Molecular Computation
A DNA-Based Model for Solving Mathematical Problems

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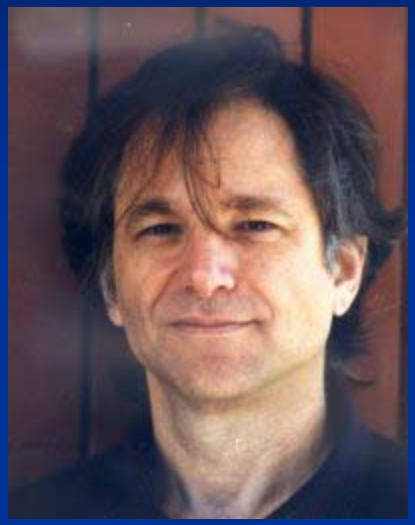
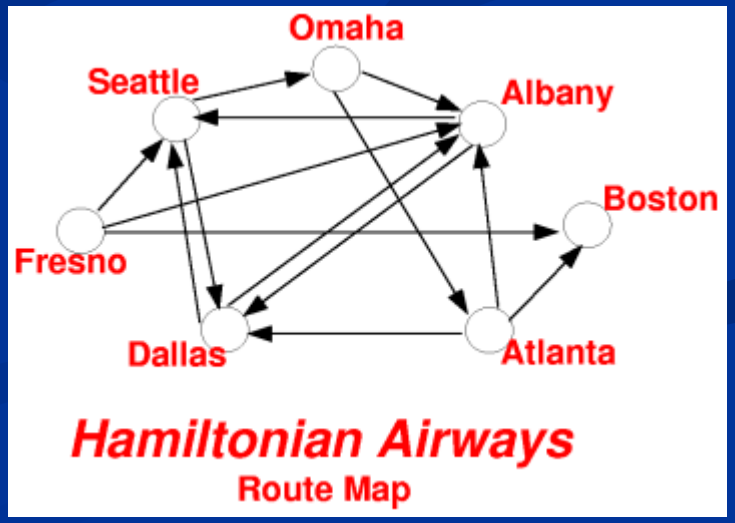
Topics

- What is DNA computing?
- What are the prerequisites for creating a DNA computing model?
- The two phases of the project
- Phase 1: Testing DNA strand binding
- The Geneseo problem
- Phase 2: Modeling the problem
- Future work

What is DNA Computing?

- An application of nanotechnology
- First developed in 1994 by Leonard Adleman
- Uses single stranded DNA molecules to represent the variables in a mathematical problem
- Selective hybridization then allows for the isolation of the correct answer





Why DNA?

- DNA has the ability to compute in *parallel*
- Standard computers compute in *series*
- This gives DNA the ability to sort through massive sets of data much quicker than a standard computer
- The key is simultaneous hybridization of DNA in solution

Example: Adding Numbers

5+3, 4+2, 3+6

Standard Computer:

5+3=8

4+2=6

3+6=9

Parallel:
5+3=8

4+2=6

3+6=9

Prerequisites

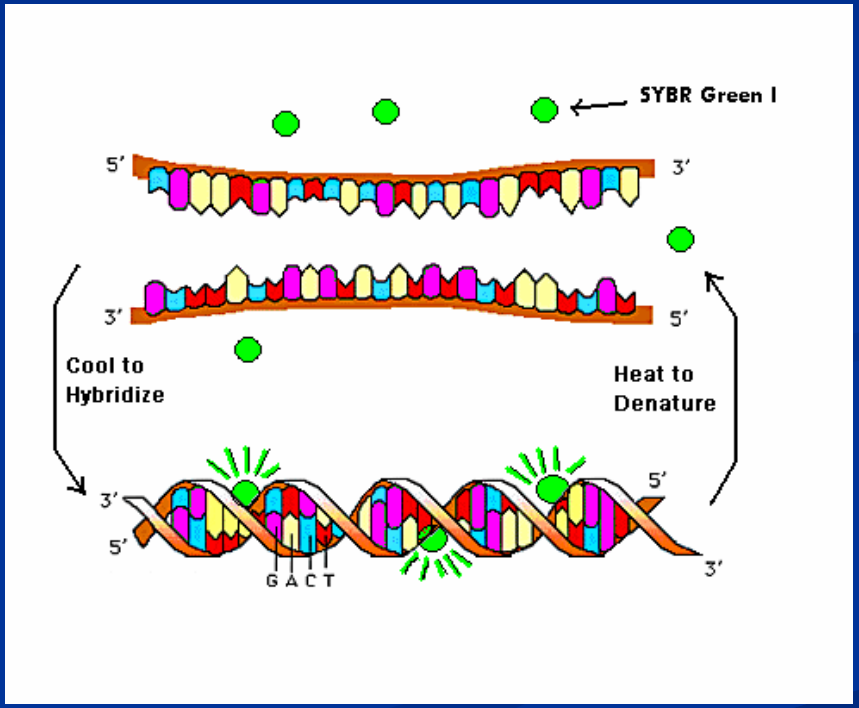
- Method for generating sequences of DNA to represent all the variables of a given problem
- Must also generate "well-behaved" strands
- Procedure for validating this method
- Strands that mis-pair when hybridizing will create errors in a DNA problem

Phase I

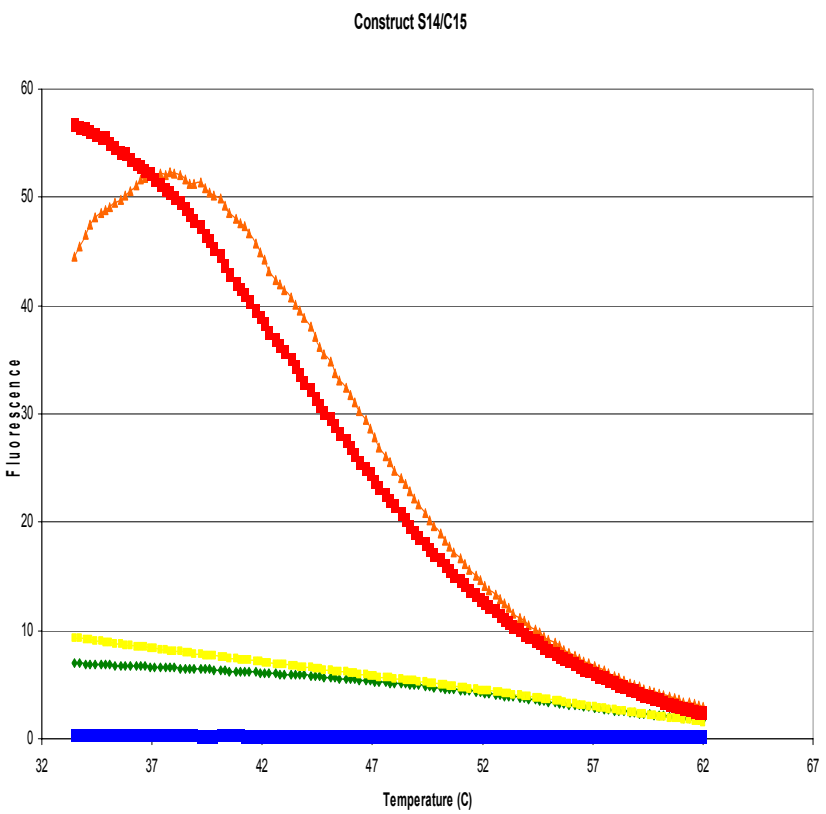
- Generated sequences using a computer algorithm developed by Dr. Anthony Macula
- Sequences were then synthetically prepared by *Invitrogen*
- Validated efficacy of the algorithm using SYBR Green I molecular dye
- This Dye binds to the minor groove of double stranded DNA (dsDNA) only

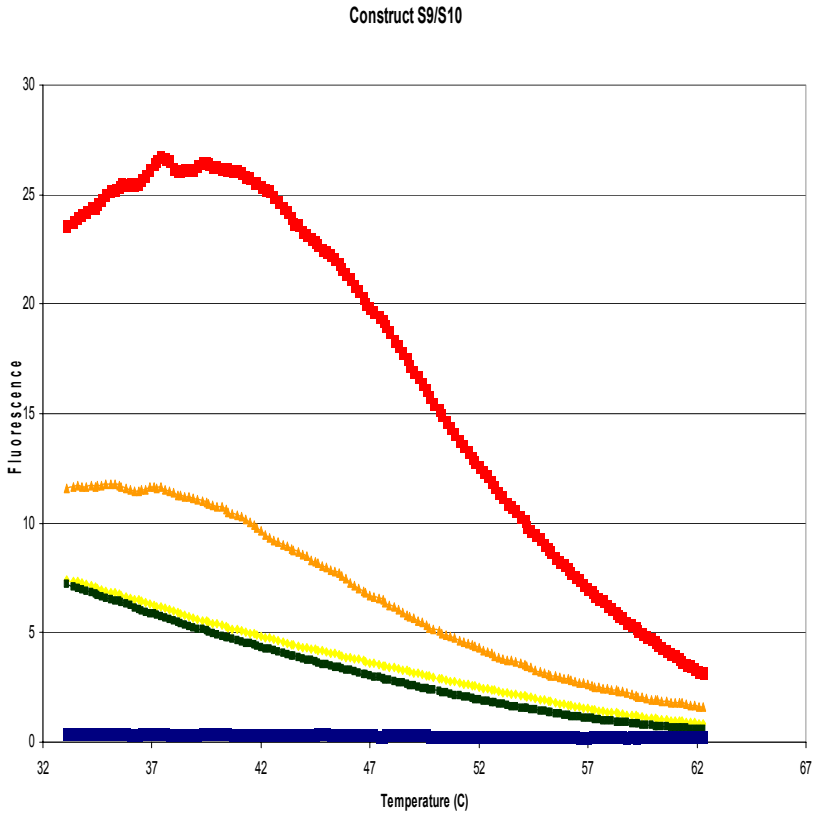
SYBR Green

- Place the generated strands in solution together
- Measure fluorescence to see if there is dsDNA present
- If there is notable fluorescence when it is not expected a DNA strand will be discarded and not used in the final experiment



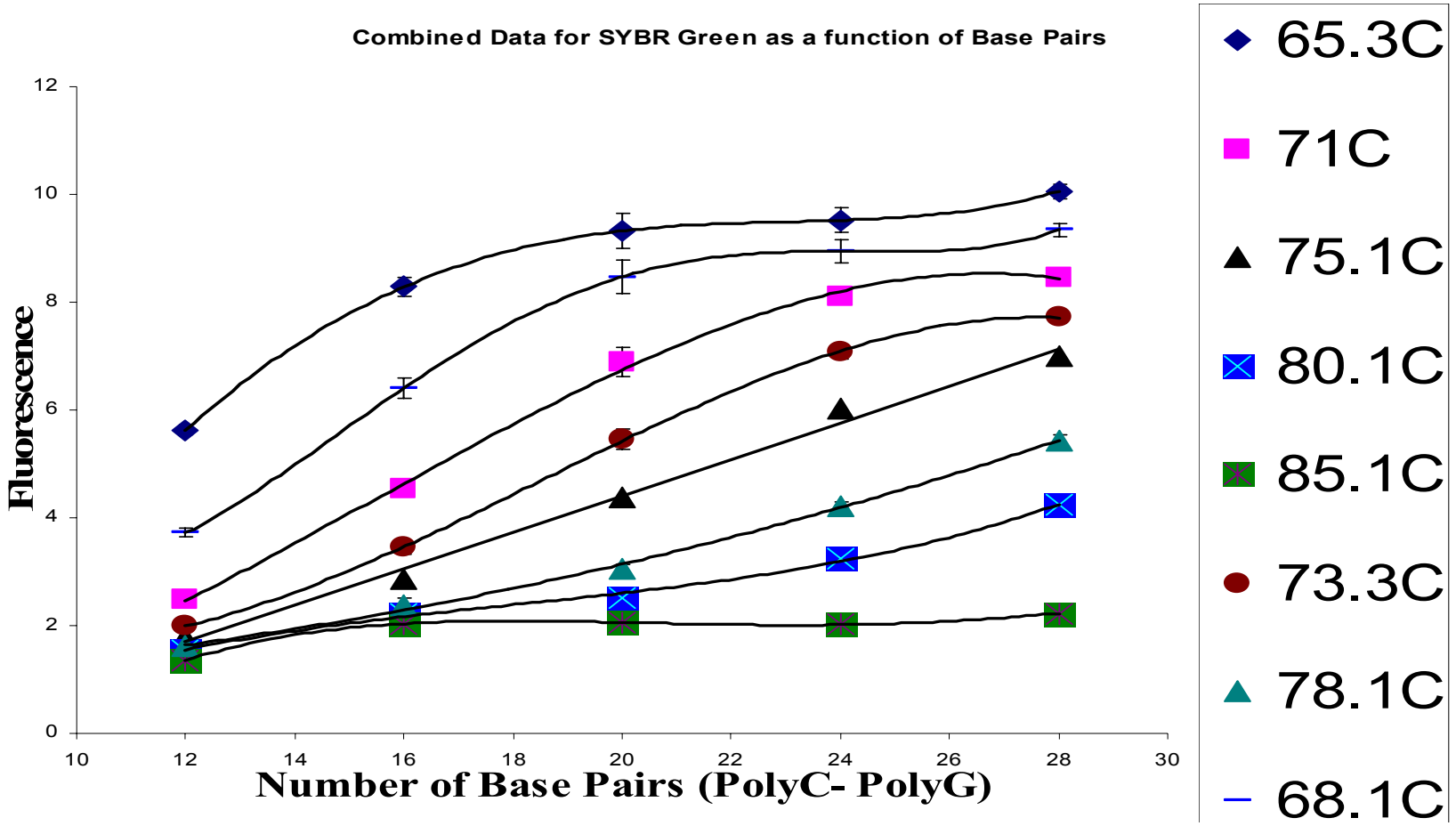
Fluorescence Experiments





Conclusion: SYBR Green was effective in screening for appropriate binding. The algorithm used to generate the sequences was efficient at producing "well-behaved" strands.

Other SYBR Experiments



The SAT Problem

- Short for *Satisfiability*
- A series of logic clauses connected by "and" statements
- Each clause must be true for the entire series to be true
- Each Variable is represented by two strands: One for TRUE and one for FALSE

In a SAT problem all clauses must be true!
Example:
1) X1 or X2
2) ~X1 or X5
3) ~AX or X3 or X4
4) X3 or ~X5
5) X4 or X5
6) ~X3 or ~X4
7) ~X2 or X3

It is easy to see that these problems can get incredibly complex as more clauses are added.

Answer: A1=T, A2=T, A3=T, A4=F, A5=T

Phase II
Modeling the Problem

- The first step is to create all the possible answers to the problem
- The individual DNA strands must be linked together to produce all possible combinations
- Ex:

10 strands to code for **T** or **F** for **5** Variables

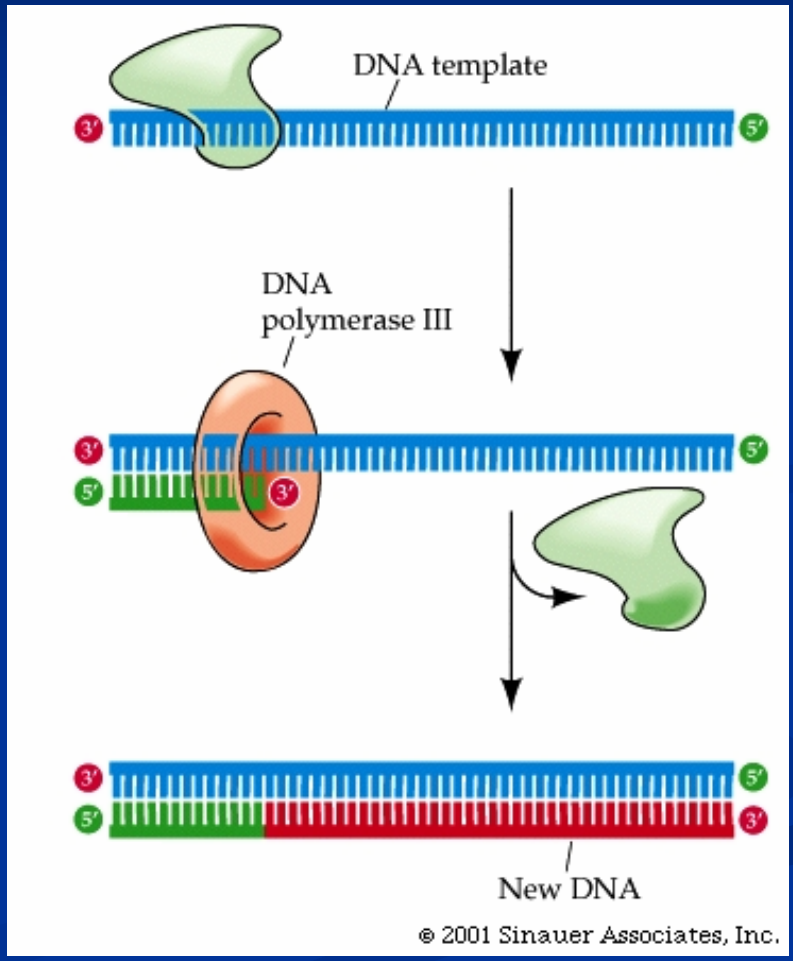
Each strand is **16 nucleotides** long there are **2^5=32** possible "solution" strands of length **80 nucleotides (16 nucleotides * 5variables)**

DNA Strands

- Library Sequences (5'—3')
- C C T T T T T T T T T T T T T T T T, T1
- T T T C C A A T T T C C T T A T, F1
- A A C A A C C A A A C C A A A A, T2
- A A A T C C T C T T T T C A A A, F2
- A C A C A C A C T T T T A C T T, T3
- A C T A T C A C A A A A T A A A, F3
- C T T A C T A T T C A T T C A T, T4
- T A A C C T A C C T C T C C T T, F4
- C T A T A C C A T C A A T T A T, T5
- T A A T T C T C A A C A T T T A, F5

Building the Answers

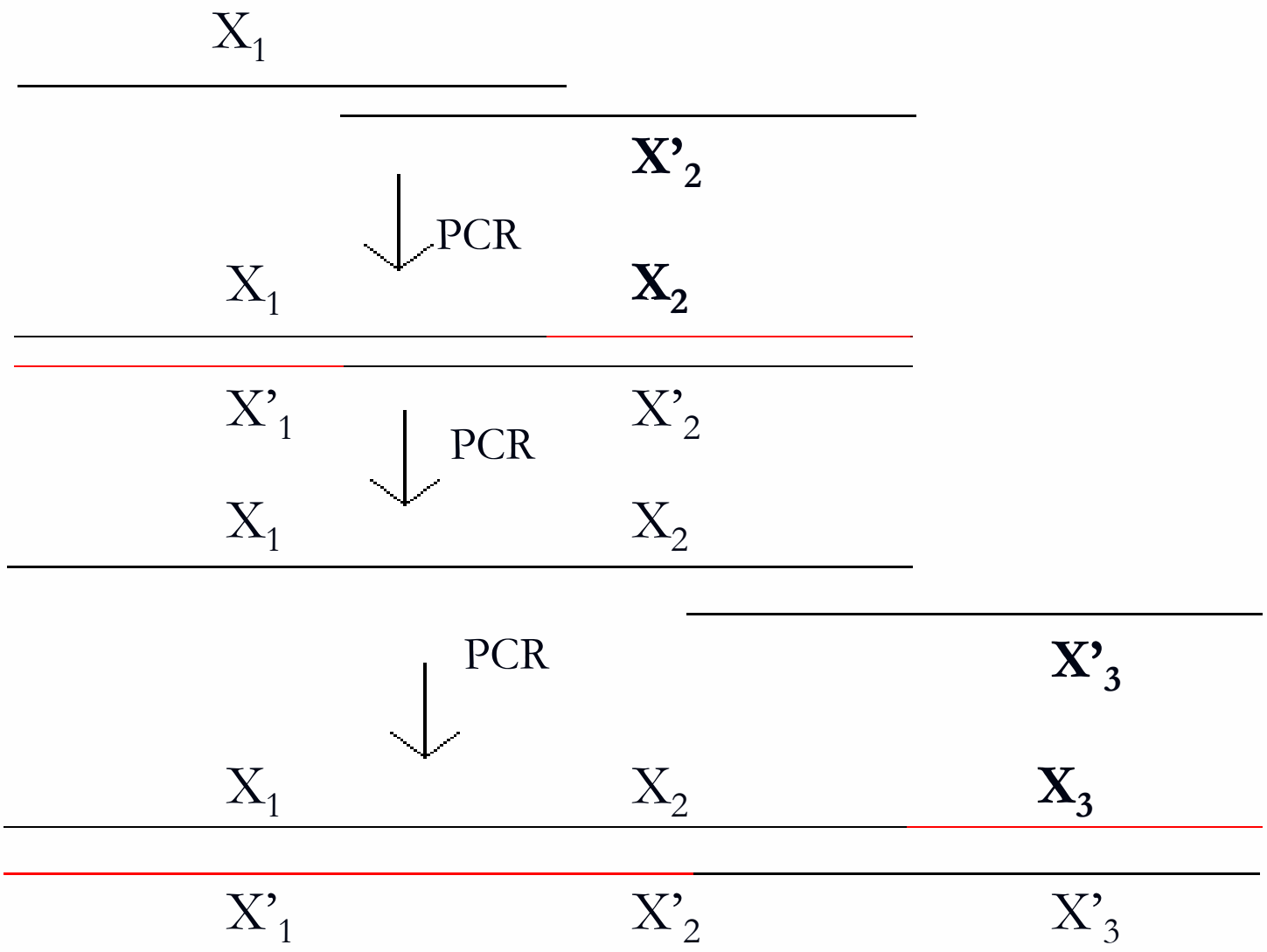
- DNA polymerase extends a DNA molecule by adding complementary bases to a primer
- We exploit this capability to create all combinations of the variable strands



Connecting the Pieces

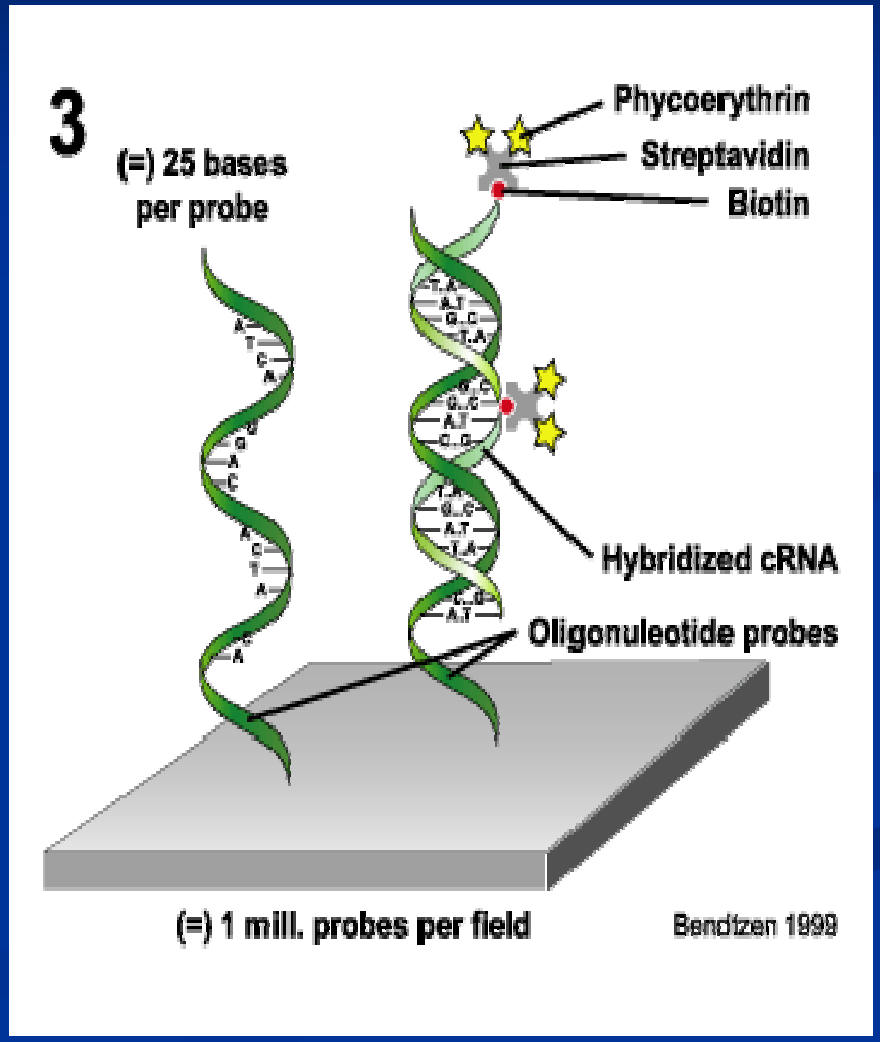
- Polymerase Chain Reaction (PCR): Repetitive heating and cooling of DNA sample to allow DNA polymerase to extend all the molecules
- Using complements to each new variable position all possible combinations of strands are created one PCR reaction at a time
- What is this slide talking about?

Stepwise PCR



Future Work

- The PCR reactions produce all 32 combinations, but it also creates their complements
- We need single-stranded DNA
- Use Biotin and Streptavidin to separate



Future Work

- Once all strands are single stranded the problem can be solved
- Bind complement sequences that make the first clause True to Streptavidin, which is also associated with metallic beads on a column
- Strands with the right combination will adhere to the column
- Pass the captured strands through successive columns representing TRUE for each clause in the problem
- Anything remaining at the end codes for the answer
- Sequence the strand

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