

DNA Microarrays

DePaul Bioinformatics Workshop

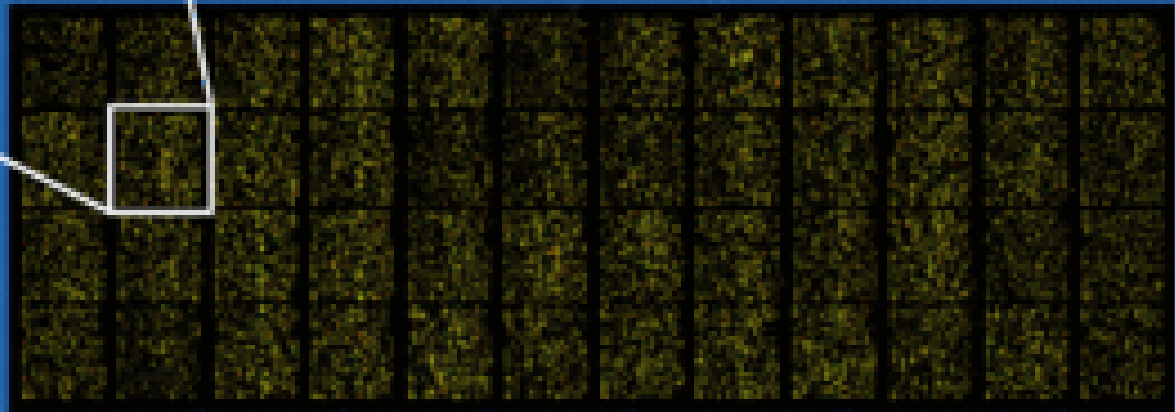
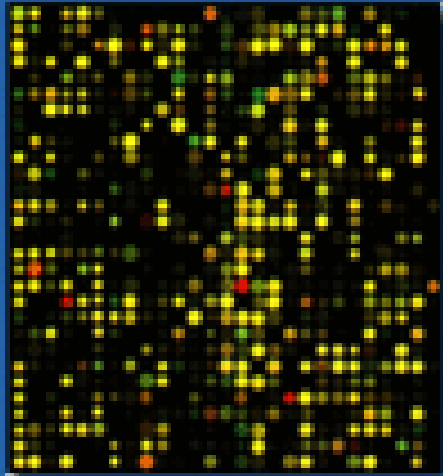
Other names you might hear...

- Gene chip
- Genome chip
- DNA chip
- Gene array

Fabrication

- Microscopic DNA spots
- Glass, plastic or silicon substrate
- Spots arranged in a grid or grids
- Each spot designed with DNA probe
- Techniques for application include pin printing, photolithography, and electrochemistry

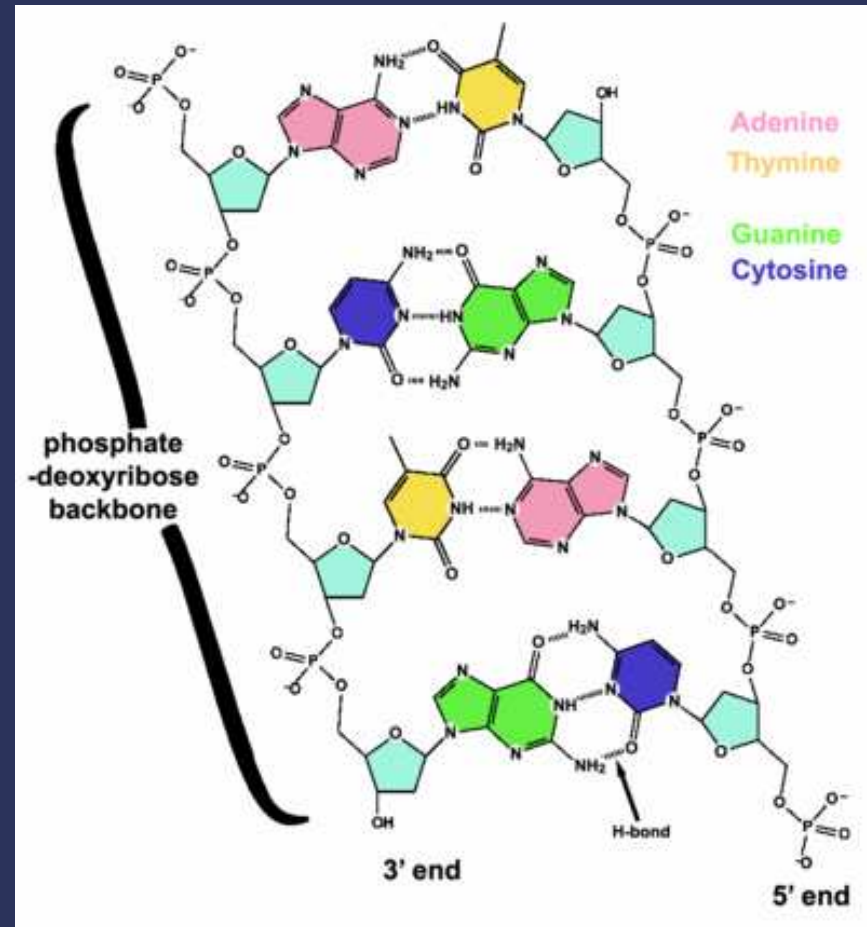
A typical microarray



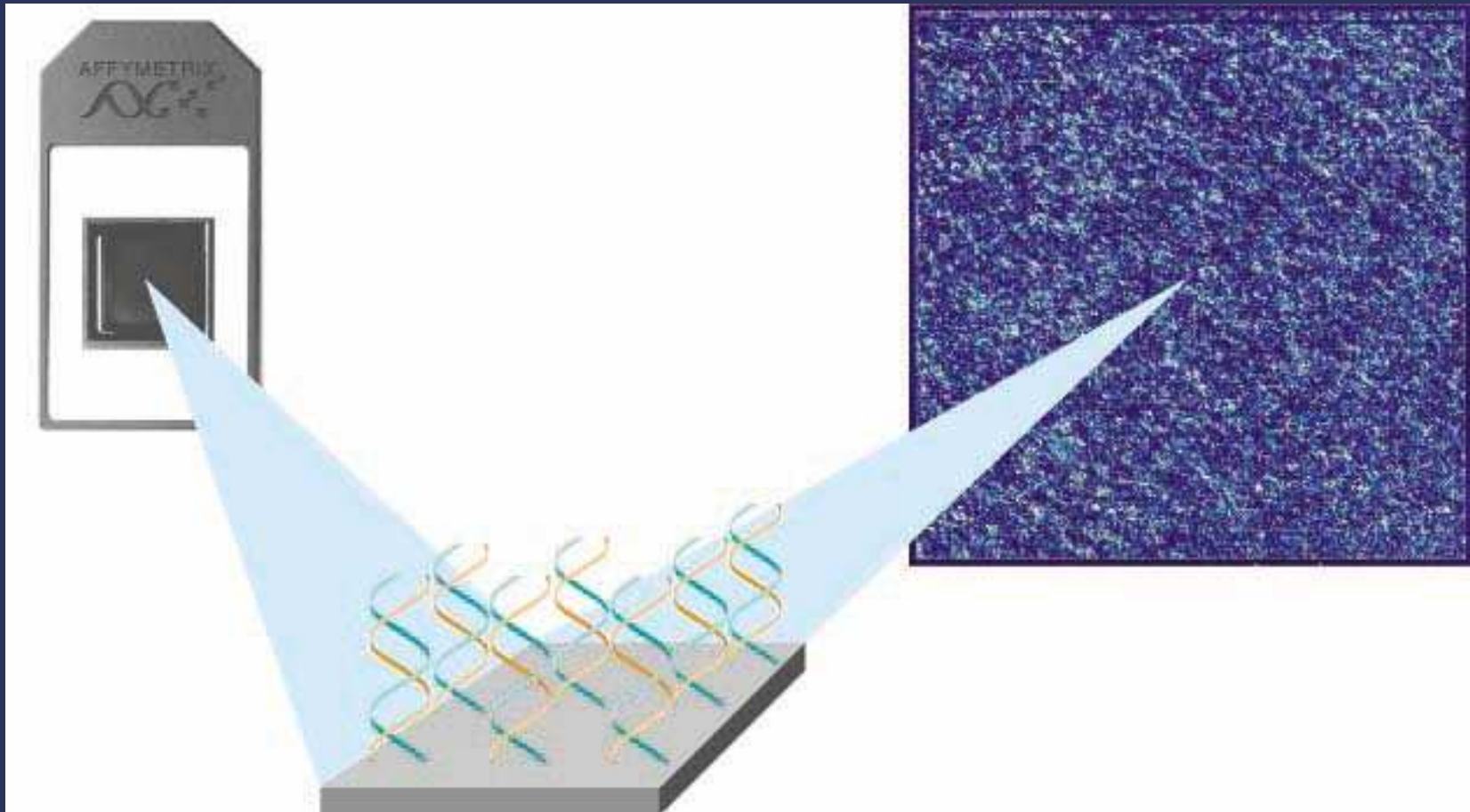
Why does it work?

- Test DNA is applied to the microarray
- The test DNA will bond to certain probes and not to others
- The test DNA is labeled with fluorophores
- Where the DNA sticks, the slide will fluoresce
- A picture of the array is then analyzed

Base pair matching



Affymetrix Chip



Problems solved

- Gene expression – used to compare an expressed and unexpressed gene
- Genome matching – used to identify mutations such as amplifications and deletions of DNA
- Classification – used to match an unknown genome against a library of known genomes

Gene expression study

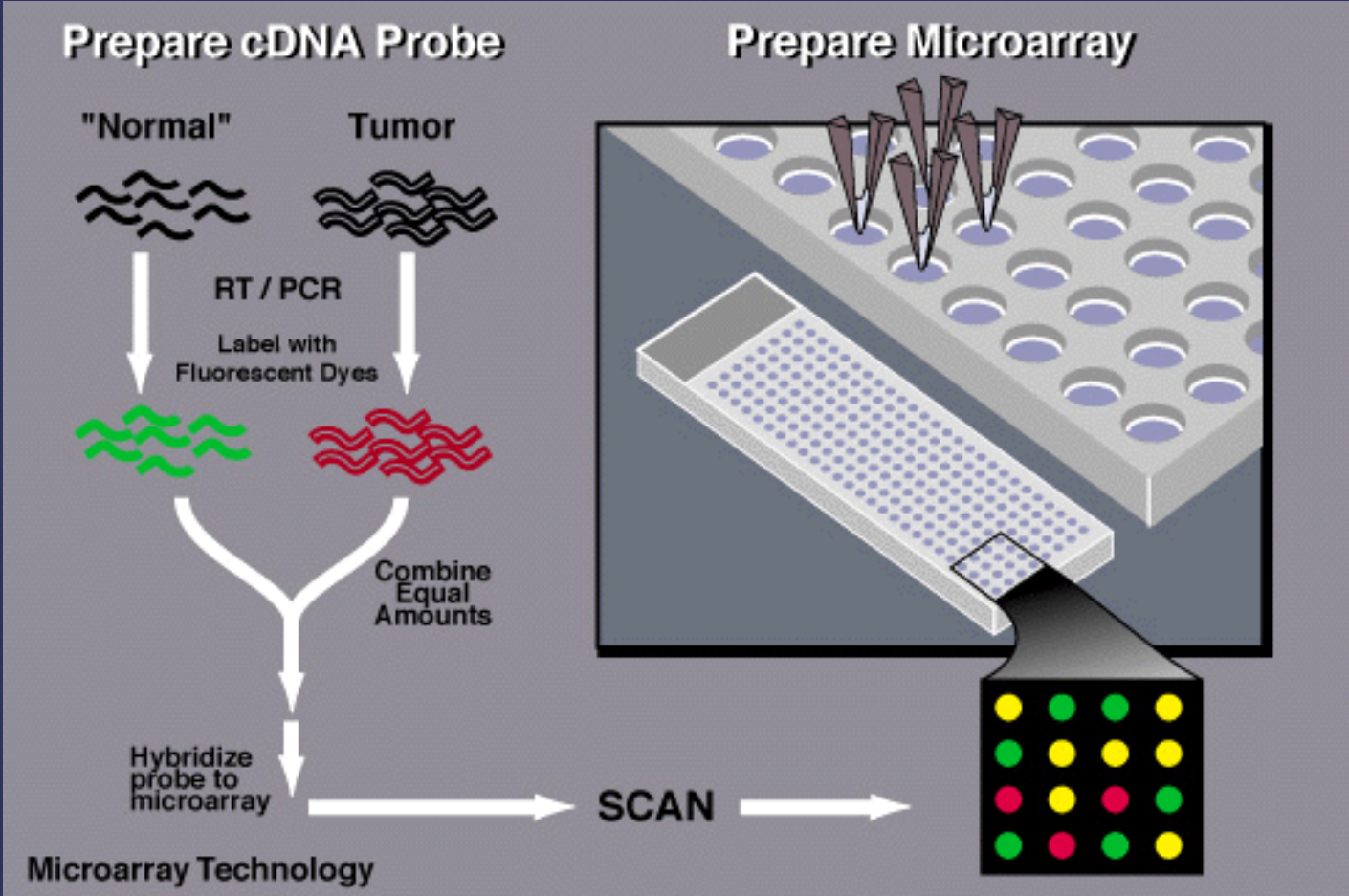


Image Processing

- Gridding – finding the address of each spot in the image
- Segmentation – separating out the spot from its local background
- Quantification – generating a number to indicate the relative brightness of the spot

Preprocessing

- Typically, spot intensities need to be normalized to remove measurement artifacts
- First step (often part of quantization) is to use a foreground/background correction
- Other techniques include quantile normalization and low-end mode matching

Statistics

- Small sample size; huge dimensionality
- Must take into account false positives – a random combination of genes producing an interesting result by accident
- Scatterplot smoothing, regression analysis, t-test

Conclusions

- Microarrays are a fundamental tool for understanding genomes
- Much work is still waiting to be done
- As our understanding improves, so will our use of microarrays