKGRIHFDLYHVIRRTINLPYTYTLEAVYEAFGKPKKEKVYAHEIAEAW  
 TGKGLERVAKYSMEDAKVTYELGREFFPMEAQLSRLVGQPLWDVSRSSSTGNLVEWYLLRK  
 AYERNELAPNKPDEREYERRLRESYAGGYVKEPEKGLWEGLVSLDFRSLYPSIIITHNVS  
 PDTLNREGCREYDVAPEVGHKFCKDFPGFIPSLLRLLDERQEIKRKMASKDPIEKKML  
 DYRQRAIKILANSILPEEWVPLIKNGKVKIFRIGDFVDGLMKANQGKVKKTGDTEVLEVA  
 GIHAFSFDKRSKKARVMAMKAVIRHRYSGNVYRIVLNSGRKITITEGHSLFVYRNGDLVE  
 ATGEDVKIGDLLAVPRSVNLPEKRERLNIVELLLNLSPEETEDIILTIPVKGRKNFFKGM  
 LRTLRLWIFGEEKRVRTASRYLRHLENLGYIRLRKIGYDIIDKEGLEKYRTLYEKLVDVVR  
 YNGNKREYLVEFNAVRDVISLMPEEELKEWRIGTRNGFRMGTFVDIDEDFAKLLGYVSE  
 GSARKWKNQTGGWSYTVRLYNENDEVLDMEHLAKKFFGKVKRGKNYVEIPKKMAYIIIFE  
 SLCGTLAENKRVPEVIFTSSKGVRAWFLEGYFIGDGDVHPSKRVRLSTKSELLVNLVL  
 LNSLGVSAIKLGYDSGVYRVYVNEELKFTEYRKKKNVYHSHIVPKDILKETFGKVFQKNI  
 SYKKFRELVENGLDREKAKRIEWLLNGDIVLDRVVEIKREYYDGYVDLSVDEDENFLA  
 GFGFLYAHNSYGYGYAKARWYCKECAESVTAWGREYIEFVRKELEEKFGFKVLYIDTD  
 GLYATIPGAKPEEIKKKALEFVDYINAKLPGLLELEYEGFYVRGFFVTKKKYALIDEEGK  
 IITRGLEIVRRDWSEIAKETQAKVLEAILKHGNVEEAVKIVKEVTEKLSKYEIPPEKLV  
 YEQITRPLHEYKAIGPHVAVAKRLAARGVKVRPGMVIIGYIVLRGDGPISKRAILAEFDL  
 RKHKYDAEYYIENQVLPVAVLRILEAFGYRKEDLRWQKTKQTGLTAWLNKKK

**FIG. 61****Pfu polymerase UniProtKB - P61875 (DPOL\_PYRFU) (SEQ ID NO:27)**

MILDVDYITEEGKPVIRLFKKENGKFKIEHDRTFRPYIYALLRDDSKIEEVKKITGERHG  
 KIVRIVDVEKVEKKFLGKPIITVWKLYLEHPQDVPTIREKVREHPAVVDIFEYDIPFAKRY  
 LIDKGLIPMEGEEELKILAFDIETLYHEGEEFGKGPIIMISYADENEAKVITWKNIDL PY  
 VEVSSSEREMIKRFLRIIREKDPDIIVTYNGDSFDFPYLAKRAEKLGIKLTIGRDGSEPK  
 MQRIGDMTAVEVKGRIHFDLYHVITRTINLPYTYTLEAVYEAFGKPKKEKVYAHEIAKAW  
 SGENLERVAKYSMEDAKATYELGKEFLPMEIQLSRLVGQPLWDVSRSSSTGNLVEWYLLRK  
 AYERNEVAPNKPSEEEYQRRRLRESYTGGFVKEPEKGLWENIVYLDFRALYPSIIITHNVS  
 PDTLNLEGCKNYDIAPQVGHKFCKDIPGFIPSLLGHLLEERQKIKTKMKETQDPIEKILL  
 DYRQKAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYIELVWKELEEKFGFKVLYI  
 DTDGLYATIPGGESEIKKKALEFVKYINSKLPGLLELEYEGFYKRGFFVTKKRYAVIDE  
 EGKVITRGLEIVRRDWSEIAKETQARVLETILKHGDVEEAVRIVKEVIQKLANYEIPPEK  
 LAIYEQITRPLHEYKAIGPHVAVAKKLAAGVKIKPGMVIIGYIVLRGDGPISNRAILAEE  
 YDPKKHKYDAEYYIENQVLPVAVLRILEGFGYRKEDLRYQKTRQVGLTSWLNKKK

**FIG. 62**

**Pyrococcus abyssi polymerase UniProtKB - P0CL77 (DPOL\_PYRAB) (SEQ ID NO:28)**

MIIDADYITEDGKPIIRIFKKEKGFEKVEYDRTRFPYIYALLKDDSAIDEVKKITAERHG  
KIVRITEVEKVQKKFLGRPIEVWKLYLEHPQDVPAIREKIREHPAVVDIFEYDIPFAKRY  
LIDKGLTPMEGNEELTFLAVDIETLYHEGEEFGKGPIIMISYADEEGAKVITWKSIDL  
PYVEVSSSEREMIKRLVKVIREKDPDVIIITNGDNFDFPYLLKRAEKLGIKPLGRDNSEPK  
MQRMGDSLAVEIKGRIHFDLFPVIRRTINLPTYTLEAVYEAFGKSKEKVYAHEIAEAW  
TGKGLERVAKYSMEDAKVTFELGKEFFPMEAQLARLVGQPVWDVSRSTGNLVEWFLLRK  
AYERNELAPNKPDEREYERRLRESYEGGYVKEPEKGLWEGIVSLDFRSLYPSIIITHNVS  
PDTLNRENCKEYDVAPQVGHFRFCKDFPGFIPSLGNLLEERQKIKKRMKESKDPVEKKLL  
DYRQRAIKILANSYGYGYAKARWYCKEAEVSTAWGRQYIDLVRRELESRGFKVLYID  
TDGLYATIPGAKHEEIKEKALKFVEYINSKLPGLLELEYEGFYARGFFVTKKKYALIDEE  
GKIVTRGLEIVRDWSEIAKETQAKVLEAILKHGNDVAVKIVKEVTEKLSKYEIPPEKL  
VIYEQITRPLSEYKAIGPHVAVAKRLAAKGVKVPGMVIGYIVLRGDGPISKRAIAIEEF  
DPKKHKYDAEYYIENQVLPAPERILRAFGYRKEDLKYQKTKQVGLGAWLKF

**FIG. 63****RB69 polymerase UniProtKB - Q38087 (DPOL\_BPR69) (SEQ ID NO:29)**

MKEFYLTVEQIGDSIFERYIDSNGRERTREVEYKPSLFAHCPESQATKYFDIYGKPCTRK  
LFANMRDASQWIKRMEDIGLEALGMDDFKLAYLSDTYNIEIKYDHTKIRVANFDIEVTSP  
DGFPEPSQAKHPIDAITHYDSIDDRFYVFDLLNSPYGNVEEWSIEIAAKLQEQGGDEVPS  
EIIDKIIYMPFDNEKELLMEYLNFWQQKTPVILTGWNVESFDIPYVYNRIKNIFGESTAK  
RLSPHRKTRVKVIENMYGSREIITLFGISVLDYIDLKFKSFTNQPSYSLDYISEFELNV  
GKLKYDGPISKLRESNHQRYISYNIIDVYRVLQIDAKRQFINLSLDMGYAKIQIQSVFS  
PIKTWDALIFNSLKEQNKVIPQGRSHPVQYPGAFVKEIPNRYKYVMSFDLTSLYPSII  
RQVNISPETIAGTFKVAPLHDYINAVAERP SDVYSCSPNGMMYYKDRDGVVPTEITKVFN  
QRKEHKGMYLAAQRNGEIIKEALHNPNLSVDEPLDVYRFD FSDEIKEKIKKLSAKSLNE  
MLFRAQRTEVAGMTAQINRKL LINSLYGALGNVWFRYYDLRNATAITTFGQMALQWIERK  
VNEYLNEVCGTEGEAFVLYGDTDSIYVSADKIIDKVGESKFRD TNHWVDFLDKFARERME  
PAIDRGFREMCEYMNNKQHLMFMDREAIAGPPLGSKGIGGFWTGKKRYALNVWDMEGTRY  
AEPKLKIMGLETQKSSTPKAVQKALKECIRMLQEGEESLQEYFKEFEKEFRQLNYISIA  
SVSSANNIAKYDVGGFPGPKCPFHIRGILTYNRAIKGNIDAPQVVEGEKVYVLP LREGNP  
FGDKCIAWPSGTEITDLIKDDVLHWMDYTVLLEKTFIKPLEGFTSAAKLDYEKKASLFDM  
FDF

**FIG. 64**

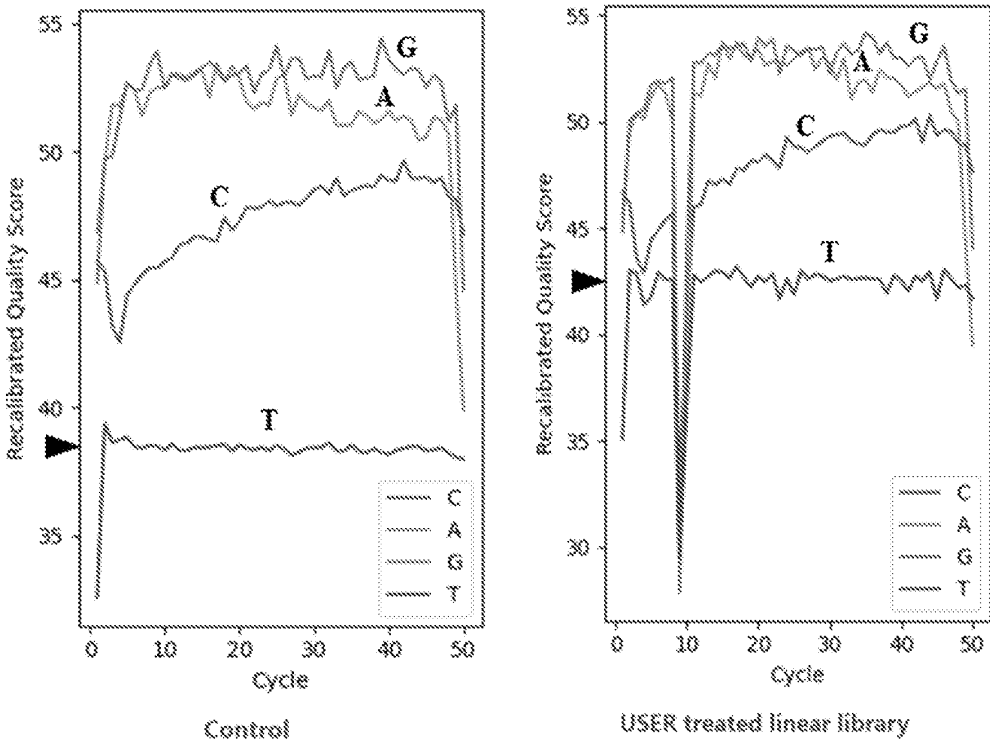


FIG. 65

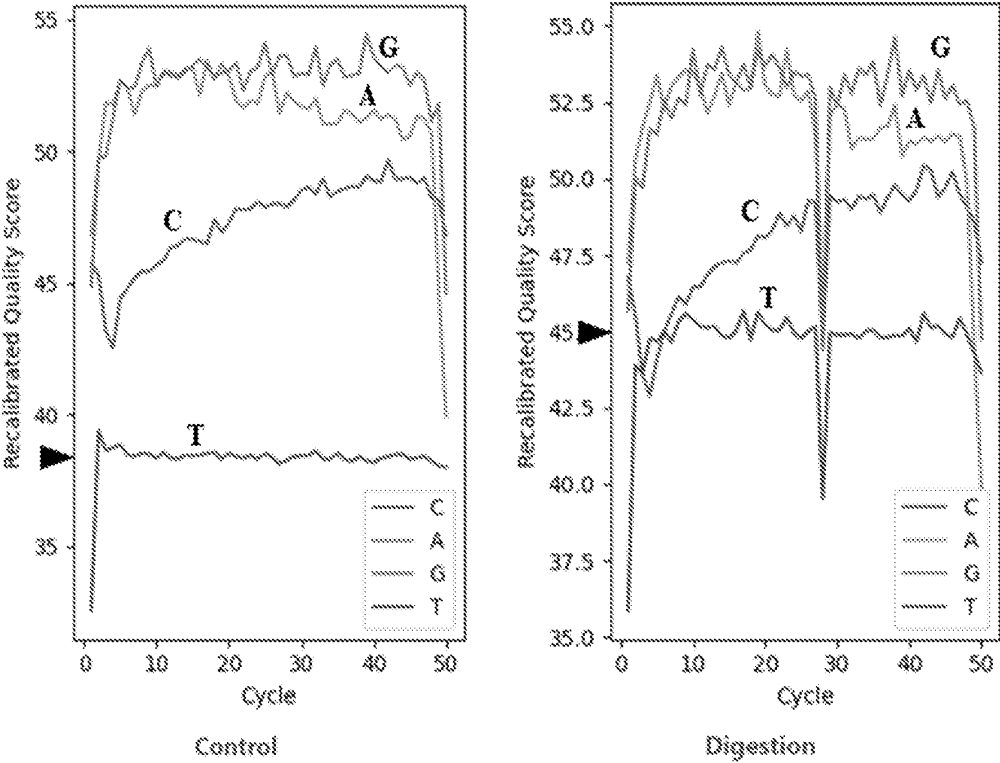


FIG. 66

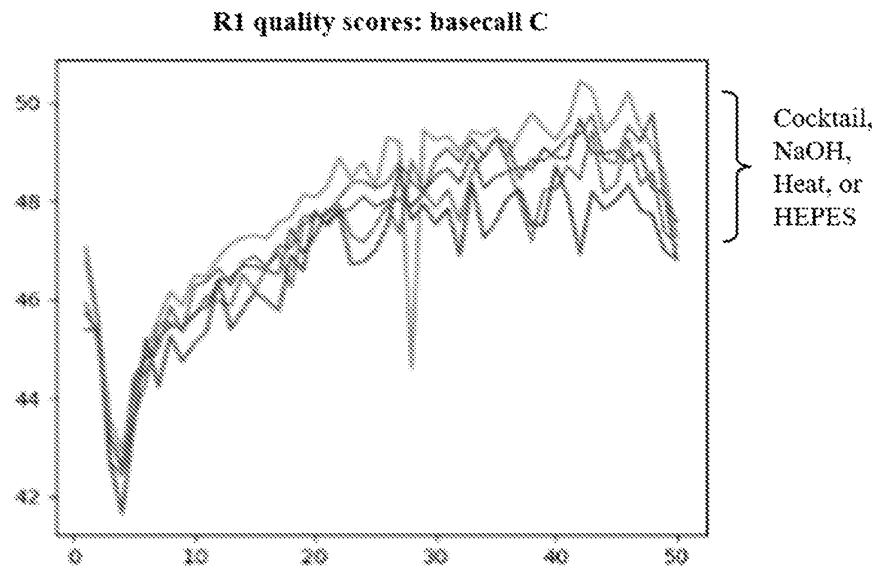


FIG. 67A

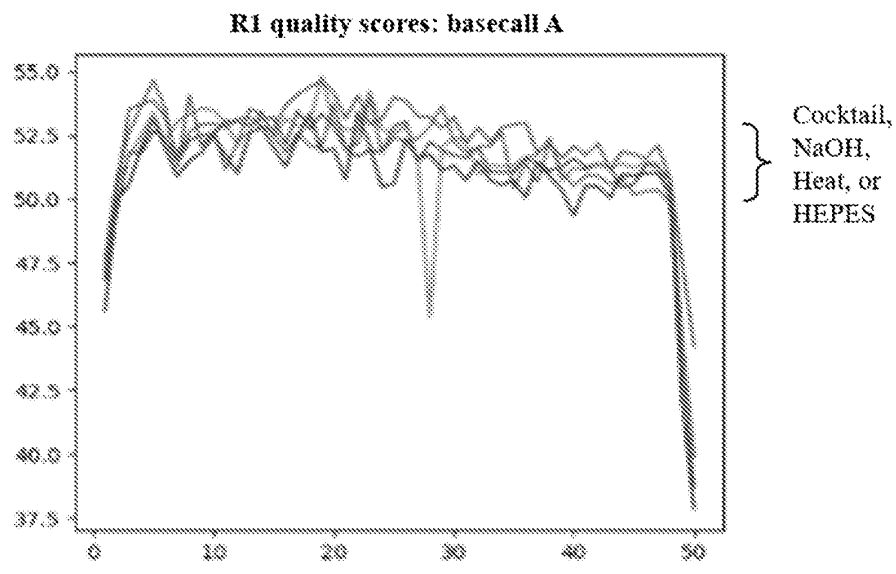


FIG. 67B

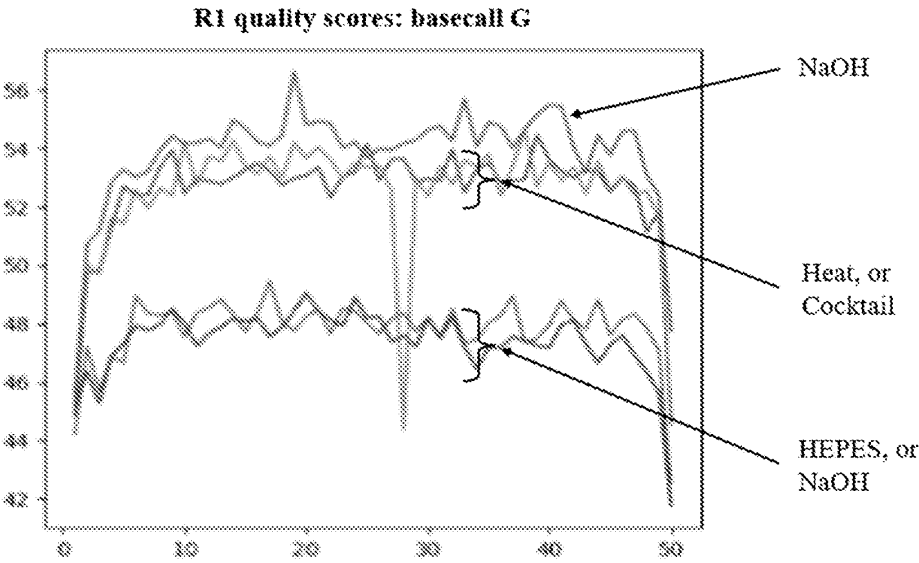


FIG. 67C

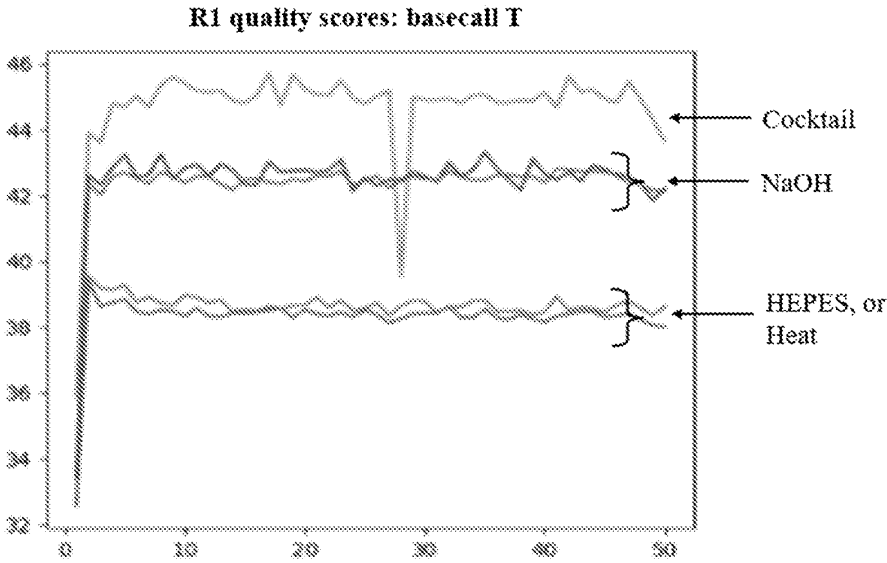


FIG. 67D

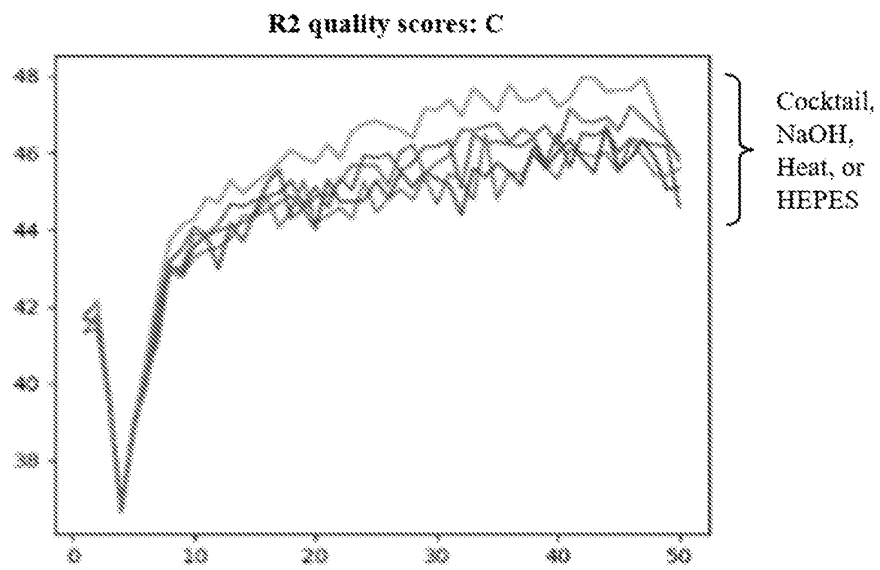


FIG. 68A

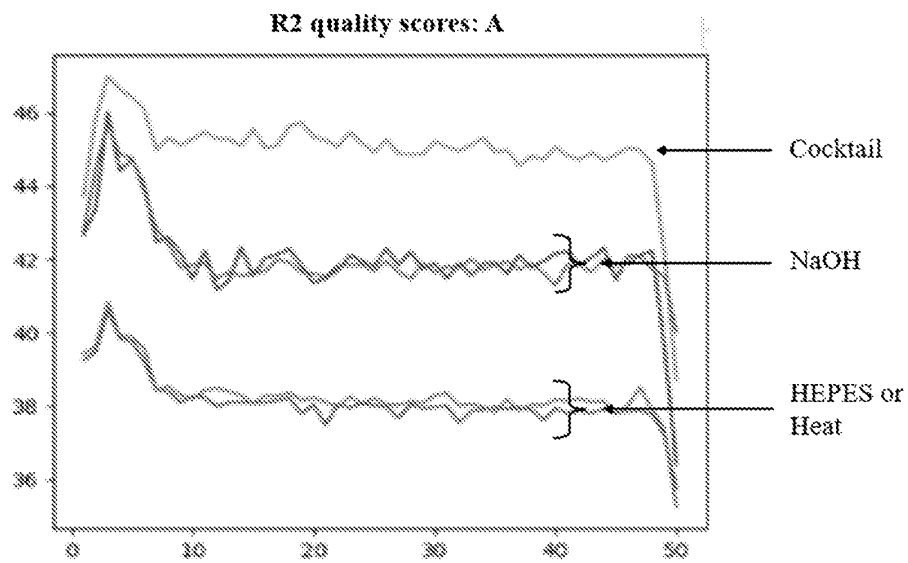


FIG. 68B

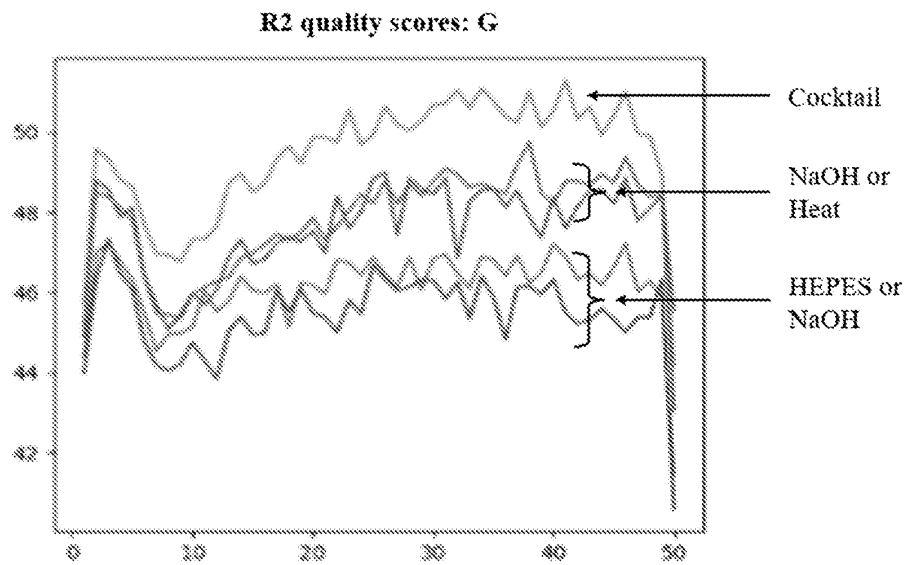


FIG. 68C

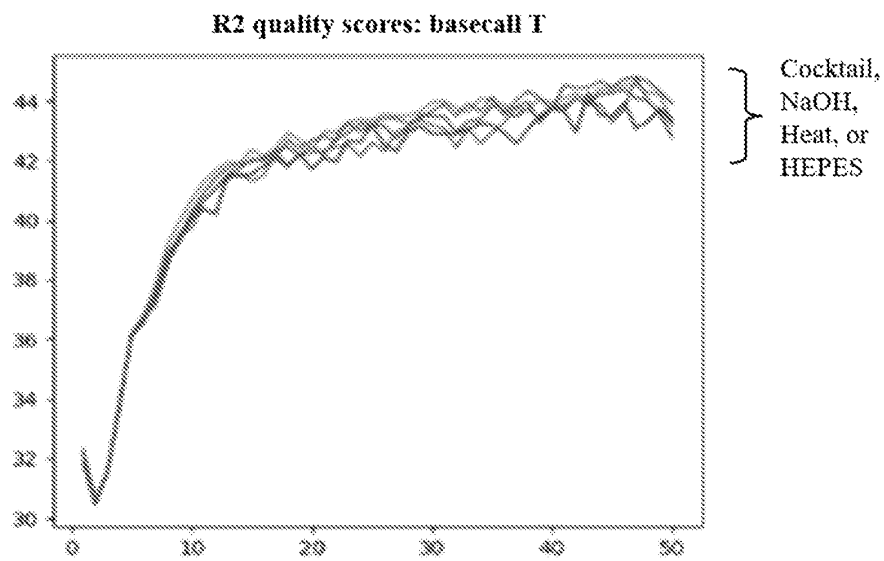


FIG. 68D

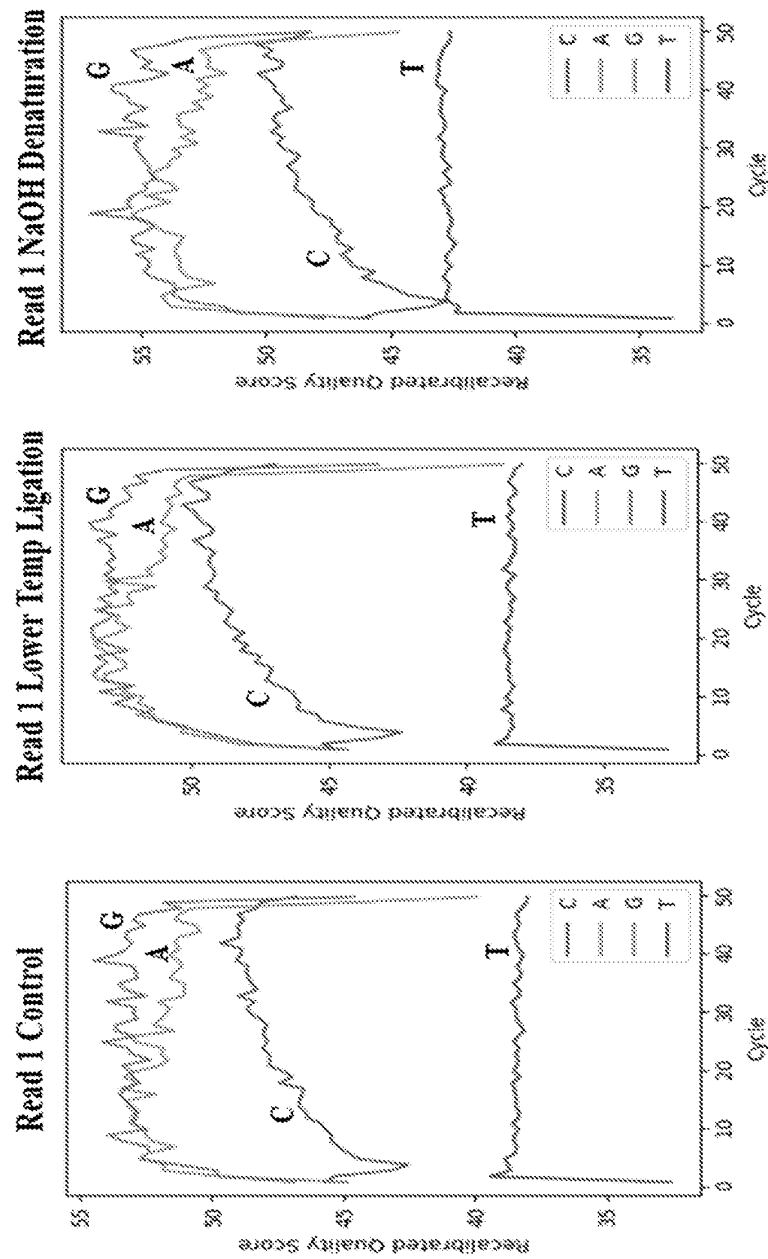


FIG. 69

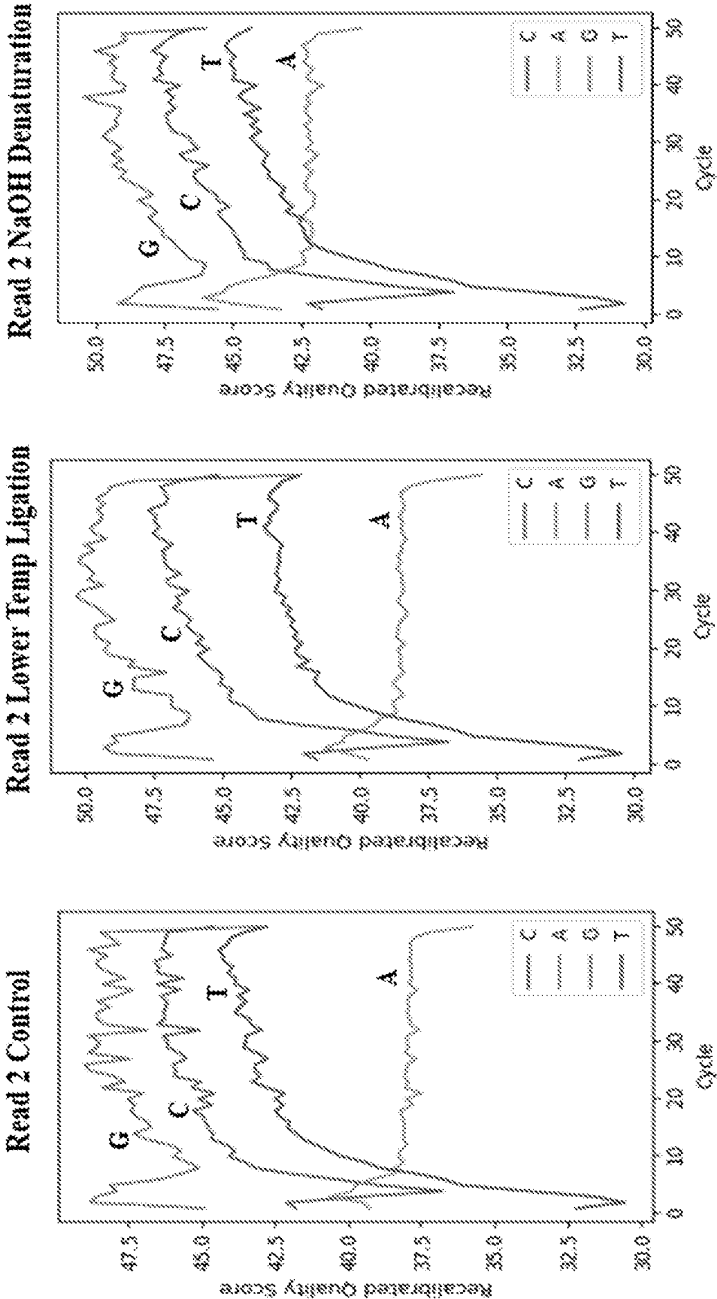


FIG. 70

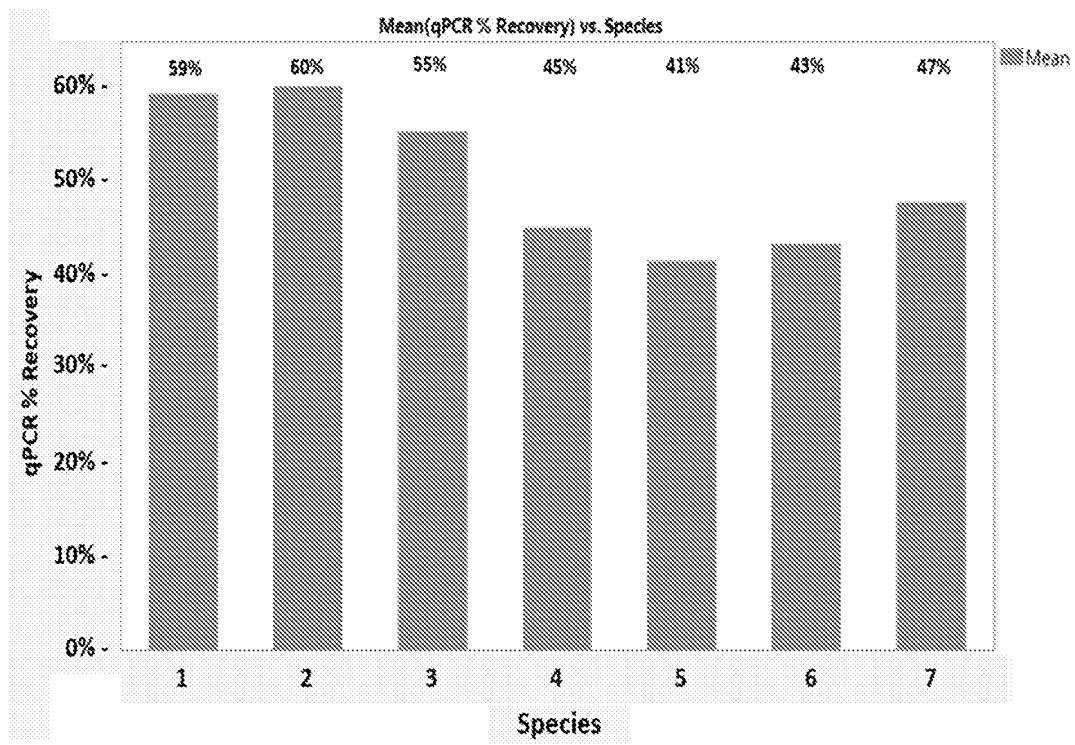


FIG. 71

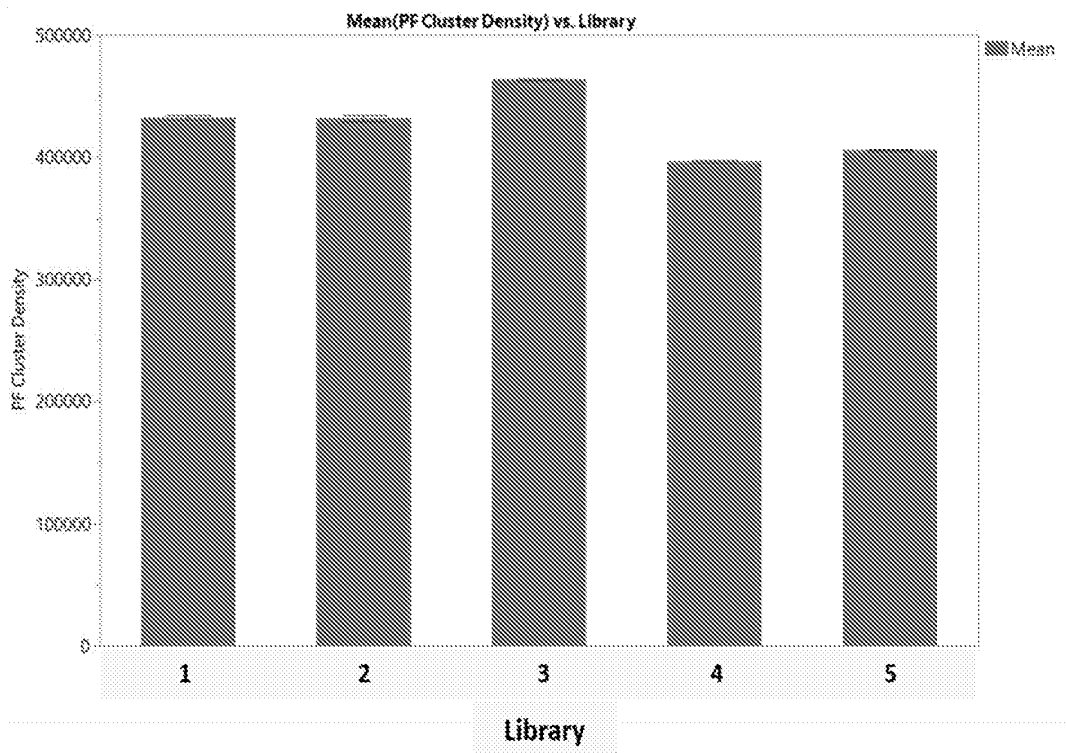


FIG. 72

TABLE A: *E. coli*

|   | USER<br>library<br>prep | USER<br>on-FC | Reads<br>(millions) | %Q30<br>R1 | %Q40<br>R1 | %Q50<br>R1 | %error<br>R1 | %Q30<br>R2 | %Q40<br>R2 | %Q50<br>R2 | % error<br>R2 |
|---|-------------------------|---------------|---------------------|------------|------------|------------|--------------|------------|------------|------------|---------------|
| 1 | NO                      | NO            | 965.6 M             | 98.4%      | 94.1%      | zero       | 0.0666%      | 97.1%      | 86.6%      | zero       | 0.1319%       |
| 2 | YES                     | NO            | 836.0 M             | 98.7%      | 94.9%      | 81.37%     | 0.0401%      | 97.9%      | 88.4%      | 75.68%     | 0.0817%       |
| 3 | YES                     | NO            | 782.8 M             | 98.6%      | 94.4%      | 80.08%     | 0.0427%      | 98.2%      | 88.9%      | 76.04%     | 0.0664%       |
| 4 | YES                     | NO            | 776.3 M             | 98.6%      | 94.5%      | 80.28%     | 0.0401%      | 98.0%      | 88.6%      | 75.66%     | 0.0692%       |
|   |                         |               |                     |            |            |            |              |            |            |            |               |
| 5 | NO                      | NO            | 627.7 M             | 99.0%      | 95.8%      | zero       | 0.0338%      | 97.8%      | 87.8%      | zero       | 0.0688%       |
| 6 | NO                      | YES           | 521.2 M             | 98.9%      | 95.2%      | 82.32%     | 0.0314%      | 97.5%      | 87.1%      | 73.17%     | 0.0645%       |
| 7 | NO                      | YES           | 657.5 M             | 98.9%      | 95.6%      | 88.66%     | 0.0320%      | 97.7%      | 88.0%      | 75.49%     | 0.0703%       |
|   |                         |               |                     |            |            |            |              |            |            |            |               |
| 8 | YES                     | YES           | 647.4 M             | 98.7%      | 94.8%      | 90.13%     | 0.0367%      | 97.2%      | 86.5%      | 72.65%     | 0.0799%       |
| 9 | YES                     | YES           | 644.7 M             | 99.0%      | 95.5%      | 88.04%     | 0.0269%      | 97.3%      | 86.8%      | 73.35%     | 0.0748%       |

TABLE B: Human

|   | USER<br>library<br>prep | USER<br>on-FC | Reads<br>(millions) | %Q30<br>R1 | %Q40<br>R1 | %Q50<br>R1 | %error<br>R1 | %Q30<br>R2 | %Q40<br>R2 | %Q50<br>R2 | % error<br>R2 |
|---|-------------------------|---------------|---------------------|------------|------------|------------|--------------|------------|------------|------------|---------------|
| 1 | NO                      | YES           | 837.8 M             | 97.9%      | 94.0%      | 81.2%      | 1.0600%      | 96.4%      | 91.6%      | 68.2%      | 1.0513%       |
| 2 | NO                      | YES           | 871.3 M             | 97.9%      | 93.9%      | 80.8%      | 1.1114%      | 96.6%      | 92.0%      | 69.3%      | 1.1713%       |

FIG. 73

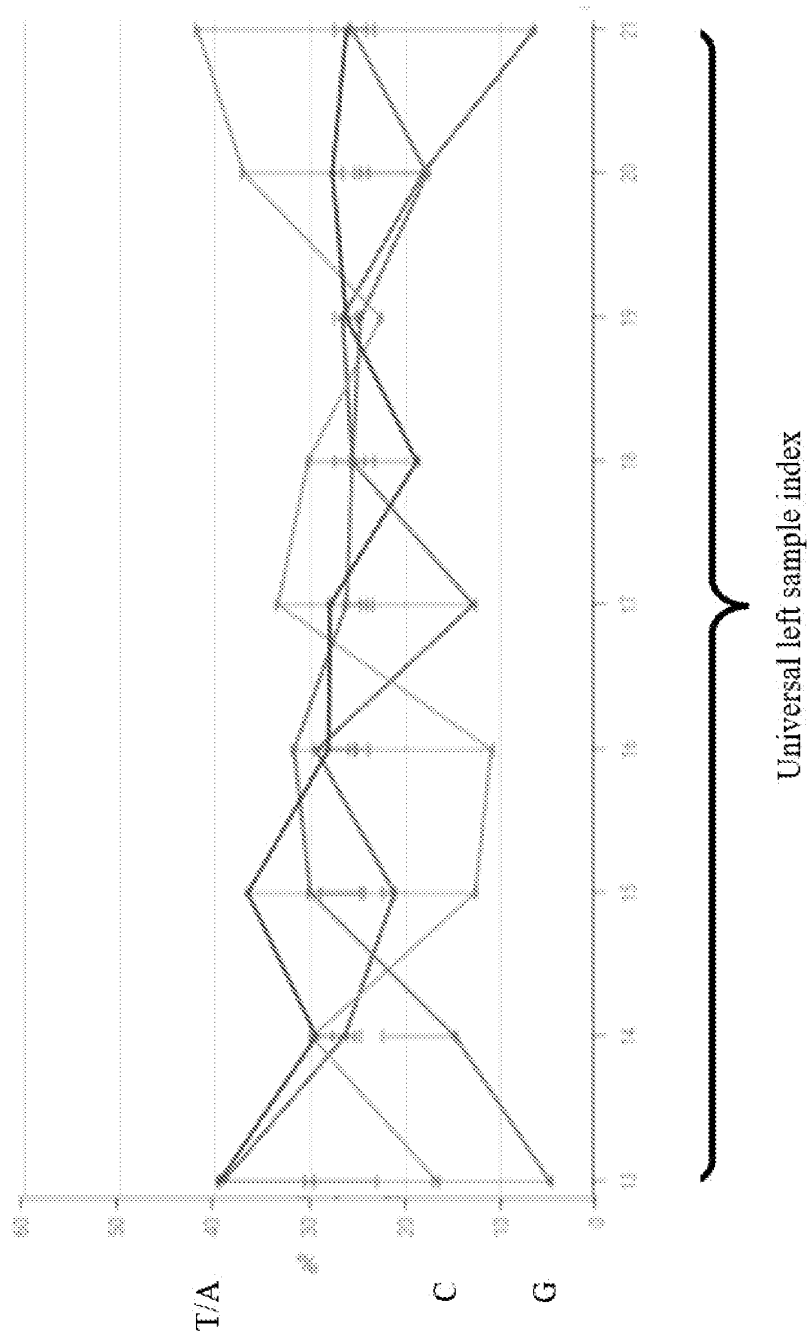


FIG. 74

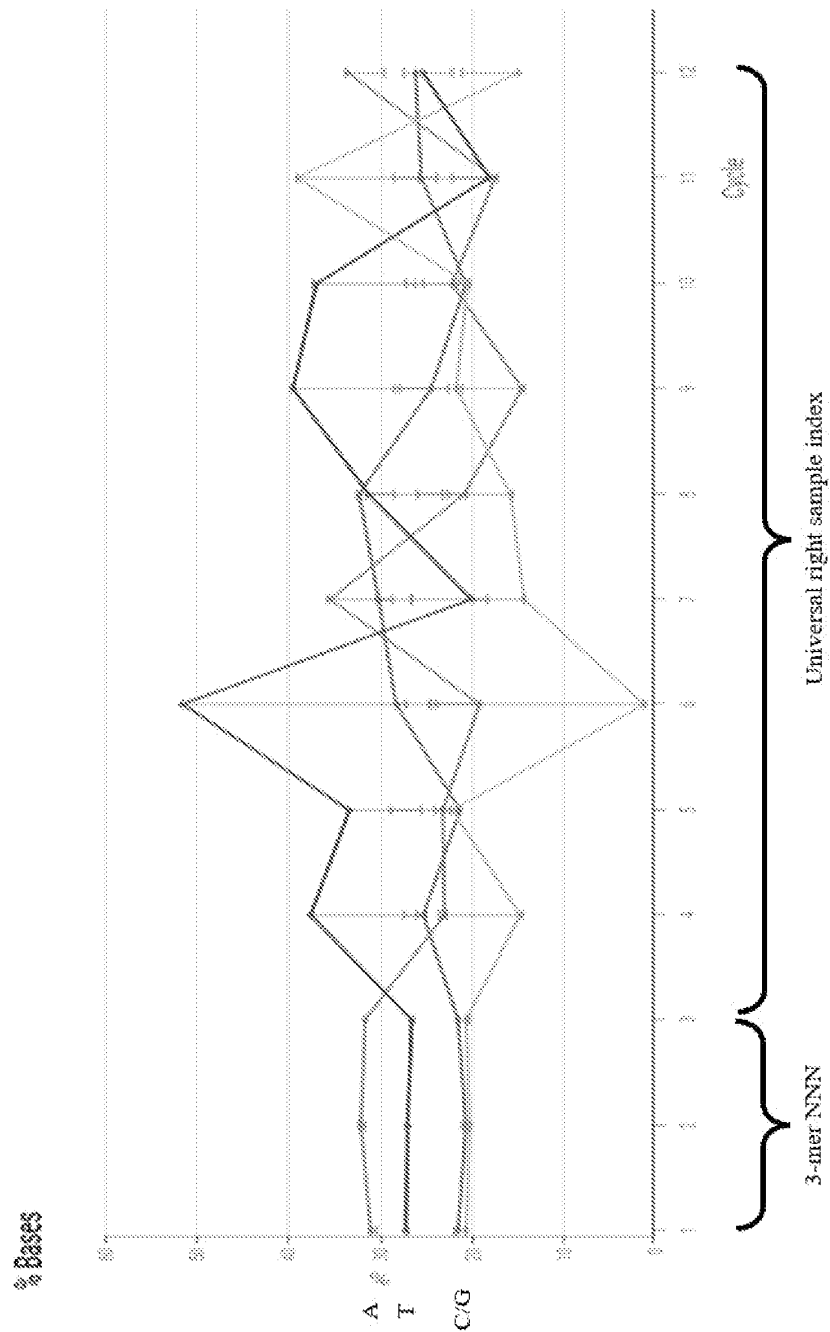


FIG. 75