## Gene Expression Analysis

#### ▲ Linear regression model: Relating two genes

- Straight line regression model:
  - (dependent variable) response gene y (e.g., ER) (independent variable, explanatory variable) predictor gene x (e.g., ps2)
- Measurement error model: repeat values i = 1,...,n,
  independent expression levels on n tumors

$$y_i = \alpha + \beta x_i + \epsilon_i$$

- $\epsilon_i$ : independent errors (sampling, measurement, lack of fit)
- Model "explains" variability in response y "due to" x
- Bivariate data  $(y_i, x_i)$  BUT focus is asymmetric: explaining y through x
- Non-causal, purely empirical
- Predictive validity: fit model and test in new cases
- Typical assumption: Gaussian (normally) distributed errors  $\epsilon \sim N(0, \sigma^2)$
- Analysis and inference:
  - Estimate parameters  $(\alpha, \beta, \sigma^2)$
  - Assess model fit adequate? good? if inadequate, how?
  - Explore implications:  $\beta, \beta x$
  - Predict new ("future") responses at new  $x_{n+1}, \ldots$

### ♠ Linear regression model: Least squares fitting

• For any chosen  $\alpha, \beta$ ,

$$Q(\alpha,\beta) = \sum_{i=1}^{n} \epsilon_i^2 = \sum_{i=1}^{n} (y_i - \alpha - \beta x_i)^2$$

measures "fit" of chosen line  $\alpha + \beta x$  to response data

- Choose  $\hat{\alpha}, \hat{\beta}$  to minimise  $Q(\alpha, \beta)$
- Least squares estimates (LSE)
- Fitted least squares line:  $\hat{y} = \hat{\alpha} + \hat{\beta}x$

#### ♠ LSE formulæ and interpretation:

- Sample variances and covariances  $s_x, s_y, s_{x,y}$
- •

$$\hat{\beta} = \frac{s_{x,y}}{s_x}, \quad \hat{\alpha} = \bar{y} - \hat{\beta}\bar{x}$$

• Or

$$\hat{\beta} = r_{x,y} \sqrt{\frac{s_y}{s_x}}$$

•  $\hat{\beta}$  is correlation coefficient corrected for relative scales of y: x

- (so units of the "fitted line"  $\hat{\alpha} + \hat{\beta}x$  are on scale of y)

• Same variability:  $s_y = s_x$  implies  $\hat{\beta} = r_{x,y}$ 

# ♠ Significance of fit, residuals, prediction

• See the more general framework of multiple regression models, in Note 3. The model here is a special case.