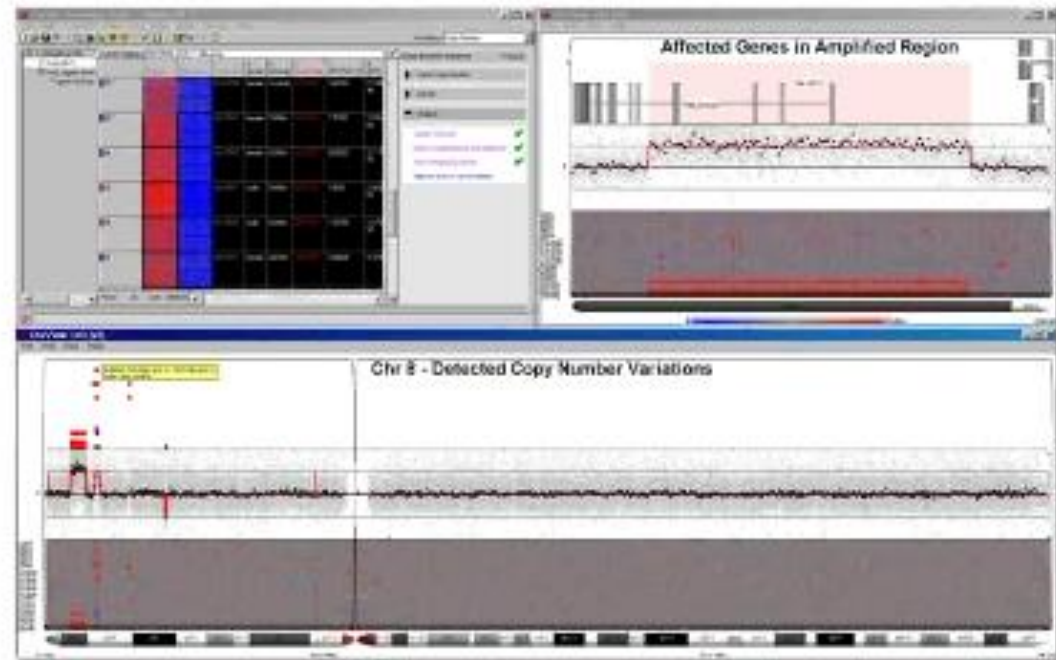


Partek[®] Genomics Suite[™]

Differential Gene Expression & Alternative Splice Detection Using the Affymetrix Exon Array

February 25, 2008
St. Louis, Missouri

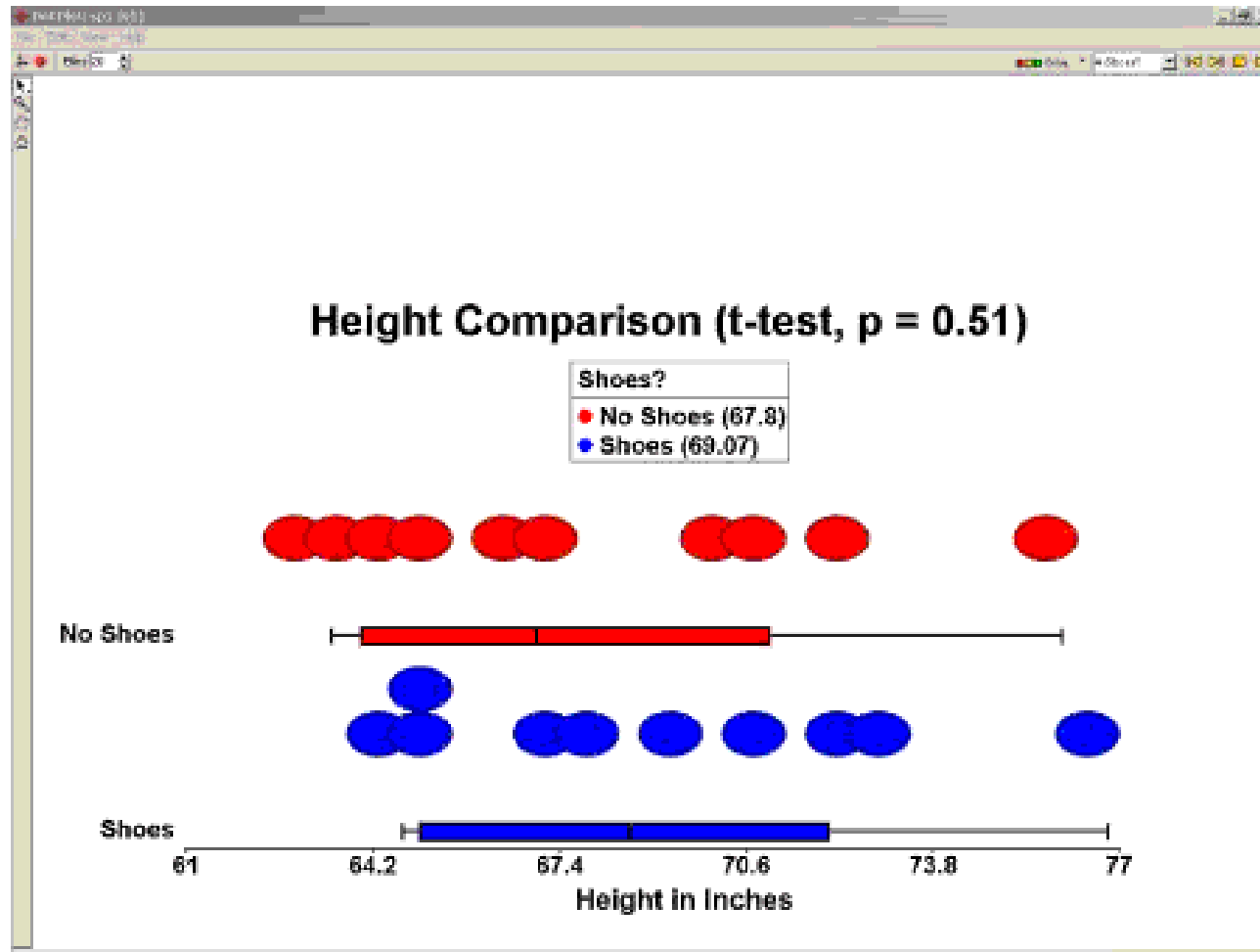
Tom Downey
President, Partek Inc.



The Shoe Experiment

- ❖ Do shoes make a person taller?
 - ❖ P.I. DJ Meyer, Partek Inc.
- ❖ The measurement:
 - ❖ Measure the height 10 people with shoes and 10 people without shoes
 - ❖ Use a “two sample” t-test to see if there is a difference between the the mean of two groups
- ❖ Conclusion
 - ❖ No “statistically significant difference” in height due to wearing shoes.

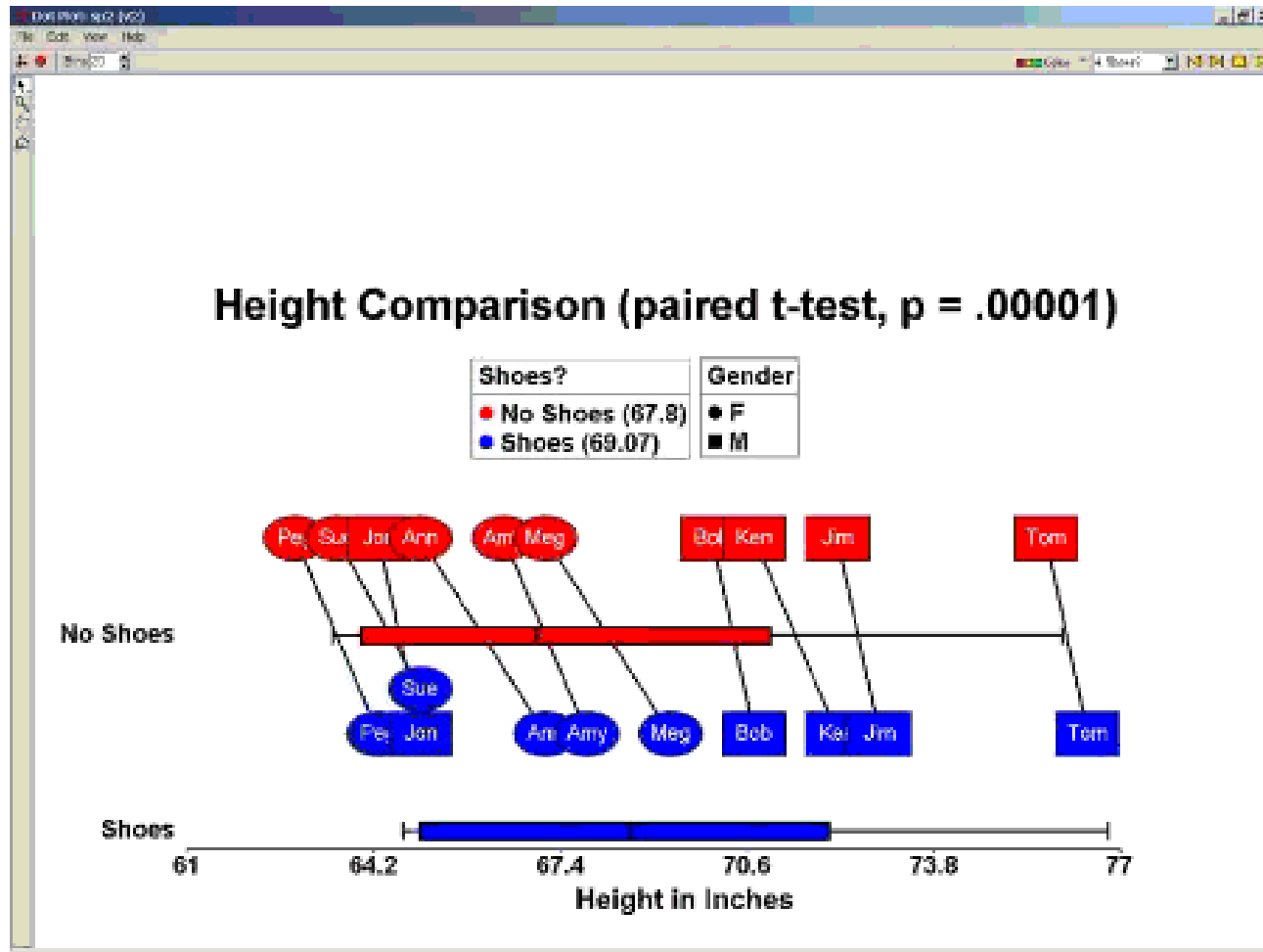
Shoe Experiment: t-Test



A simple t-test does not have the power to correctly identify this pattern without a very large sample size, because it assumes multiple samples from the same individual are independent when they are not.

(Fold-change = 1.02)

Shoe Experiment: Paired t-Test

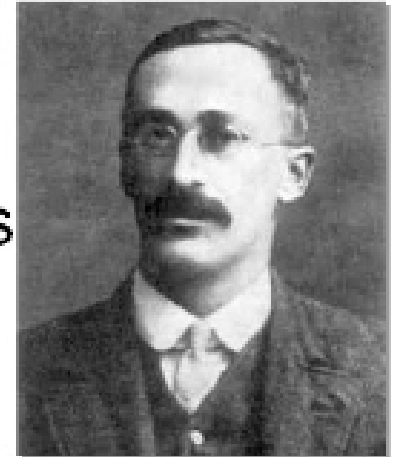


The paired t-test provides substantially more statistical power by removing person-to-person differences from the noise.

T-Test is simple ANOVA

$$y = \mu + S + \varepsilon$$

- ❖ T-test invented in 1908 by “Student” (Gosset)
- ❖ Here is how to write the “linear model”:
 - ❖ y = Gene expression
 - ❖ μ = Mean height
 - ❖ S = Wearing Shoes? (2 levels: “shoes” vs. “no shoes”)
 - ❖ ε = Error (noise)



Paired t-test is a 2-way ANOVA

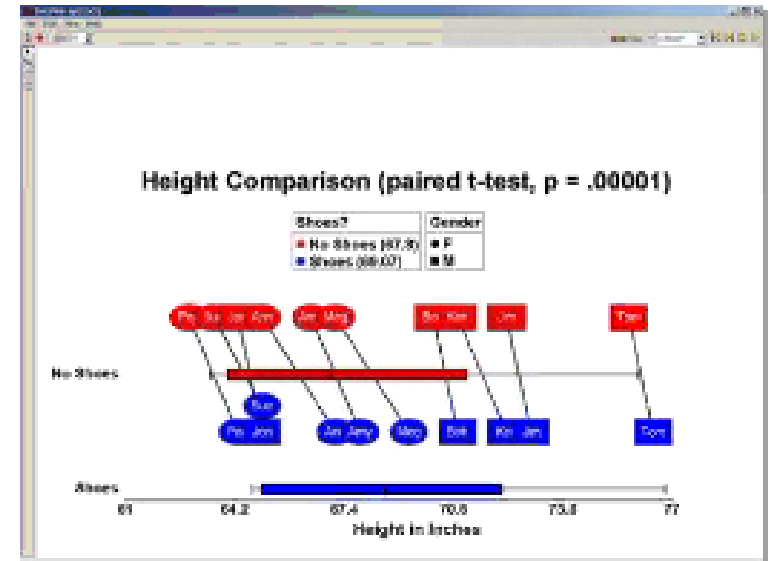
$$y = \mu + S + P + \varepsilon$$

Differential "Height Expression" due to Shoe Effect

❖ The linear model:

- ❖ y = Expression
- ❖ μ = Mean height
- ❖ S = Shoes (2 levels)
- ❖ P = Person (10 levels)
- ❖ ε = Error (noise)

ANOVA invented by Fisher in 1923



Gender Effects?

□ Let's have a little fun and explore the effect of sex ;)

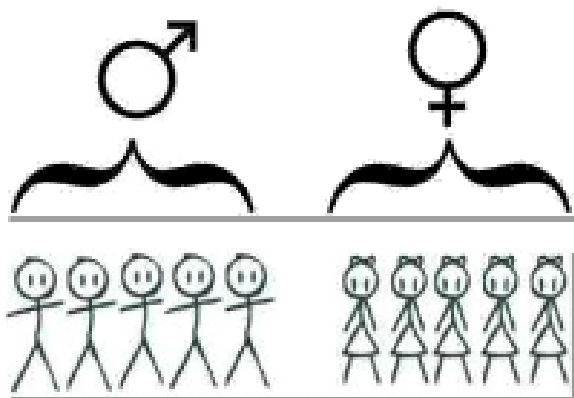
□ 3-way ANOVA

$$y = \mu + S + G + P(G) + \varepsilon$$

□ Once person is known, gender already known

■ Thus the p-value for Tissue Type remains unchanged

■ We get the estimate of gender effect for free!

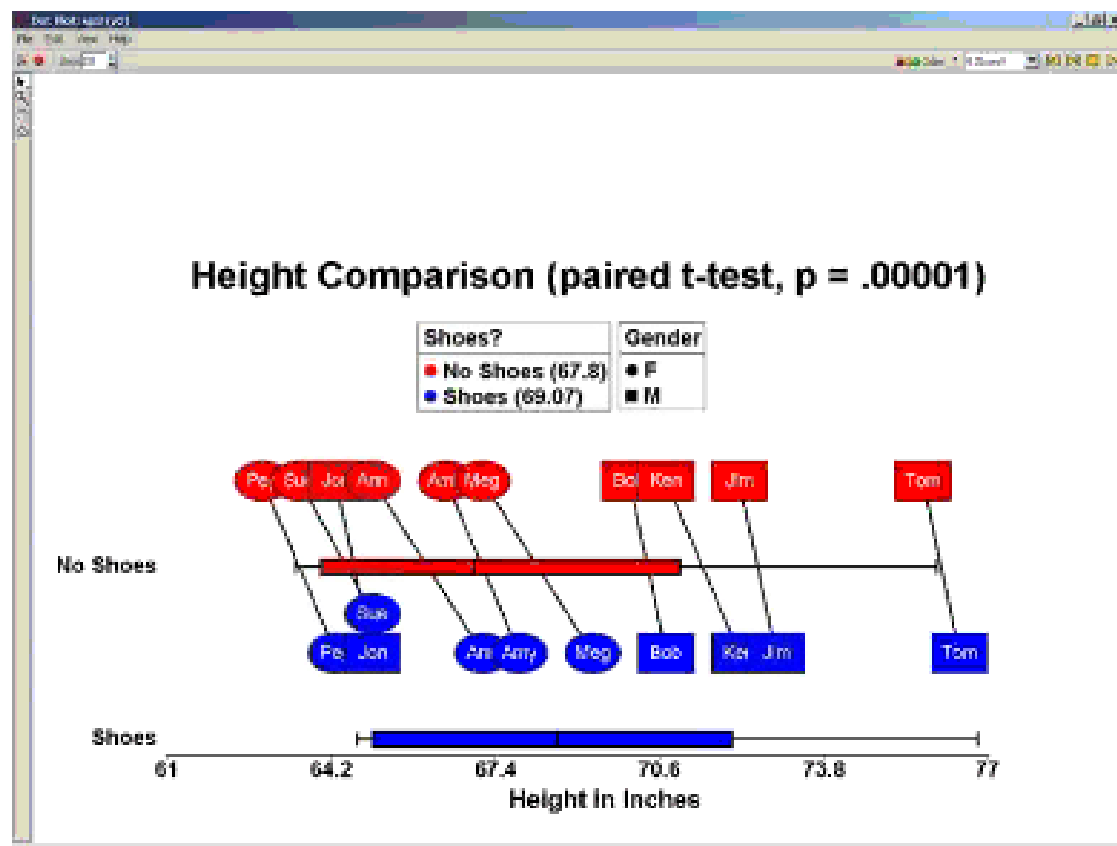


Add Gender (3-way ANOVA)

$$y = \mu + S + G + P(G) + \varepsilon$$

- ❖ $p(\text{Shoes})=1e-5$
- ❖ $p(\text{Gender})=.04$
- ❖ $p(\text{Person})=2e-9$

- ❖ *It appears ($p=.04$) that men (at Partek) are significantly taller than women*



Explore Gender/Shoe Interaction...

- ❖ *Do shoes have the same effect on men & women*

$$y = \mu + S + G + S * G + P(G) + \varepsilon$$

- ❖ $p(\text{Shoes}) = 1e-8$
- ❖ $p(\text{Gender}) = .04$
- ❖ $p(\text{Person}) = 2e-12$
- ❖ $p(\text{Shoe} * \text{Gender}) = 7e-5$

- ❖ *Wow! Shoes affect women's height more than men's!*
- ❖ *Also note that p-values for shoe effect are even smaller because we explained more "noise"*

