1. Study design, resources and cost, variability, confounding.

**Case Study 3**

**Experimental Design 1**

This is not a good design. The aim of this study is to identify clinically relevant subgroups of patients (clustering method). Two different dyes, in this case, make it is much more difficult to compare between dye-groups. Also, it is difficult to compare between arrays. This design costs half the number of arrays but has less power. Only unrelated samples on the same array are comparable but has dye bias issue.

**Experimental Design** **2**

This one is an appropriate design and costs 60 arrays. The reference sample on each array can serve as the quality control, and the baseline for normalization. In this way, it is meaningful to carry out comparison and clustering with less confounding and full power.

**Experimental Design 3**

This one is an appropriate design and costs 60 Affymetrix arrays. The Affymetrix array is designed in the way for comparison between samples (normalization). It also comes with corresponding statistical methods.

**Case Study 4**

**Experimental Design 1**

This is not appropriate. The normalization method comes with Affymetrix can not deal with global changes which is expected to see alongside the time course. It may remove all variances come from different time points. Thus, this design can not answer the scientific question.

**Experimental Design 2**

This is an appropriate and robust design. We have a cross-arrays reference sample for quality control and normalization. The intensity ratio on each array is good to compare between arrays.

**Experimental Design 3**

The loop design is also appropriate. What’s more, each sample is tested twice in this design. However, compared with design 2, this one requires more complex data analysis and the loop is more fragile to one bad array occurred amid.