



# Principles in the design of multiphase experiments with a later laboratory phase: orthogonal designs

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# Outline

1. Primary experimental design principles
2. Factor-allocation description for standard designs.
3. Principles for simple multiphase experiments.
4. Principles leading to complications, even with orthogonality.
5. Summary



# 1) Primary experimental design principles

- **Principle 1** (Evaluate designs with skeleton ANOVA tables)
  - Use whether or not data to be analyzed by ANOVA.
- **Principle 2** (Fundamentals): Use randomization, replication and blocking or local control.
- **Principle 3** (Minimize variance): Block entities to form new entities, within new entities being more homogeneous; assign treatments to least variable entity-type.
- **Principle 4** (Split units): confound some treatment sources with more variable sources if some treatment factors:
  - i. require larger units than others,
  - ii. are expected to have a larger effect, or
  - iii. are of less interest than others.

# A standard athlete training example

- 9 training conditions — combinations of 3 surfaces and 3 intensities of training — to be investigated.
- Assume the prime interest is in surface differences
  - intensities are only included to observe the surfaces over a range of intensities.
- Testing is to be conducted over 4 Months:
  - In each month, 3 endurance athletes are to be recruited.
  - Each athlete will undergo 3 tests, separated by 7 days, under 3 different training conditions.
- On completion of each test, the heart rate of the athlete will be measured.
- Randomize 3 intensities to 3 athletes in a month and 3 surfaces to 3 tests in an athlete.
  - A split-unit design, employing Principles 2, 3 and 4(iii).



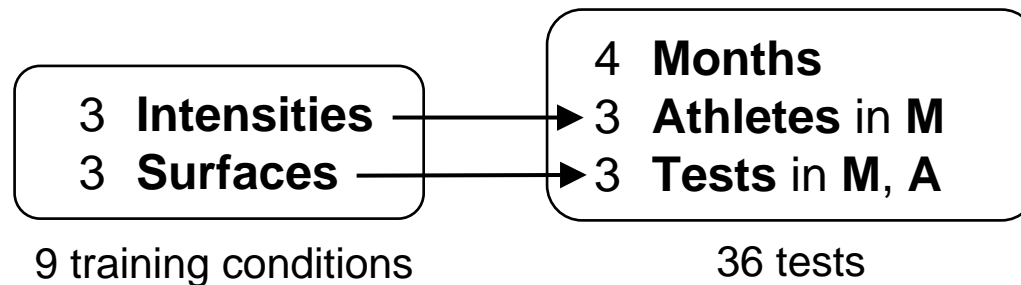
## 2) Factor-allocation description for standard designs

(Nelder, 1965; Brien, 1983; Brien & Bailey, 2006)

- Standard designs involve a single allocation in which a set of treatments is assigned to a set of units:
  - treatments are whatever are allocated;
  - units are what treatments are allocated to;
  - treatments and units each referred to as a set of objects;
- Often do by randomization using a permutation of the units.
  - More generally treatments are allocated to units e.g. using a spatial design or systematically
- Each set of objects is indexed by a set of factors:
  - Unit or unallocated factors (indexing units);
  - Treatment or allocated factors (indexing treatments).
- Represent the allocation using factor-allocation diagrams that have a **panel** for each set of objects with:
  - a list of the factors; their numbers of levels; their nesting relationships.

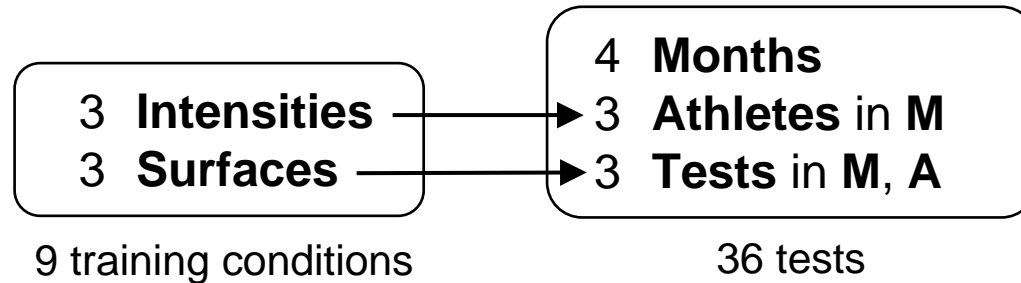
# Factor-allocation diagram for the standard athlete training experiment

- One allocation (randomization):
  - a set of training conditions to a set of tests.



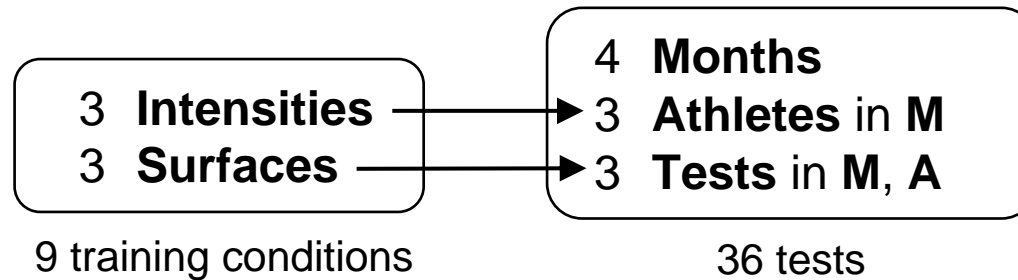
- The set of factors belonging to a set of objects forms a **tier**:
  - they have the same status in the allocation (randomization):
  - {Intensities, Surfaces} or {Months, Athletes, Tests}
  - Textbook experiments are two-tiered.
- A crucial feature is that diagram automatically shows EU and restrictions on randomization/allocation.

# Some derived items



- Sets of generalized factors (terms in the mixed model):
  - Months, Months $\wedge$ Athletes, Months $\wedge$ Athletes $\wedge$ Tests;
  - Intensities, Surfaces, Intensities $\wedge$ Surfaces.
- Corresponding types of entities (groupings of objects):
  - month, athlete, test (last two are Eus);
  - intensity, surface, training condition (intensity-surface combination).
- Corresponding sources (in an ANOVA):
  - Months, Athletes[M], Tests[M $\wedge$ A];
  - Intensities, Surfaces, Intensities#Surfaces.

# Skeleton ANOVA



tests tier		training conditions tier		E[MSq]		
source	df	source	df	$\sigma_{MAT}^2$	$\sigma_{MA}^2$	$\sigma_M^2$
Months	3			1	3	9
Athletes[M]	8	Intensities	2	1	3	$q_I(\mu)$
		Residual	6	1	3	
Tests[M^A]	24	Surfaces	2	1		$q_S(\mu)$
		I#S	4	1		$q_{IS}(\mu)$
		Residual	18	1		

- Intensities is confounded with the more-variable Athletes[M] & Surfaces with Tests[M^A].



### 3) Principles for simple multiphase experiments

- Suppose in the athlete training experiment:
  - in addition to heart rate taken immediately upon completion of a test,
  - the free haemoglobin is to be measured using blood specimens taken from the athletes after each test, and
  - the specimens are transported to the laboratory for analysis.
- The experiment is two phase: testing and laboratory phases.
  - The outcome of the testing phase is heart rate and a blood specimen.
  - The outcome of the laboratory phase is the free haemoglobin.
- How to process the specimens from the first phase in the laboratory phase?

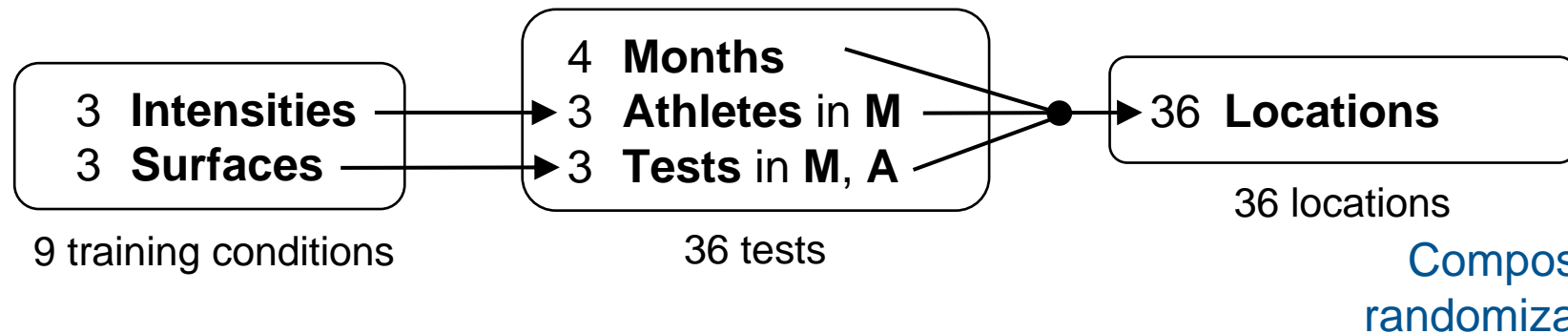


# Some principles

- **Principle 5** (Simplicity desirable): assign first-phase units to laboratory units so that each first-phase source is confounded with a single laboratory source.
  - Use composed randomizations with an orthogonal design.
- **Principle 6** (Preplan all): if possible.
- **Principle 7** (Allocate all and randomize in laboratory): always allocate all treatment and unit factors and randomize first-phase units and lab treatments.
- **Principle 8** (Big with big):
  - Confound big first-phase sources with big laboratory sources, provided no confounding of treatment with first-phase sources.

# A simple two-phase athlete training experiment

- Simplest is to randomize specimens from a test to locations (in time or space) during the laboratory phase.



locations tier		tests tier		training conditions tier		E[MSq]				
source	df	source	df	source	df	$\sigma_L^2$	$\sigma_{MAT}^2$	$\sigma_{MA}^2$	$\sigma_M^2$	
Locations	35	Months	3			1	1	3	9	
		Athletes[M]	8	Intensities	2	1	1	3	$q_I(\mu)$	
				Residual	6	1	1	3		
		Tests[M^A]	24	Surfaces	2	1	1			$q_S(\mu)$
				I#S	4	1	1			$q_{IS}(\mu)$
				Residual	18	1	1			

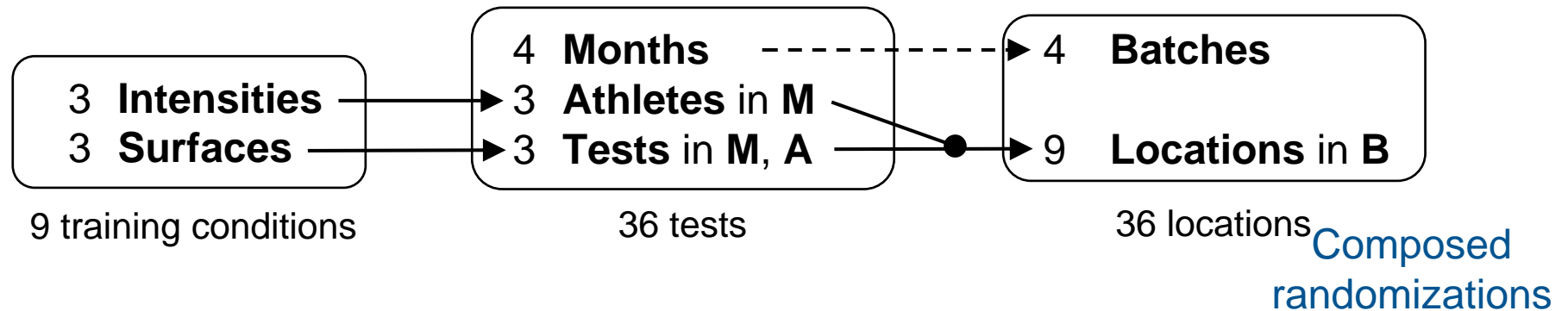
# A simple two-phase athlete training experiment (cont'd)

locations tier		tests tier		training conditions tier		E[MSq]			
source	df	source	df	source	df	$\sigma_L^2$	$\sigma_{MAT}^2$	$\sigma_{MA}^2$	$\sigma_M^2$
Locations	35	Months	3			1	1	3	9
		Athletes[M]	8	Intensities	2	1	1	3	$q_I(\mu)$
				Residual	6	1	1	3	
		Tests[M^A]	24	Surfaces	2	1	1		$q_S(\mu)$
				l#S	4	1	1		$q_{lS}(\mu)$
				Residual	18	1	1		

- No. tests = no. locations = 36 and so tests sources exhaust the locations source.
- Cannot separately estimate locations and tests variability, but can estimate their sum.
- But do not want to hold blood specimens for 4 months.

# A simple two-phase athlete training experiment (cont'd)

- Simplest is to align lab-phase and first-phase blocking.



locations tier		tests tier		training conditions tier		E[MSq]					
source	df	source	df	source	df	$\sigma_{BL}^2$	$\sigma_B^2$	$\sigma_{MAT}^2$	$\sigma_{MA}^2$	$\sigma_M^2$	
<b>Batches</b>	<b>3</b>	Months	3			1	<b>9</b>	1	3	9	
Locations[B]	32	Athletes[M]	8	Intensities	2	1	1	3	$q_I(\mu)$		
				Residual	6	1	1	3			
		Tests[M^A]	24	Surfaces	2	1	1	$q_S(\mu)$			
				I#S	4	1	1	$q_{IS}(\mu)$			
				Residual	18	1	1				

- Note Months confounded with Batches (i.e. Big with Big).

# The multiphase law

- DF for sources from a previous phase can never be increased as a result of the laboratory-phase design.
- However, it is possible that first-phase sources are split into two or more sources, each with fewer degrees of freedom than the original source.

locations tier		tests tier		training conditions tier		E[MSq]					
source	df	source	df	source	df	$\sigma_{BL}^2$	$\sigma_B^2$	$\sigma_{MAT}^2$	$\sigma_{MA}^2$	$\sigma_M^2$	
Batches	3	Months	3			1	9	1	3	9	
Locations[B]	32	Athletes[M]	8	Intensities	2	1		1	3	$q_I(\mu)$	
				Residual	6	1		1	3		
		Tests[M^A]	24	Surfaces	2	1		1			$q_S(\mu)$
				I#S	4	1		1			$q_{IS}(\mu)$
				Residual	18	1		1			

- DF for first phase sources unaffected.



## 4) Principles leading to complications, even with orthogonality

### ■ **Principle 9** (Use pseudofactors):

- An elegant way to split sources (as opposed to introducing grouping factors unconnected to real sources of variability).

### ■ **Principle 10** (Compensating across phases):

- Sometimes, if something is confounded with more variable first-phase source, can confound with less variable lab source.

### ■ **Principle 11** (Laboratory replication):

- Replicate laboratory analysis of first-phase units if lab variability much greater than 1<sup>st</sup>-phase variation;
- Often involves splitting **product** from the first phase into **portions** (e.g. batches of harvested crop, wines, blood specimens into aliquots, drops, lots, samples and fractions).

### ■ **Principle 12** (Laboratory treatments):

- Sometimes treatments are introduced in the laboratory phase and this involves extra randomization.



## 5) Summary

- Have provided 4 standard principles and 8 principles specific to orthogonal, multiphase designs.
- In practice, will be important to have some idea of likely sources of laboratory variation.
- Are laboratory treatments to be incorporated?
- Will laboratory replicates be necessary?



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Web address for link to Multitiered experiments site: <http://chris.brien.name/multitier>