

Constructing experimental designs with the edibble R-package

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Table of Contents

1 Experimental design basics 🗣

2 Current state of experimental design tools 💷 🕨

3 Software design for an everyday user 💷 🕨

4 The grammar of experimental designs with edibble 🔤 🗭 🔶

These slides made using R powered by HTML/CSS/JS can be found at emitanaka.org/slides/stats4bio2021/edibble



Experimental design basics

Experiment

Essential scientific endeavors to collect data to explore, understand or verify phenomena.

Experimental data

The gold standard in data collection.

(provided that experimental design is satisfactory)

Comparative experiments

Collecting data to compare the effects of different conditions under a *controlled environment* with the goal of drawing generalisable conclusions

Designing comparative experiments

"

... to identify data-collection schemes that achieve sensitivity and specificity requirements despite biological and technical variability, while keeping time and resource costs low.

- Krzywinski & Altman (2014)

Planning the controlled environment such that there is a higher confidence that effects can be attributed to selected conditions

Krzywinski, M., Altman, N. Designing comparative experiments. Nat Methods 11, 597–598 (2014). https://doi.org/10.1038/nmeth.2974

Basic terminology in comparative experiments modified versions of Bailey (2008)

A **treatment** (\mathcal{T}) is the entire description of the condition applied to an experimental unit.

Experimental unit (Ω) is the smallest unit that the treatment can be independently applied to.

Observational unit (Ω_o) is the smallest unit in which the response will be measured on.

- Not to be confused with responses *Y*.
- May or may not be the same as experimental unit.

- **Block**, also called **cluster**, is the unit that group some other units (e.g. experimental units) such that the units within the same block (cluster) are more alike (homogeneous).
- A **design** $(D : \Omega \to T)$ is the allotment of treatments to particular set of units.
- A **plan** or **layout** is the design translated into actual units. *Randomisation* is usually involved in the translation process.

Bailey, R. (2008). Design of Comparative Experiments (Cambridge Series in Statistical and Probabilistic Mathematics). Cambridge: Cambridge University Press. doi:10.1017/CB09780511611483

Experimental structures as defined by Bailey (2008)

Unit structure means meaningful ways of dividing up experimental units (Ω) and observational units (Ω_o) .

For example:

- Unstructured
- Blocking

Treatment structure means meaningful ways of dividing up \mathcal{T} .

For example:

1

- **Unstructured**: no grouping within ${\mathcal T}$
- Factorial: all combinations of at least two factors
- Factorial + control

Unreplicated experiments



- Experimental units: 3 cows
- Observational units: 3 cows
- Observation: milk yield
- Treatments: 3 types of supplements
- Allotment: supplements → cows
- Replication: 1 each

Conclusion: See produces most \bigcirc therefore supplement for higher milk yield from cows out of the three supplements tested

How confident will you be of this conclusion?

• No individual experimental units are the same (with some exceptions)

Treatment replications



- Experimental units: 6 cows
- Observational units: 6 cows
- Observation: milk yield
- Treatments: 3 types of supplements
- Allotment: supplements → cows
- Replication: 2 each

Conclusion: spectra produces most $\stackrel{\frown}{\bigcirc}$ on average therefore significant is the most effective supplement for higher milk yield from cows out of the three supplements tested

How confident will you be of this conclusion now?

• Treatment replications here allow us to estimate experimental unit (or error) variation

Plan 1 Treatment allocation for nested unit structure





- Units: 2 pens with 3 cows each
- Observational units: 6 cows
- Treatments: 3 types of supplements
- Allotment: supplements → cows

Are the treatment means of say,
and a comparable?

How would you distribute the

treatments?

Plan **2** Treatment allocation for nested unit structure





- Every treatment appears once in each pen
- This is a better design since each treatment appears in every pen so you can be more confident that the treatment means are not due to the conditions of particular pens

Systematic designs

- Experimental units: 6 cows
- Observational units: 6 cows
- Observation: milk yield
- Treatments: 3 types of supplements
- Allotment: supplements → cows
- Replication: 2 each
- Assignment: systematic order

• What could go wrong with this?

- The order of the experimental units may be **confounded** with some extraneous factor
- Like say, the order of the experimental units was determined by the speed (fast to slow) of the cow to get to the feed
- This means that the more active cows are given and leasat active ones are given

Randomised designs

- Experimental units: 6 cows
- Observational units: 6 cows
- Observation: milk yield
- Treatments: 3 types of supplements
- Allotment: supplements → cows
- Replication: 2 each
- Assignment: random order

- Randomisation protects you against bias and potential unwanted confounding with extraneous factors
- Bias comes in many forms: obvious to not-so obvious, known to unknown, and so on.
- Randomisation doesn't mean it'll completely shield you from all biases!
- You can get a systematic order by chance! This doesn't mean you should keep on randomising your design until get the layout you want! You should instead add another unit structure before randomisation.

Factorial treatment structure 1



- Experimental units: 12 plots
- Observational units: 12 plots
- Observation: wheat yield
- Treatments: combination of:
 - Water: irrigated or rain-fed
 - Fertilizer: type A or type B
- Allotment:
 - Water \rightarrow plots
 - Fertilizer → plots
- Assignment: random order

How many treatments are there?



Factorial treatment structure 2



- Experimental units: 12 plots
- Observational units: 12 plots
- Observation: wheat yield
- Treatments: combination of:
 - Water: irrigated or rain-fed
 - Fertilizer: type A or type B
- Allotment:
 - Water and fertilizer → plots
- Assignment: random order



Factorial treatment structure, nested unit structure, and treatment constraint













- Units: 6 strips with 2 plots each
- Observational units: 12 plots
- **Observation**: wheat yield
- Treatments: combination of:
 - Water: irrigated or rain-fed
 - Fertilizer: type A or type B
- Allotment:
 - Water → strip
 - Fertilizer → plot
- Assignment: random order

Some classical "named" experimental designs

- A Completely Randomised Design
- **B** Randomised Complete Block Design
- **C** Factorial Design
- **D** Split-Plot Design

A Completely Randomised Design (CRD)



- Experimental units: 6 cows
- Observational units: 6 cows
- Observation: milk yield
- **Treatments**: 3 types of supplements
- Allotment: supplements → cows
- Replication: 2 each
- Assignment: random order

B Randomised Complete Block Design (RCBD)





- Units: 2 pens with 3 cows each
- Observational units: 6 cows
- **Treatments**: 3 types of supplements
- Allotment: supplements → cows, with restriction such that each treatment appears once in each pen
- Assignment: random order

C Factorial Design



- Experimental units: 12 plots
- Observational units: 12 plots
- **Observation**: wheat yield
- Treatments: combination of:
 - Water: irrigated or rain-fed
 - Fertilizer: type A or type B
- Allotment:
 - Water and fertilizer → plots
- Assignment: random order

D Split-Plot Design













- Units: 6 strips with 2 plots each
- Observational units: 12 plots
- Observation: wheat yield
- Treatments: combination of:
 - Water: irrigated or rain-fed
 - Fertilizer: type A or type B
- Allotment:
 - Water → strip
 - Fertilizer → plot
- Assignment: random order



Current state of experimental design tools

CRAN Task View of Design of Experiments

& Analysis of Experimental Data

contains



based on the ctv package version 0.8.5

In contrast, only a handful of libraries exist in Python (namely pyDOE, pyDOE2, dexpy, experimenter and GPdoemd).

Design of experiments area appear to have the least collaboration



Thanks to Dewi Lestari Amaliah for the graph!

Authors tend to work in silos → limited knowledge sharing across silos perhaps

Topic 🔶	# of packages	% of packages connected within topic	Averag # c author
Analysis of Pharmacokinetic Data	18	16.67	
Hydrological Data and Modeling	96	21.88	~
Design of Experiments (DoE) & Analysis of Experimental	109	24.77	26/76

Top downloaded R-packages in the design of experiments



agricolae is one of the top downloaded

(total download based on logs from the RStudio CRAN mirror scrubbed by Danyang Dai)

agricolae

a case of classical named randomised designs

A agricolae::design.crd

Completely randomised design for t = 3 treatments with 2 replicates each

```
trt <- c("A", "B", "C")</pre>
agricolae::design.crd(trt = trt, r = 2)
## $parameters
## $parameters$design
## [1] "crd"
##
## $parameters$trt
## [1] "A" "B" "C"
##
## $parameters$r
## [1] 2 2 2
##
```



B agricolae::design.rcbd

Randomised complete block design for t = 3 treatments with 2 blocks

```
trt <- c("A", "B", "C")
agricolae::design.rcbd(trt = trt, r = 2)</pre>
```

```
## $parameters
## $parameters$design
## [1] "rcbd"
##
## $parameters$trt
## [1] "A" "B" "C"
##
## $parameters$r
## [1] 2
##
```



C agricolae::design.ab()

Factorial design for $t = 3 \times 2$ treatments with 2 replication for each treatment

```
agricolae::design.ab(trt = c(3, 2), r = 2, design = "crd")
```

```
## $parameters
## $parameters$design
## [1] "factorial"
##
## $parameters$trt
## [1] "1 1" "1 2" "2 1" "2 2" "3 1" "3 2"
##
## $parameters$r
## [1] 2 2 2 2 2 2
##
```

Note *not* A/B testing!



D agricolae::design.split()

Split-plot design for $t = 2 \times 4$ treatments with 2 replication for each treatment

```
trt1 <- c("I", "R"); trt2 <- LETTERS[1:4]
agricolae::design.split(trt1 = trt1, trt2 = trt2, r = 2, design = "crd")</pre>
```

```
## $parameters
## $parameters$design
## [1] "split"
##
## $parameters[[2]]
## [1] TRUE
##
## $parameters$trt1
```



Good design considers units and treatments first, and then allocates treatments to units. It does not choose from a menu of named designs.

–Rosemary Bailey (2008)

AlgDesign

a case of optimised (model-based) designs

AlgDesign::gen.factorial()

• First, a helper function to create the treatment (and replicate) combinations:

dat

##		irrigation	fertilizer	variety
##	1	1	1	1
##	2	2	1	1
##	3	3	1	1
##	4	1	2	1
##	5	2	2	1
##	6	2	0	1

AlgDesign::optFederov

• Optimum design with 14 trials using Federov's exchange algorithm

```
## [1] 0.2343815
##
## $A
## [1] 6.25
##
```

CCa
AlgDesign::optBlock()

• An optimal design with 3 blocks of size 9.

```
AlgDesign::optBlock(frml = \sim ., # assume additive effects
                    withinData = dat,
                     blocksizes = rep(9, 3),
                    criterion = "D")
## $D
## [1] 0.1924501
##
## $diagonality
## [1] 0.866
##
## CDlooka
```

What were the experiments about? Context is key in experimental design

Units and allocation are often *implicitly* understood



Software design for an everyday user

Benefits of programming

- Computational reproducibility
- 2 Allows greater flexibility



3 Can promote higher order thinking if the software is designed with the user in mind

Software design for users

- A user interacts with the **software** interface
- The interface design can make a huge difference to an everyday user

Orawing faces 1 Specific instructions for the computer

Drawing a happy face

```
library(grid)
# face shape
grid.circle(x = 0.5, y = 0.5, r = 0.5)
# eyes
grid.circle(x = c(0.35, 0.65)),
            y = c(0.6, 0.6),
            r = 0.05,
            gp = gpar(fill = "black"))
# mouth
grid.curve(x1 = 0.4, y1 = 0.4,
           x2 = 0.6, y2 = 0.4,
           square = FALSE)
```



Brawing faces 1 Specific instructions for the computer

Drawing a sad face

```
library(grid)
# face shape
grid.circle(x = 0.5, y = 0.5, r = 0.5)
# eyes
grid.circle(x = c(0.35, 0.65)),
            y = c(0.6, 0.6),
            r = 0.05,
            gp = gpar(fill = "black"))
# mouth
grid.curve(x1 = 0.4, y1 = 0.4,
           x^2 = 0.6, y^2 = 0.4,
           square = FALSE,
           curvature = -1)
```



Orawing faces 2 Functional instructions for the computer

Use functions to draw faces

```
face1 <- function() {</pre>
  grid::grid.circle(x = 0.5, y = 0.5, r = 0.5)
  qrid::grid.circle(x = c(0.35, 0.65),
                    y = c(0.6, 0.6),
                    r = 0.05.
                    gp = gpar(fill = "black"))
  grid::grid.curve(x1 = 0.4, y1 = 0.4,
                   x^2 = 0.6, y^2 = 0.4,
                   square = FALSE)
face2 <- function() {</pre>
  grid::grid.circle(x = 0.5, y = 0.5, r = 0.5)
  grid::grid.circle(x = c(0.35, 0.65),
                    y = c(0.6, 0.6),
                    r = 0.05.
                     gp = gpar(fill = "black"))
  grid::grid.curve(x1 = 0.4, y1 = 0.4,
                   x^2 = 0.6, y^2 = 0.4,
                   square = FALSE,
```

curvature = -1)



Urawing faces Human-centered design

Adapt computational systems for human use with syntactic sugar



• Now what do you expect for the output?

- Functions are named after emotions
- Emotion is a surrogate for describing the entire face

What if you want to draw a face that is winking? ③ ... with a grin? ④

... or with the tongue out? 💬

The differences between facial features are small, but you need an **entire new function** that contains instructions for the *whole* face and a **new function name**.

• How would you design the system to draw faces?

Orawing faces 4 Rethinking function arguments as facial parts

Let's reframe how we think

Orawing faces 4 Rethinking function arguments as facial parts

Let's reframe how we think

https://github.com/emitanaka/portrait

library(portrait)

- Let's *reframe* how we think
- A face is made up of:
 - eyes
 - mouth
 - shape

③ Drawing faces **④** Rethinking function arguments as facial parts

Let's reframe how we think

https://github.com/emitanaka/portrait

library(portrait)

- Let's *reframe* how we think
- A face is made up of:
 - eyes
 - mouth
 - shape

face(eyes = "googly", mouth = "smile", shape = "round") face(eyes = "round", mouth = "sad", shape = "oval")





- We can easily make large number of faces with a single function
- It makes users think about faces based on facial features
- But what about hair, nose and other facial features?

Crawing faces 4 Rethinking function arguments as facial parts

Let's reframe how we think

- A face is made up of:
 - eyes
 - mouth
 - shape
 - hair 🖜
 - nose 🖜

•	Adding	more	arguments:
---	--------	------	------------

face(eyes = "googly", mouth = "smile", shape = "round", hair = "none", nose = "simple") face(eyes = "googly", mouth = "smile", shape = "round", hair = "mohawk", nose = "simple")





But about other facial features?

Rethink everything as an object

Rethink everything as an object

library(portrait)
face()



Rethink everything as an object

library(portrait)
face() +
 cat_shape()



Rethink everything as an object

```
library(portrait)
face() +
  cat_shape() +
  cat_eyes()
```



Rethink everything as an object

library(portrait)
face() +
 cat_shape() +
 cat_eyes() +
 cat_nose()



Rethink everything as an object

library(portrait)
face() +
 cat_shape() +
 cat_eyes() +
 cat_nose() +
 cat_whiskers()



Rethink everything as an object

```
library(portrait)
face() +
    dog_shape() +
    cat_eyes(fill = "red") +
    cat_nose() +
    cat_whiskers()
```



Rethink everything as an object



Software design for everyday users

- 1 Imperative instructions for the computer \rightarrow more work for humans
- 2 Recipe functions \rightarrow One function to draw one complete face
- 3 Syntactic syntax → Make it easier for humans to read code
- A function with multiple arguments →
 One function to draw multiple complete faces
- 5 Finite number of functions to draw *infinite* possible *incomplete* and complete faces

The tool **you choose** to use can **enforce a certain way of thinking** and may restrict you on what you can do. 59/76



library(edibble)
start_design("My experiment")

My experiment

library(edibble)
start_design("My experiment") %>%
 set_units(wholeplot = 4)

My experiment └─wholeplot (4 levels)

library(edibble)
start_design("My experiment") %>%
 set_units(wholeplot = 4) %>%
 set_units(subplot = nested_in(wholeplot, 2))

My experiment └wholeplot (4 levels) └subplot (8 levels)

library(edibble)
start_design("My experiment") %>%
 set_units(wholeplot = 4,
 subplot = nested_in(wholeplot, 2))

My experiment └wholeplot (4 levels) └subplot (8 levels)

```
library(edibble)
start_design("My experiment") %>%
  set_units(wholeplot = 4,
        subplot = nested_in(wholeplot, 2)) %>%
  set_trts(water = c("irrigated", "rainfed"),
        fertilizer = c("A", "B"))
```

My experiment -wholeplot (4 levels) -subplot (8 levels) -water (2 levels) -fertilizer (2 levels)

```
library(edibble)
start_design("My experiment") %>%
  set_trts(water = c("irrigated", "rainfed"),
        fertilizer = c("A", "B")) %>%
   set_units(wholeplot = 4,
        subplot = nested_in(wholeplot, 2))
```

My experiment water (2 levels) fertilizer (2 levels) wholeplot (4 levels) Subplot (8 levels)

library(edibble)
start_design("My experiment") %>%
 set_trts(water = c("irrigated", "rainfed")) %>%
 set_units(wholeplot = 4) %>%
 set_trts(fertilizer = c("A", "B")) %>%
 set_units(subplot = nested_in(wholeplot, 2))

My experiment -water (2 levels) -wholeplot (4 levels) -subplot (8 levels) -fertilizer (2 levels)

My experiment wholeplot (4 levels) Subplot (8 levels) water (2 levels) fertilizer (2 levels) Allotment:

- water ~ wholeplot
- fertilizer ~ subplot

My experiment wholeplot (4 levels) Subplot (8 levels) water (2 levels) fertilizer (2 levels) Allotment: • water ~ wholeplot

• fertilizer ~ subplot Assignment: random

#	An edibble:	8 x 4		
	wholeplot	subplot	water	fertilizer
	<unit(4)></unit(4)>	<unit(8)></unit(8)>	<trt(2)></trt(2)>	<trt(2)></trt(2)>
1	wholeplot1	subplot1	irrigated	А
2	wholeplot1	subplot2	irrigated	В
3	wholeplot2	subplot3	irrigated	А
4	wholeplot2	subplot4	irrigated	В
5	wholeplot3	subplot5	rainfed	В
6	wholeplot3	subplot6	rainfed	А
7	wholeplot4	subplot7	rainfed	В
8	wholeplot4	subplot8	rainfed	A

#	An edibble	e: 8 x 4		
	block	subplot	water	fertilizer
	<unit(2)></unit(2)>	<unit(8)></unit(8)>	<trt(2)></trt(2)>	<trt(2)></trt(2)>
1	block1	subplot1	irrigated	А
2	block1	subplot2	irrigated	В
3	block1	subplot3	rainfed	В
4	block1	subplot4	rainfed	А
5	block2	subplot5	rainfed	А
6	block2	subplot6	irrigated	В
7	block2	subplot7	rainfed	В
8	block2	subplot8	irrigated	А

 The resulting design is what we call "randomised complete block design"

```
library(edibble)
start_design("Modified design") %>%
  set_units(block = 2,
            subplot = nested_in(block, 4)) %>%
 set_trts(water = c("irrigated", "rainfed"),
           fertilizer = c("A", "B")) %>%
 allot_trts(water:fertilizer ~ subplot) %>%
 assign_trts("random", seed = 1) %>%
  set_rcrds_of(subplot = c("yield", "disease"),
               block = "manager") %>%
 serve_table()
```

 The functions are reminiscent of the fundamental experimental terminology

An edibble: 8 x 7 block subplot water fertilizer yield disease manager <unit(2)> <unit(8)> <trt(2)> <trt(2)> <rcrd> <rcrd> <rcrd> 1 block1 subplot1 irrigated A 2 block1 subplot2 irrigated B 3 block1 subplot3 rainfed B 4 block1 subplot4 rainfed A 5 block2 subplot5 rainfed A 6 block2 subplot6 irrigated B 7 block2 subplot8 irrigated A 8 block3 subplot8 irrigated A 8 block4 subplot8 irrigated A
The grammar of experimental design with edibble

```
out <- start_design("Modified design") %>%
set_units(block = 2,
           subplot = nested_in(block, 4)) %>%
set_trts(water = c("irrigated", "rainfed"),
          fertilizer = c("A", "B")) %>%
allot_trts(water:fertilizer ~ subplot) %>%
 assign_trts("random", seed = 1) %>%
 set_rcrds_of(subplot = c("yield", "disease"),
              block = "manager") %>%
expect_rcrds(yield = to_be_numeric(with_value(">=", 0)),
              disease = to_be_factor(levels = c("none", "moderate", "severe"))
serve_table()
```

export_design(out, file = "design-layout.xlsx", overwrite = TRUE)

• The exported file has data validation features embedded

There are more (not-well documented) features in edibble More on those on Thursday!

- Our understanding of experimental design is growing and so the tool should evolve with better understanding
- The idea for edibble was conceived early 2019, the code base was released publicly on 31st Dec 2020.
- Since its initial public realease, underlying structure in edibble has evolved drastically for the better
- The development of a good tool is a community effort so...

Get in touch!

- The purpose of edibble is to help you plan experiments better
- edibble gets better with feedback
 - Slides: emitanaka.org/slides/stats4bio2021/edibble
 - **R** Package documentation: edibble.emitanaka.org
 - Source code: github.com/emitanaka/edibble
 - emi.tanaka@monash.edu 🕑 @statsgen
- Feature requests or issues with edibble? Submit or upvote here: github.com/emitanaka/edibble/issues, send me an email or tell me now!