

## **Regulation of Cell Binding and Entry by DNA Origami mediated Spatial Distribution of Aptamers**

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**Table S1** Assembly of the DNA origami nanoboxes (DONs). All the DNA staple strands sequence were used for the construction of DONs, following the design previously described.<sup>1</sup> (red: modified with Cy5 fluorophore at 5' end)

| Staple       | Sequence                                         |
|--------------|--------------------------------------------------|
| Face strains |                                                  |
| A-13,118     | ATACAGTAACAGTACCTTAACGTCAGATGAATTTTTTTGAGTA<br>A |
| A-17,14      | ATTACCTGTTTTGGATTATACTTCTGAAATAATCCT             |
| A-17,46      | CAAAATCGACCTACCATATCAAAATCCTGATT                 |
| A-17,78      | GGATTCGCCAGAAATAAAGAAATTAACCACCA                 |
| A-23,31      | GGGTTAGACGCAGAGGCGAATTATTCATTTC                  |
| A-23,63      | ACGTAAAACTGATTGCTTTGAATACCAAGTTA                 |
| A-23,95      | TTTCAGGTTTTTACATCGGGAGAAACAATAAC                 |
| A-37,14      | GATTGTTTTTTTGATTAGAGCCGTCAATGCACTAAC             |
| A-37,46      | ATCAGATGGATTTAGAAGTATTAGATTGAGGA                 |
| A-37,78      | GAAGGAGCGACAACCTCGTATTAACTGGTCAG                 |
| A-37,110     | CATTATCATATTAATTTTAAAAGTTTTTTGAACCTC             |
| A-43,31      | CATTTGAGATGGCAATTCATCAATTAATGGAA                 |
| A-43,63      | AACAATTCGGAATTATCATCATATTTATTTGC                 |
| A-43,95      | CCGAACGTTTTTGCGGAACAAAGAGCGTAGAT                 |
| A-57,14      | AACTAATATTTTCGAACCACCAGCAGAACATTA AAA            |
| A-57,46      | AGGTTATCGGCGGTCAGTATTA ACTAATGCGC                |
| A-57,78      | TTGGCAAACCACGCTGAGAGCCAGACAGACAA                 |
| A-57,110     | AAATATCATAAAGCATCACCTTGCTTTTCCTTCTGA             |
| A-63,31      | AGAGGTGATAAAATATCTTTAGGAAGATAATA                 |
| A-63,63      | CAACAGTGTCAACAGTTGAAAGGAACTTTACA                 |
| A-63,95      | GAAAAATCAACCCTCAATCAATATTCCTTTGC                 |
| A-77,14      | ATACCGAATTTTGAAATACCTACATTTTAGGAAAAA             |
| A-77,46      | GAACTGATAAATGGATTATTACATCCAGAAC                  |

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|-----------|-----------------------------------------------------|
| A-77,78   | TATTTTTGTCACACGACCAGTAATAAGAACTC                    |
| A-77,110  | CCTGAAAGCCAACAGAGATAGAACTTTTTTGATTAG                |
| A-83,31   | ATCGTCTGAGCCCTAAAACATCGCGATAAAAC                    |
| A-83,63   | TTCACCAGAATGGCTATTAGTCTTACCGCCTG                    |
| A-83,95   | CATTCTGGCGTAAGAATACGTGGCCAGCAAAT                    |
| A-97,14   | CGCTCATGTTTTTTTTTAGACAGGAACGGAGGCCGATTAAAGG<br>GATT |
| A-97,46   | AATATTACGAAGTGTTTTTATAATCCTCGTTA                    |
| A-97,78   | AAACTATCTAAAAGAGTCTGTCCAGGTTGCTT                    |
| A-97,110  | TAATAACATTGTAGCAATACTTCTTTTTTCGCTTAAT               |
| A-103,31  | AATCCTGACGCCAGCCATTGCAACGACGCTCA                    |
| A-103,63  | CCACCGAGGGCCTTGCTGGTAATATTGGCAGA                    |
| A-103,95  | ATTAACCGTCACTTGCCTGAGTAGAAAAGGGA                    |
| A-117,46  | GAATCAGAGCGGGAGCTAAACAGGTACGCCAG                    |
| A-117,78  | TGACGAGCACGTATAACGTGCTTTCAGTGAGG                    |
| A-117,110 | GCGCCGCTACAGGGCGCGTACTATTCACGCAA                    |
| B-13,31   | GCCCCGATTTAGAGCTTGACGGGGTGAACCA                     |
| B-13,63   | GCGAACGTGGCGAGAAAGGAAGGGAAAAACCG                    |
| B-13,7    | TTCACTAAATCGGAACCCTCGAGGTG                          |
| B-13,95   | GAAAGGAGCGGGCGCTAGGGCGCTTTTTTTAAAGAA                |
| B-27,14   | CCGTAAAGTTTTGGCGAAAATCCTGTTTCTGGTTTG                |
| B-27,46   | TCACCCAATCGGCAAAATCCCTTAGGCCCTGA                    |
| B-27,78   | TCTATCAGCCCGAGATAGGGTTGAGACGGGCA                    |
| B-27,110  | CGTGGACTGAACAAGAGTCCACTATTTTGGCGCCAG                |
| B-33,31   | TTCCGAAAATCAAGTTTTTTGGGGTAAAGGGA                    |
| B-33,63   | AAGAATAGGGCGATGGCCCACTACGAAAGCCG                    |
| B-33,95   | CCAGTTTGCCAACGTCAAAGGGCGAAGAAAGC                    |
| B-47,14   | CCCCAGCATTTTTTAACTCACATTAATTGTGCCTAAT               |
| B-47,46   | GAGAGTTGCGCTTTCAGTCGGGACGAGCCGG                     |

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|-----------|----------------------------------------------------|
| B-47,78   | ACAGCTGATGCATTAATGAATCGGATTGTTAT                   |
| B-47,110  | GGTGGTTTGGCGGTTTGC GTATTGTTTTGTAATCAT              |
| B-53,31   | TCACTGCCCAGCAAGCGGTCCACGGATGGTGG                   |
| B-53,63   | GTGCCAGCTTGCCCTTCACCGCCTTAAATCAA                   |
| B-53,95   | CGGGGAGATTCTTTTCACCAGTGAGTGTTGTT                   |
| B-67,14   | GAGTGAGCTTTTTTTGGGTAACGCCAGGGCTGCAAGG              |
| B-67,46   | AAGCATAAGTTGTAAAACGACGGCGCTATTAC                   |
| B-67,78   | CCGCTCACTGCCTGCAGGTCGACTTGTTGGGA                   |
| B-67,110  | GGTCATAGTACCGAGCTCGAATTCTTTTCAAAGCGC               |
| B-73,31   | GTCACGACAGTGTAAGCCTGGGGCGTTGCGC                    |
| B-73,63   | AGCTTGCAAATTCCACACAACATAAACCTGTC                   |
| B-73,95   | TCCCCGGGCTGTTTCCTGTGTGAACCAACGCG                   |
| B-87,14   | CGATTAAGTTTTTGGCGCATCGTAACCGTCACGTTGG              |
| B-87,46   | GCCAGCTGGGGGACGACGACAGTAACAAACGG                   |
| B-87,78   | AGGGCGATCGCACTCCAGCCAGCTGCGAGTAA                   |
| B-87,110  | CATTCGCCGGTGCCGGAACCAGGTTTTCTGTAGCC                |
| B-93,31   | CAGTTTGAGCGAAAGGGGGATGTGTTTTCCCA                   |
| B-93,63   | AGGAAGATCGGTGCGGGCCTCTTCCAGTGCCA                   |
| B-93,95   | CCGCTTCTATT CAGGCTGCGCAACCTAGAGGA                  |
| B-107,14  | TGTAGATGTTTTATTTAAATTGTAAACGTTAATATT               |
| B-107,46  | CGGATTGAATTCGCATTAAATTTTTGTAAAT                    |
| B-107,78  | CAACCCGTTTTTTAACCAATAGGAACGCCATC                   |
| B-107,110 | AGCTTTCATTCGCGTCTGGCCTTCTT                         |
| B-113,31  | TTGTTAAACCGTAATGGGATAGGTGCATCTGC                   |
| B-113,63  | CAGCTCATCGGATTCTCCGTGGGATCGGCCTC                   |
| B-113,95  | AAAAATAATCAACATTAAATGTGATTCCGGCA                   |
| C-13,118  | TTTACAAAGGCTATCAGGCTATTTTTGAGAGATCTTTTACATTA<br>TG |
| C-17,14   | ATCAGAAATTTTAAGATTCAAAAGGGTGGAGTAATG               |

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|----------|----------------------------------------------|
| C-17,46  | TAGCATGTGTCAAATCACCATCAATAGAACCC             |
| C-17,78  | ACAAGAGATCTAGCTGATAAATTAAGCCTTTA             |
| C-17,110 | CTATCAGGCTATTTTTGAGAGATCTTTTACATTATG         |
| C-23,31  | CGGAGACACAATCATATGTACCCCGGTTGATA             |
| C-23,63  | TCAACCGTATCGATGAACGGTAATCGTAA AAC            |
| C-23,95  | GAGGGTAGTCATTGCCTGAGAGTCTGGAGCAA             |
| C-37,14  | TGTAGGTATTTTTCTACTAATAGTAGTAAAAAGGTG         |
| C-37,46  | TCATATATAATCATACAGGCAAGGTTTAGCTA             |
| C-37,78  | TTTCAACGTTAAGCAATAAAGCCTTTAGATAC             |
| C-37,110 | ACCCTGTAATCGGTTGTACCAA AATTTT-AATTCTGC       |
| C-43,31  | ATCCAATATTTAAATGCAATGCCTAGAAAGGC             |
| C-43,63  | TAGCAAAACAAGGATAAAAATTTTTATGATAT             |
| C-43,95  | AAAGCTAAATACTTTTGCGGGAGAATGCCGGA             |
| C-57,14  | GCATCAATTTTTGCGGATGGCTTAGAGCATAAGAGG         |
| C-57,46  | TATTTTCAATGCTGTAGCTCAACAGGATTAGA             |
| C-57,78  | ATTCGCACTAAAGTACGGTGTCTGAACCAGA              |
| C-57,110 | GAACGAGTATAACAGTTGATTCCCTTTTCAAATATC         |
| C-63,31  | TGAATATATTTGGGGCGCGAGCTGGCATT AAC            |
| C-63,63  | ATATGCAAAATGGTCAATAACCTGCAAAGAAT             |
| C-63,95  | CATTCCATAGATTTAGTTTGACCACAGAGCAT             |
| C-77,14  | TCATTTTTTTTTGTTTCAGAAAACGAGAATCAAATGC        |
| C-77,46  | GAGTACCTATCAGGTCTTTACCCTCGGAATCG             |
| C-77,78  | CCGGAAGCAGCAAAGCGGATTGCAAAAATGTT             |
| C-77,110 | GCGTTTTAGAAGCCCGAAAGACTTTTTTGCAAAAGA         |
| C-83,31  | AATCAAAATTAATTGCTCCTTTTGTTAATTGC             |
| C-83,63  | TAGTCAGAAACTCCAACAGGTCATGTTTTAA              |
| C-83,95  | ATTAAGAGATTTCGAGCTTCAAAGCGGAAGTTT            |
| C-97,14  | TTTAAACATTTTAACTAATGCAGATACATAGGAATACCACATTC |
| C-97,46  | TCATAAATTACGAGGCATAGTAAGATTACAGG             |

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|-----------|--------------------------------------------------|
| C-97,78   | TAGACTGGCCCTCGTTTACCAGACACGTTAAT                 |
| C-97,110  | AGTTTTGCATAGCGAGAGGCTTTTTTTTATACCAG              |
| C-103,31  | AAAGGAATATTCATTGAATCCCCCTGACCATA                 |
| C-103,63  | TATCATAAATAGCGTCCAATACTGGACTATTA                 |
| C-103,95  | AAACCAAACAGAGGGGGTAATAGTTCAAAAAG                 |
| C-117,46  | TAGAAAGATTCATCAGTTGAGATTTAACGCCA                 |
| C-117,78  | AAAACGAAC TAACGGAACAACATTAGCAACAC                |
| C-117,110 | TCAGGACGTTGGGAAGAAAAATCTGACGATAA                 |
| D-13,102  | TTGCAGGGAGTTAAAGATTCGGTCGCTGAGGCTTTTCGAGGT<br>GA |
| D-17,30   | AGCAACGGATGAGGAAGTTTCCATGGCACCAA                 |
| D-17,62   | TCAGCAGCGAAAGACAGCATCGGAACGAGGGT                 |
| D-23,15   | ACTTTTTCCTACAGAGGCTTTGAG                         |
| D-23,47   | TAAAATACGACAACAACCATCGCCTAGTTGCG                 |
| D-23,79   | ACCGATATGCCGCTTTTGCGGGATCGTCACCC                 |
| D-37,30   | CCTAAAAC TCTTTGACCCCCAGCGGATTTGTA                |
| D-37,62   | CCGACAATGTAATGCCACTACGAATAAACGGG                 |
| D-37,94   | ATTTCTTATTTATCAGCTTGCTTTTTTTAAAGGAAT             |
| D-43,15   | AACACTCAGAAAGAGGCAAAAGAATTTTGACTAAAG             |
| D-43,47   | AAGCGCGAAAGGCTCCAAAAGGAGGAAAATCT                 |
| D-43,79   | TGTATCGGAACAGCTTGATACCGACACGCATA                 |
| D-57,30   | TCATCGCCCATGTTACTTAGCCGGCGAACTGA                 |
| D-57,62   | CCAAAAAAAACAAAGTACAACGGAATTATACC                 |
| D-57,94   | TGCGAATAATAGAAAGGAACAAC TTTTTTCGTCTTT            |
| D-63,15   | ACCTGCTCTGATAAATTGTGTCGATTTTACACTAA              |
| D-63,47   | GCAGACGGAAACAAC TTTCAACAGTGTATGGG                |
| D-63,79   | GAGTGAGAATAATTTTTTCACGTTCTTTAAT                  |
| D-77,30   | CCAAC TTTGCGCATAGGCTGGCTGGATATTCA                |
| D-77,62   | ATTTTGCTTCAATCATAAGGGAACAACGAGGC                 |

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|----------|--------------------------------------------------|
| D-77,94  | CCAGACGTACGATCTAAAGTTTTGTTTTGTACCGTA             |
| D-83,15  | CAGACCAGGAAAGAGGACAGATGATTTTAATCCGCG             |
| D-83,47  | CAAGAGTAGCATTCCACAGACAGCAACTACAA                 |
| D-83,79  | TTAGCGTATAGTAAATGAATTTTCTTTCAGCG                 |
| D-97,30  | TTACCCAAAAGGCTTGCCCTGACGGAGATGGT                 |
| D-97,62  | CGCCTGTAATCTTGACAAGAACCGACCTTCAT                 |
| D-97,94  | ACACTGAGCCCAATAGGAACCCATTTTTTTAGTACC             |
| D-103,15 | CAGTGAATATCAACGTAACAAAGCTTTTACGGTGTA             |
| D-103,47 | CAGAACGAGAGCCACCACCCTCATAGAACCGC                 |
| D-103,79 | ATAGCAAGTTTCGTCACCAGTACACCTCATAG                 |
| D-117,30 | TTAATTTCAACTTTAATCATTGTGTTTTTGCTCATT             |
| D-117,62 | CACCCTCAGTAGTAAATTGGGCTTAGAAACAC                 |
| D-117,94 | GCCACCCTCAGAACCGCCACCCTCTTTCAGGG                 |
| E-13,118 | AAACATGAAAGTATTAGGAACCTATTATTCTGTTTTGGCAGGT<br>C |
| E-17,14  | AAGTATAGTTTTTTGATGATACAGGAGTGCGTCATA             |
| E-17,46  | AGGCGGATTTAACGGGGTCAGTGCAAGCGCAG                 |
| E-17,78  | GGATTAGGCGTATAAACAGTTAATAACAAATA                 |
| E-23,31  | AATAAGTTAAGTGCCGTCGAGAGGGTTGATAT                 |
| E-23,63  | ACAGTGCCATTAGCGGGGTTTTGCTCAGTACC                 |
| E-23,95  | CCTATTTTCAGAGGCTGAGACTCCTCAAGAGAA                |
| E-37,14  | CATGGCTTTTTTACCGCCTCCCTCAGAGCAGAGCCA             |
| E-37,46  | TCTCTGAACGCCACCCTCAGAGCCTGCCATCT                 |
| E-37,78  | AATCCTCACCACCAGAACCACCACGCATTTTC                 |
| E-37,110 | AGACGATTATTGACAGGAGGTTGATTTTCTTTAGCG             |
| E-43,31  | CTCAGAACTTTACCGTTCCAGTAAGTACTGGT                 |
| E-43,63  | CAGAGCCGTAAAGCCAGAATGGACTTGAGTA                  |
| E-43,95  | CCGCCAGCGGCCTTGATATTCACAGCCCCCTG                 |
| E-57,14  | CCACCGGATTTTTTTAGAGCCAGCAAAATTTGAGCCA            |

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|-----------|----------------------------------------------|
| E-57,46   | TTTCATAAACCATTAGCAAGGCCGTTTCATTAA            |
| E-57,78   | GGTCATAGAACCATCGATAGCAGCGAGGGAGG             |
| E-57,110  | TCAGACTGACAGAATCAAGTTTGCTTTTGCCAAAGA         |
| E-63,31   | GCACCATTTCAAATCACCGGAACCCGCCACC              |
| E-63,63   | ACCAATGACCCCCTTATTAGCGTTACCACCCT             |
| E-63,95   | CAGTAGCGTAGCGCGTTTTTCATCGCAGAGCCG            |
| E-77,14   | TTTGGGAATTTTCAAACGTAGAAAATACTTACGCAG         |
| E-77,46   | AGGTGAATACATATAAAAGAAACGCCCCAAAAG            |
| E-77,78   | GAAGGTAATAAGTTTATTTTGTTCAGGAAACCG            |
| E-77,110  | CAAAAGGGCATATGGTTTACCAGCTTTTAGTAAGCA         |
| E-83,31   | AGGTGGCATATCACCGTCACCGACCACCAGTA             |
| E-83,63   | CCACGGAAATATTGACGGAAATTAGAAACGTC             |
| E-83,95   | AGAAAATTCGACATTCAACCGATTACCGTAAT             |
| E-97,14   | TATGTTAGTTTTATTGAGCGCTAATATCACAAAGTCAGAGGGTA |
|           | TT                                           |
| E-97,46   | AACTGGCAAGAATTGAGTTAAGCCCATTAGAC             |
| E-97,78   | AGGAAACGAAACAATGAAATAGCATACAGAGA             |
| E-97,110  | GATAGCCGAGCCCTTTTTAAGAAATTTTGTTTAAC          |
| E-103,31  | AACCCACATGATTAAGACTCCTTAATACATAA             |
| E-103,63  | AGAGCAAGCAATAATAACGGAATACAAAGACA             |
| E-103,95  | CTTACCGAAACAAAGTTACCAGAACAATCAAT             |
| E-117,46  | GGGAGAATTAAGTGAACACCCTGAAGAGAGAT             |
| E-117,78  | GAATAACATAAAAACAGGGAAGCGCAATAATA             |
| E-117,110 | GTCAAAAATGAAAATAGCAGCCTTATAGCTAT             |
| F-13,102  | TTGCTCAACAGTAGGGCTCCAGTATAAAGCCAACTTTTGCGTT  |
|           | AAA                                          |
| F-17,30   | TCGAGCCATAAAGTAATTCTGTCCTGCAGAAC             |
| F-17,62   | AACGCCAACATGTAATTTAGGCAGAGGCATTT             |
| F-23,15   | ACAAAAGGGTAATAAGAGAATATATT                   |

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|----------|---------------------------------------|
| F-23,47  | ACAATAAAGTTTAGTATCATATGCTTACTAGA      |
| F-23,79  | AATTCTTATAATTGAGAATCGCCATATTTAAC      |
| F-37,30  | GCGCCTGTAATAATATCCCATCCTCGGCTGTC      |
| F-37,62  | AAAAGCCTCAACATGTTTCAGCTAAAGACGACG     |
| F-37,94  | TAAGAATACCGTGTGATAAATAAGTTTTAAAGAACG  |
| F-43,15  | ACAAGAAATTATCAACAATAGATATTTTAAGTACCG  |
| F-43,47  | AGCATGTATCTGACCTAAATTTAATTAGTTAA      |
| F-43,79  | AATACCGAAACACCGGAATCATAAGTTATACA      |
| F-57,30  | TTTCCTTAGCACTCATCGAGAACAATTACCGC      |
| F-57,62  | TTTCATCTGAAACCAATCAATAATAATTTACG      |
| F-57,94  | CGAGAAAAAATCCAATCGCAAGACTTTTCAAAATCA  |
| F-63,15  | CAAGTACCTCATTCCAAGAACGGGTTTTAGTCCTGA  |
| F-63,47  | GTTTTTATGGGTTATATAACTATAACCTCCGG      |
| F-63,79  | CTGATGCACTTTTTCAAATATATTTGGTTTGA      |
| F-77,30  | GCCCAATATATTCTAAGAACGCGAGTTTTGAA      |
| F-77,62  | CTTAGGTTTTTTCATCGTAGGAATCAGCAAGCC     |
| F-77,94  | TAGGTCTGTCAATAGTGAATTTATTTTTGTAAATCG  |
| F-83,15  | TTATCCGGGCAAGCAAATCAGATATTTTTATTAAAC  |
| F-83,47  | AGCGAACCAGCGATAGCTTAGATTGAATCCTT      |
| F-83,79  | GAGAAGAGAGAGACTACCTTTTTATGTAAATG      |
| F-97,30  | GCCTTAAAAATTTTATCCTGAATCTAATTTGC      |
| F-97,62  | GAAAACATTCCCGACTTGCGGGAGGGCGTTTT      |
| F-97,94  | TCGCTATTGAATAACCTTGCTTCTTTTTAACAAAAT  |
| F-103,15 | CCAGCTACTCAAGATTAGTTGCTATTTTTAGAAAGGC |
| F-103,47 | GCTAACGATGGAAACAGTACATAAGAATTACC      |
| F-103,79 | ATGTGAGTAATTAATTTCCCTTAAAGACGCT       |
| F-117,30 | CAGTTACAAAATAAACAGCCATATTTTTTTTTGCAC  |
| F-117,62 | TTTTTTAAGCGTCTTTCCAGAGCCTTACCAAC      |
| F-117,94 | TAATTACATTTAACAATTTCAATTTATCAATAT     |

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Linker strains

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AB-117,14 TAAAGGGATTTCACATAAATCGGAACCCTCGAGGTG  
BA-13,31 GCCCCCGATTTGCGGGAGCTAAACAGGTACGCCAG  
AB-117,46 GAATCAGATTTTTTTAGAGCTTGACGGGGTGAACCA  
BA-13,63 GCGAACGTTTTACGTATAACGTGCTTTCAGTGAGG  
AB-117,78 TGACGAGCTTTGGCGAGAAAGGAAGGGAAAAACCG  
BA-13,95 GAAAGGAGTTTACAGGGCGCGTACTATTCACGCAA  
AB-117,11 GCGCCGCTTTTCGGGCGCTAGGGCGCTTTTTTTTAAAGAA

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R-A-97,14 CGCTCATGTTTTTTTAGACAGGAACGGAGGCCGAT  
BC-107,14 TGTAGATGTTTTATTAAATTGTAAACGTTTGGTTGATA  
CB-23,31 CGGAGACACAATCATATGTACCCCTTTTAAATATT  
BC-107,46 CGGATTGAATTCGCATTAAATTTTTTTCGTAAAAC  
CB-23,63 TCAACCGTATCGATGAACGGTAATTTTTGTAAAT  
BC-107,78 CAACCCGTTTTTTAAACCAATAGGATTTTGGAGCAA  
CB-23,95 GAGGGTAGTCATTGCCTGAGAGTCTTTACGCCATC  
BC-107,11 AGCTTTCATTCGCGTCTGGCCTTCTTTTACAAAGG

0

R-C-13,118 CTATCAGGCTATTTTTGAGAGATCTTTACATTATG  
CE-117,46 TAGAAAGATTCATCAGTTTGCAGCCTTATAGCTAT  
EC-117,110 GTCAAAAATGAAAATATTTTTGAGATTTAACGCCA  
CE-117,78 AAAACGAACATAACGGATTTGGGAAGCGCAATAATA  
EC-117,78 GAATAACATAAAAACATTTACAACATTAGCAACAC  
CE-117,110 TCAGGACGTTGGGAAGTTTCACCCTGAAGAGAGAT  
EC-117,46 GGGAGAATTAACCTGAATTTAAAAATCTGACGATAA  
AE-23,31 GGGTTAGACGCAGAGGTTTAGACTCCTCAAGAGAA  
EA-23,95 CCTATTTACAGAGGCTGTTTCGAATTATTCATTCA  
AE-23,63 ACGTAAAACTGATTGCTTTGGTTTTGCTCAGTACC

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|------------|-------------------------------------------------------------|
| EA-23,63   | ACAGTGCCATTAGCGGTTTTTTGAATACCAAGTTA                         |
| AE-23,95   | TTTCAGGTTTTTACATTTTTCGAGAGGGTTGATAT                         |
| EA-23,31   | AATAAGTTAAGTGCCGTTTCGGGAGAAACAATAAC                         |
| DE-117,30  | TTAATTTCTTTTATTGAGCGCTAATATCACAAAGTCAGAGGGTA                |
| ED-97,14   | TATGTTAGTTTTTAACTTTAATCATTGTGTTTTTGCTCATT                   |
| DE-117,86  | CAGAACCGTTTTACCGCCTCCCTCAGAGCAGAGCCA                        |
| ED-37,14   | CATGGCTTTTTTCCACCCTCTTTCAGGGATAGCAAG                        |
| R-D-97,94  | ACACTGAGCCCAATAGGAACCCATT                                   |
| R-D-97,102 | TTTCGTCACCAGTACACCTCATAG                                    |
| R-D-117,10 | TTTAGTACCGCCACCCT                                           |
| 2          |                                                             |
| AD-37,110  | TTTTGAGTAACATTATCATATTAATTTTTTTTTTAAGTTTTGTTT<br>TGTACCGTA  |
| DA-77,94   | TTTCGTCTTTCCAGACGTACGATCTATTTTTTTTTTAAAAGTTT<br>TTTGAACCTC  |
| AD-77,110  | TTCCTTCTGACCTGAAAGCCAACAGATTTTTTTTCTTGCTTTTT<br>TTAAAGGAAT  |
| DA-37,94   | TTCGAGGTGAATTTCTTATTTATCAGTTTTTTTTTGATAGAACTT<br>TTTTGATTAG |
| R-A-13,118 | ATACAGTAACAGTACCTTAACGTCAGATGAATTT                          |
| R-D-57,94  | TGCGAATAATAGAAAGGAACAACCTTT                                 |
| R-A-57,110 | AAATATCATAAAGCATCACCTTGCTT                                  |
| R-D-13,102 | TTGCAGGGAGTTAAAGATTCGGTCGCTGAGGCTT                          |
| DC-63,15   | ACCTGCTCTGATAAATTGTGTCGATTTAATTCTGC                         |
| CD-37,110  | ACCCTGTAATCGGTTGTACCAAATTTTACACTAA                          |
| DC-103,15  | CAGTGAATATCAACGTAACAAAGCTTTGCAAAAGA                         |
| CD-77,110  | GCGTTTTAGAAAGCCCGAAAGACTTTTTTACGGTGTA                       |
| BD-27,110  | CGTGGACTGAACAAGAGTCCACTATTTGCGGGAT                          |
| DB-23,79   | ACCGATATGCCGCTTTTTTGCGCCAGGGTG GTTT                         |

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|------------|-----------------------------------------------------------------------|
| BD-67,110  | GGTCATAGTACCGAGCTCGAATTCTTTTACGAGGGT                                  |
| DB-13,70   | CGTCACCCTCAGCAGCGAAAGACAGCATCGGATTTTCAAAGC<br>GC                      |
| R-B-47,110 | GGCGGTTTGCGTATTGTTTTGTAATCAT                                          |
| EF-23,111  | TTATTCTGTTTTTTTAACAATTTCATTTATCAATAT                                  |
| FE-117,94  | TAATTACATTTTGGCAGGTCAGACGATTATTGACAGGAGGTTG<br>ATTTTCTTTAGCG          |
| EF-77,110  | CAAAAGGGCATATGGTTTACCAGCTTTTCAGTTACA                                  |
| FE-97,30   | GCCTTAAAAATTTTATCCTGAATCTAATTTGCTTTTAGTAAGCA                          |
| R-E-13,118 | AAACATGAAAGTATTAGGAACCTA                                              |
| R-F-117,22 | AAATAAACAGCCATATTTTTTTTTTGCAC                                         |
| C-37,14    | TGTAGGTATTTTTCTACTAATTTTTTTTACAAGAAATTATCAAC<br>AATAGATATTTTAAGTACCG  |
| F-63,15    | CAAGTACCTCATTCCAAGAACGGGTTTTAGTCCTGATTTTTTT<br>TTAGTAGTAAAAAGGTG      |
| CF-77,14   | TCATTTTTTTTTGTTTCAGAATTTTTTTTTTATCCGGGCAAGCAA<br>ATCAGATATTTTTATTAAAC |
| FC-103,15  | CCAGCTACTCAAGATTAGTTGCTATTTTTAGAAAGGCTTTTTTTT<br>AACGAGAATCAAATGC     |
| AF-37,14   | GATTGTTTTTTGTAAATCGTCGCTATT                                           |
| AF-57,14   | AACTAATATTTCAAAATCATAGGTCTG                                           |
| AF-77,14   | ATACCGAATTTAAAGAACGCGAGAAAA                                           |
| R-A-43,7   | TTGATTAGAGCCGTCAATGCACTAAC                                            |
| R-A-63,7   | TTCGAACCACCAGCAGAACATTAAAA                                            |
| R-A-83,7   | TTGAAATACCTACATTTTAGGAAAAA                                            |
| R-F-37,94  | TAAGAATACCGTGTGATAAATAAGTT                                            |
| R-F-57,94  | AATCCAATCGCAAGACTT                                                    |
| R-F-97,94  | GAATAACCTTGCTTCTTTTTAACAAAAT                                          |
| R-F-77,94  | TCAATAGTGAATTTATT                                                     |

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|           |                                         |
|-----------|-----------------------------------------|
| BF-47,14  | CCCCAGCATTTTTTAACAACGCCAACATGTAATTT     |
| FB-23,79  | AATTCTTATAATTGAGAATCGCCATATTTTTTAACTCAC |
| BF-87,14  | CGATTAAGTTTTTGCATTTTCGAGCCA             |
| FB-13,44  | AGGCAGAGTTTTGGCGCATCGTAACCGTCACGTTGG    |
| R-B-57,13 | ATTAATTGTGCCTAATGAGTGAGCTT              |
| R-B-73,7  | TTTTGGGTAAACGCCAGGGCTGCAAGG             |
| R-F-23,23 | TAAAGTAATTCTGTCCTGCAGAAC                |

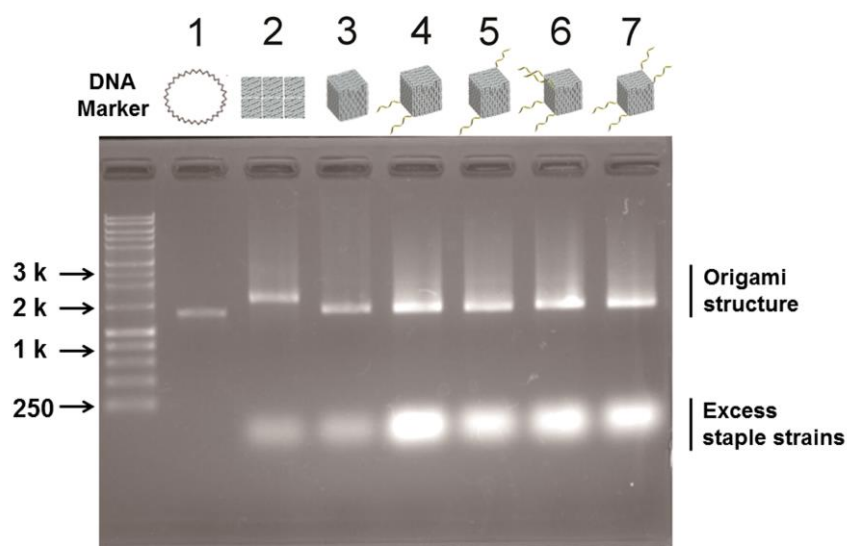
Table S2 Arranging the spatial distribution of aptamers with specific density and orientation on the surface of DONs. DNA staples AB-117,14; AB-117,110; AE-23,31; EA-23,95; BC-107,14; BC-107,110; CE-117,46;CE-117,110 from the staple mix shown above were selectively removed and replaced with the corresponding aptamer-tethered staple strains in order to construct specific aptamer-DONs. (Red: AS1411 aptamer sequence; Blue: spacer sequence)

| Aptamer-tethered staple | Sequence                                                                   |
|-------------------------|----------------------------------------------------------------------------|
| apt-AB-117,14           | GGTGGTGGTGGTTGTGGTGGTGGTGGttttTAAAGGGATTT<br>CACTAAATCGGAACCCTCGAGGTG      |
| apt-AB-117,110          | GGTGGTGGTGGTTGTGGTGGTGGTGGttttGCGCCGCTTTT<br>CGGGCGCTAGGGCGCTTTTTTTTAAAGAA |
| apt-AE-23,31            | GGTGGTGGTGGTTGTGGTGGTGGTGGttttGGGTTAGACG<br>CAGAGGTTTAGACTCCTCAAGAGAA      |
| apt-AE-23,95            | GGTGGTGGTGGTTGTGGTGGTGGTGGttttTTTCAGGTTTT<br>TACATTTTTCGAGAGGGTTGATAT      |
| apt-BC-107,14           | GGTGGTGGTGGTTGTGGTGGTGGTGGttttTGTAGATGTTT<br>TATTAAATTGTAAACGTTTGGTTGATA   |
| apt-BC-107,110          | GGTGGTGGTGGTTGTGGTGGTGGTGGttttAGCTTTCATTC<br>GCGTCTGGCCTTCTTTTACAAAGG      |
| apt-CE-117,46           | GGTGGTGGTGGTTGTGGTGGTGGTGGttttTAGAAAGATT                                   |

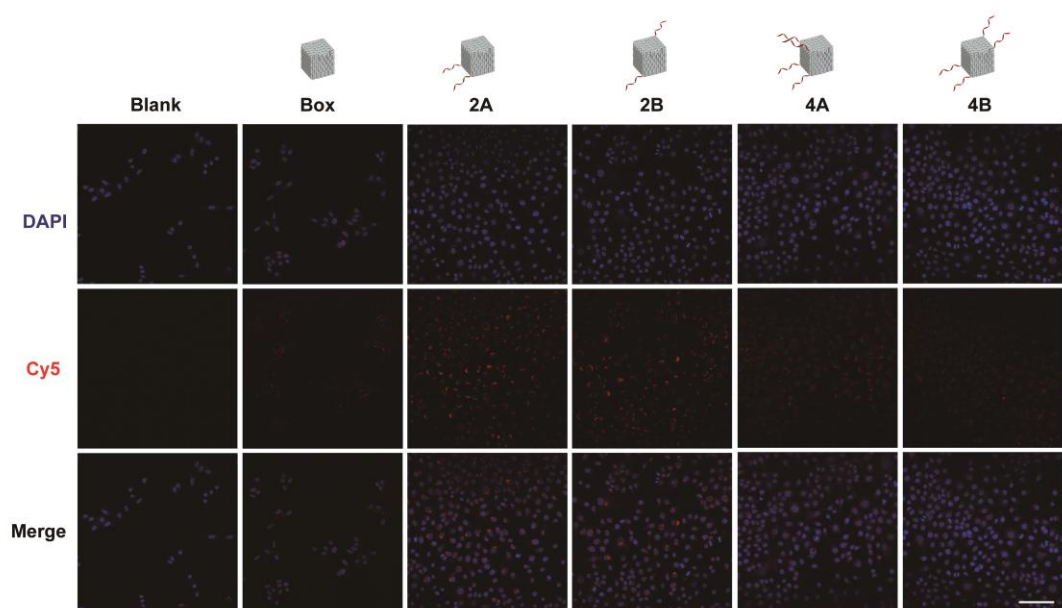
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|                |                            |
|----------------|----------------------------|
|                | CATCAGTTTGCAGCCTTATAGCTAT  |
| apt-CE-117,110 | GGTGGTGGTGGTTGTGGTGGTGGTGG |
|                | ttttTCAGGACGTT             |
|                | GGGAAGTTTCACCCTGAAGAGAGAT  |

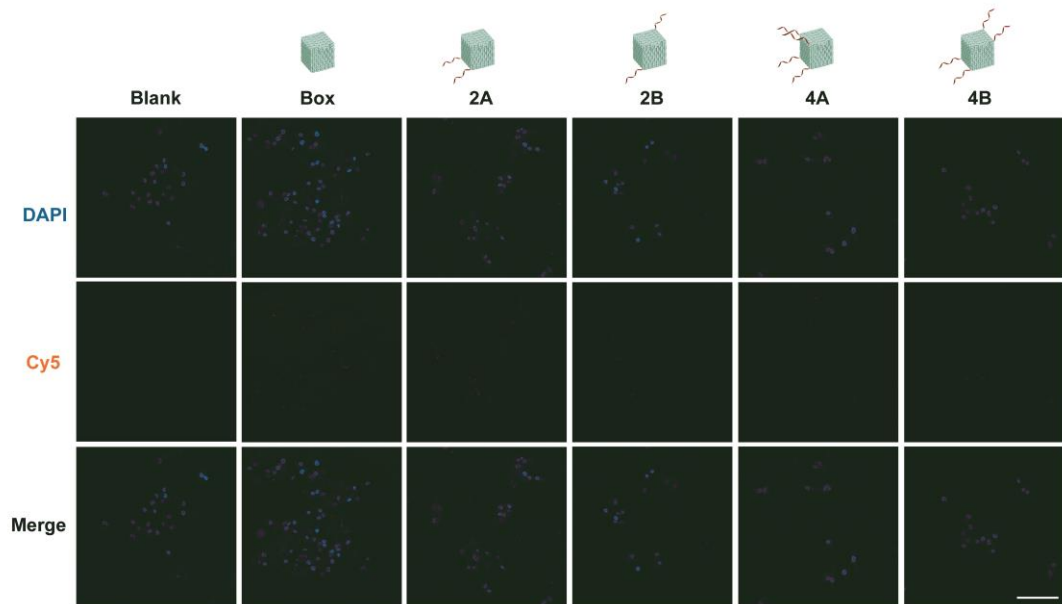
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**Figure S1** Agarose gel electrophoresis of DONs anchored with spatial distributed aptamers. Lane 1: M13 single strain; Lane 2: Assembly of DONs without linker strains; Lane 3: Unmodified DONs (Box); Lane 4 to Lane 7: different groups of aptamer DONs.



**Figure S2** Representative confocal images of HeLa cells cultured with Cy5-labeled DONs for 2 hours. Blue fluorescence: cell nuclei stained with DAPI. Red fluorescence: DONs tagged with Cy5. Scale bars: 50  $\mu$ m.



**Figure S3** Typical confocal images of MCF-7 cells incubated with Cy5-labeled DONs for 2 hours. Blue fluorescence: cell nuclei stained with DAPI. Red fluorescence: DONs tagged with Cy5. Scale bars: 50  $\mu$ m.