TAGGED SPLIT-AND-POOL

DNA tag

3' 5'

Building block (BB)

x 20 different BBs

Pooled

Split into 200 wells

200 different BB 2s (1 per well)

Well B

Well B

DNA tag 2

Well A

Well A

Pool 200 wells

DNA-encoded library of 4,000 molecules
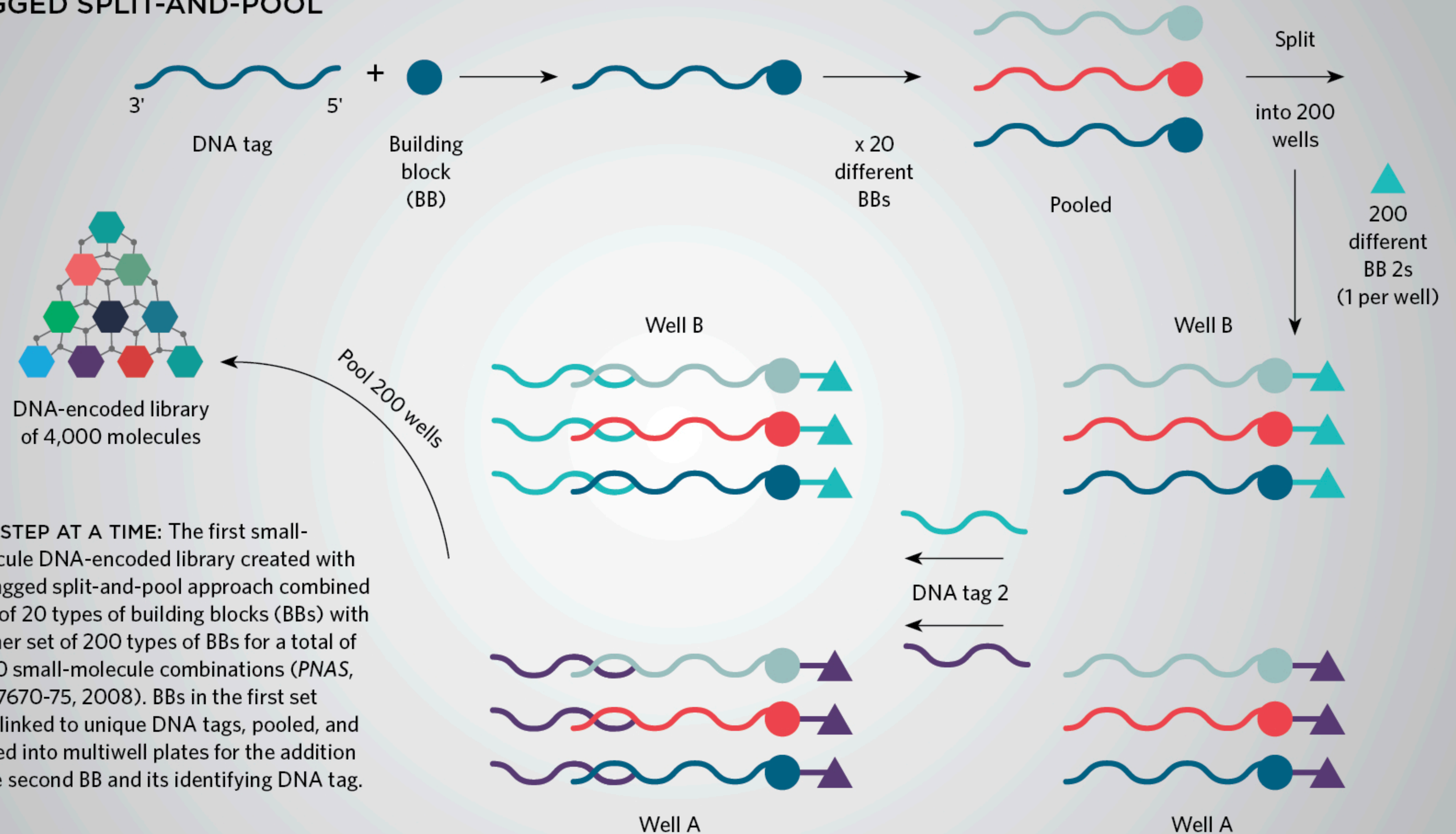
ONE STEP AT A TIME: The first small-molecule DNA-encoded library created with the tagged split-and-pool approach combined a set of 20 types of building blocks (BBs) with another set of 200 types of BBs for a total of 4,000 small-molecule combinations (*PNAS*, 105:17670-75, 2008). BBs in the first set were linked to unique DNA tags, pooled, and divided into multiwell plates for the addition of the second BB and its identifying DNA tag.