

Amsterdam Public Health



**Ecological Momentary Assessment
In Mental Health Research:**

**A practical introduction,
with examples in R**

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A Practical Introduction, With Examples in R

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Preface

Given known limitations of retrospective self-report questionnaires, such as recall bias and poor generalisability of assessment results to real-life situations, mental health researchers increasingly adopt alternative assessment methods. One of the promising alternatives is Ecological Momentary Assessment (EMA), in which emotions and behaviours are repeatedly sampled in everyday life, through wearable electronic devices.

Conducting an EMA study can be a challenge. Researchers, who are new to the field, face a dazzling array of options related to the electronic wearables, outcomes selection, study design considerations, ethical and regulatory constraints, data management, statistical analysis, and study reporting. Although standards are emerging, clear guidelines for EMA research do not - at present - exist.

This research manual provides a practical introduction to EMA-research. It was written for the Amsterdam School of Public Health (APH), to aid beginning researchers looking for practical advice in conducting EMA studies. It provides an overview of EMA instruments, outcomes, methods and analytical techniques, guidelines for EMA-studies, and a catalogue of EMA research in the APH consortium.

The manual comprises six parts:

- Part I introduces EMA and R. Chapter 1 defines EMA, and discusses the opportunities and some of the challenges of EMA research. Chapter 2 introduces R, which, as this manual aims to show, is an indispensable tool for the EMA researcher.
- Part II focuses on EMA study design (chapter 3), EMA instruments (chapter 4) and EMA data management (Chapter 5).
- Part III introduces EMA data analysis techniques: Feature Extraction (chapter 6), Mixed Modelling (chapter 7), and Network Analysis (chapter 8).
- Part IV details the momentary assessment of key mental health variables: Mood (chapter 9) and Activity (chapter 10).
- In part V, the application of the preceding material is illustrated in three case studies: The critical Slowing Down study (CSD; chapter 11), an EMA pilot study of suicidal ideation (the CASPAR study; chapter 12), and a study into a new GPS-based measure of activity (the Home Range Estimation-study; chapter 13).
- Part VI provides three catalogues of EMA resources. Chapter 14 lists EMA research groups, chapter 15 lists EMA instruments, and chapter 16 summarises R extensions (packages) that are useful in EMA data analysis.

The manual was written in Bookdown (Xie, 2016, 2018). Sources are freely available at ‘github’, via https://github.com/jruwaard/aph_ema_handbook. Please post your comments and suggestions there, or via e-mail, through aph.ema@gzingeest.nl.

Part I

Introduction

Chapter 1

What is EMA?

Ecological Momentary Assessment (EMA) has many aliases. It is known as ‘experience sampling’ (Larson and Csikszentmihalyi, 1983), ‘ambulatory assessment’ (Ebner-Priemer and Trull, 2009) or ‘Ambulatory self-reporting’ (Conner and Barrett, 2012), ‘real-time data capturing’, the ‘continuous unified electronic diary method’ (Ellis-Davies et al., 2012), and as the ‘intensive-longitudinal study design’ (Bolger and Laurenceau, 2013). The different terms stress different aspects of EMA research. All terms, however, refer to research methods that involve the repeated sampling of people’s current thoughts, emotions, behaviour, physiological states, and context, in their natural environment, typically (but not necessary) via electronic wearable devices (Shiffman et al., 2008).

EMA has been around for many years. Already in the 1980’s, early pioneers used electronic devices to elicit responses from study participants to tap into (mental) health processes in everyday life (see, e.g., Csikszentmihalyi and Larson, 2014). Recent years, however, have witnessed a large increase in EMA research. Rapid technological developments, a marked interest in the individual, and a wide recognition of the need to study health-related processes in real-life situations have all contributed to this.

With the increased adoption of EMA comes a growing need for methodological guidelines. EMA studies have unique characteristics that require specialised research skills, related to study design and statistical analysis. In many cases, these skills are not part of the standard curriculum of academic departments. This book was written to fill this gap.

1.0.1 Self-report versus Observational EMA

In EMA research, there are two forms of data collection: EMA based on self-report (active) and EMA based on observational (passive) data. Self-report requires participants to provide information, for example by rating their current mood, activities or social interaction on items that are presented to them during EMA. For observational EMA, information is collected through wearables or logfiles without active involvement of participants, for example on heart-rate, activity, smartphone use or engagement on social media. Some studies combine both forms of data collection, for example by using both a self-report sleep diary and an accelerometer in order to study sleeping patterns (Van Der Meijden et al., 2016).

1.0.1.1 Self-report EMA

1.0.1.2 Observational EMA

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1.0.2 Time-contingent and signal-contingent sampling

EMA sampling may focus on a single time-point (signal-contingent sampling), an event (event-contingent sampling), or a combination of both (Conner and Lehman, 2012).

In *signal-contingent sampling*, participants respond to questions when they are prompted to do so by a signal. Signal-contingent sampling can follow a fixed or a random scheme. In a fixed scheme, participants are prompted at fixed time-points, for example at 9:30, 12:30, and 16:30. In a random scheme, prompts are sent at random time points, typically in pre-set intervals, for example, participants could be prompted to complete two assessments per day, one at a random time point between 10:00 and 14:00, and one at a random time point between 14:00 and 16:00. Using pre-set intervals ensures that participants do not receive several prompts within a limited time-frame (Piasecki et al., 2007). In addition, it ensures that participants are not bothered by prompts at inappropriate times (e.g., most participants do not appreciate prompts after 22:00 and before 7:30).

In *event-contingent sampling*, study participants complete an assessment whenever a specific event occurs, such as a panic attack or alcohol consumption. One option is to simply instruct the participants to do so. In that case, it is important to be clear, in the instructions, to provide a clear definition of the target event, and to stress the importance to rate each event. In some cases, it may be possible to trigger event-based prompts automatically, for example by linking a self-report EMA questionnaire to an automatically detected change in activity level (Smyth and Stone, 2003).

1.1 Why EMA?

EMA aims to “minimize recall bias, maximize ecological validity, and allow study of microprocesses that influence behavior in real-world contexts.” (Shiffman et al., 2008). Recall bias refers to the concern that with retrospective self-report information, participants’ current state might affect the way they remember past events or emotions (Shiffman et al., 2008; Moore et al., 2016). The idea of EMA is evaluate participants’ *current state*, rather than reflect on past experiences. By making sure participants are measured in their own environment (daily life), rather than in a research specific context, such as a lab or mental healthcare centre, EMA is thought to provide *ecological valid* information that is not distorted by context.

1.1.1 Focus on the Individual

Finally, EMA offers a unique opportunity to study change in individuals with repeated sampling. By doing this, EMA offers a quantitative method for idiographic research (Allport, 1937), measuring characteristics of individuals across time and context (within-subject change) (Shiffman et al., 2008). This contrasts with more classic, nomothetic research, in which individuals are grouped together in order to study universal characteristics.

[Nomothetic vs Ideographic research] Donec sed lectus at sem ultrices commodo. Proin a viverra metus, nec scelerisque odio. Morbi viverra tristique libero vel fringilla. Sed at varius erat, id consequat nibh. Ut eget leo blandit orci posuere tincidunt ac sed erat. Aenean metus metus, eleifend ut facilisis a, fringilla ut neque.

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??? Fermi–Pasta–Ulam–Tsingou problem ???

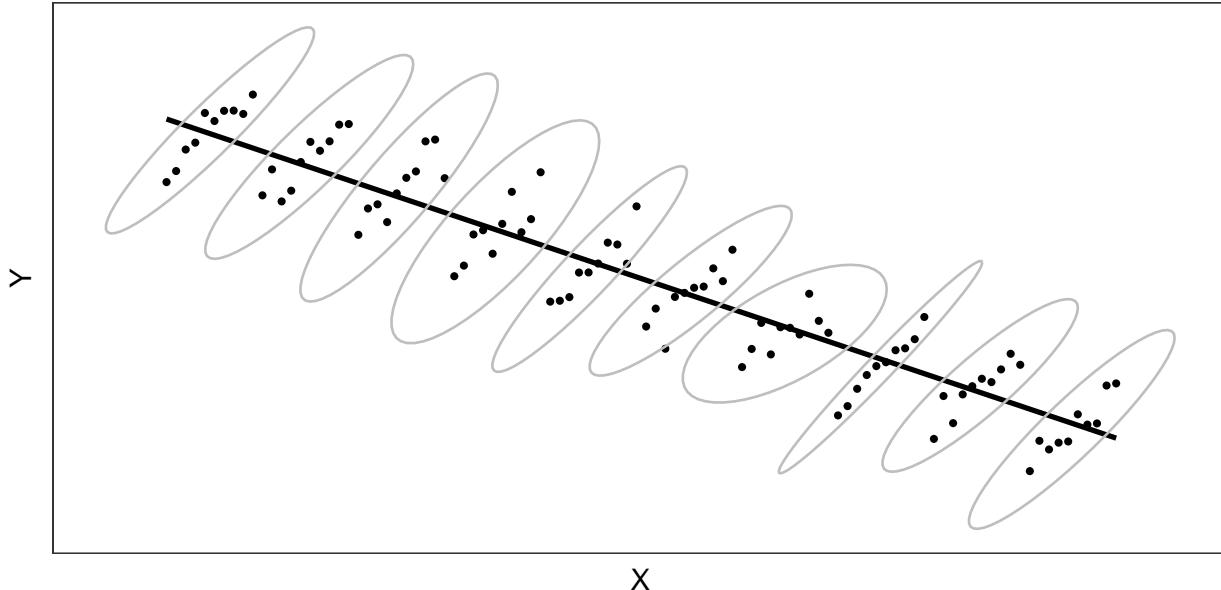


Figure 1.1: An extreme case of how individual effects may be different from group effects: the effect of x on y is positive for individuals (marked by ellipses), but negative for the group (as illustrated by the negative regression line).

1.1.2 Focus on mental health dynamics

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[State versus trait] Donec sed lectus at sem ultrices commodo. Proin a viverra metus, nec scelerisque odio. Morbi viverra tristique libero vel fringilla. Sed at varius erat, id consequat nibh. Ut eget leo blandit orci posuere tincidunt ac sed erat. Aenean metus metus, eleifend ut facilisis a, fringilla ut neque. Nunc hendrerit cursus eleifend.

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1.1.3 Focus on Real Life

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1.1.4 Focus on the Context

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1.2 Clinical Applications

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1.3 Further Reading

Table 1.1: Reviews of EMA studies targeting specific Mental Health Conditions

Disorder	Reference to Review
Anxiety	Walz et al. (2014)
Depression / Mood disorders	aan het Rot et al. (2012), Ebner-Priemer et al. (2009), Telford et al. (2012), Wenzel and Miller (2010), Wichers et al. (2011)
Eating disorders	Engel et al. (2016), Haedt-Matt and Keel (2011)
Psychosis	Oorschot et al. (2012)
Substance abuse	Shiffman (2009)
Well-being	Cornet and Holden (2018)

Chapter 2

R & RStudio

In this chapter, you will learn how to install and use two programs that are indispensable for the management and analysis of EMA data: R and RStudio.

2.1 What are R and RStudio?

R is a programming language and software environment for statistical computing and data visualisation. RStudio is a powerful user interface to R. It has many useful features that greatly simplify R-work. We strongly advise you to adopt the R/RStudio-combo.

2.2 Why R?

R, some may have told you, is for data scientists, methodologists, and scientific programmers only. It has a steep learning curve. If you are trained in SPSS, it will take time to become as productive in R as in SPSS. Why then, should you invest in R?

- Unlike SPSS, R is free. It does not eat up your budget. Why pay for something that you can get for free?
- R is cutting-edge. Methodological innovations first appear in R. Network analyses, for example (see Chapter 9), can be run in R, but not (yet) in SPSS. For some analyses, you need this alternative.
- Mastering R improves your connection to the statisticians in your team. They probably prefer R over SPSS. It is more efficient and less error-prone to all speak the same language.
- R is great for data-management. Clinical research, and especially EMA research, requires hundreds of operations on multiple raw data files. R excels at that. SPSS, frankly, does not. If you care about reproducible research (which you should), R can be a great help in putting it into practice.
- R can be used at different levels. If you want to be a basic user, that's fine. However, if you want to dive deeper, you will find that you can easily do so. You can study source code to understand a particular technique better. You can code new functions. R allows you to grow.
- R's user base is expanding every year. Chances are high that R will be the standard in your next workplace. R will look great on your CV.

You don't have to be a programmer or methodologist to use R. Yes, it takes time to master its full potential, but you should be able to run basic analyses in it within a week. This chapter will get you started.

2.3 Installing R & RStudio

Both R and RStudio are available, at no costs, for all major operating systems.

- Download R from the Comprehensive R Archive Network (CRAN), at <https://cran.r-project.org/bin/>
- Download RStudio from <http://rstudio.org>

Install R first, and RStudio second. If you install the programs in this order, RStudio will automatically find R on your computer.

If you installed R or RStudio previously, please update. This book assumes you will be working with version 3.4.2 (or higher) of R, and version 1.1.414 (or higher) of RStudio.

2.4 Interacting with R through the RStudio console

If you open RStudio, you will be presented with the interface shown in Figure 2.1. Rstudio's main window is divided in four panes (subwindows), which further contain several tabbed windows.



Figure 2.1: The RStudio Interface

Commands are sent to R starts in the bottom-left pane, named “Console”. To test this, move your cursor to the bottom line, immediately after the prompt sign (“>”). Next, type the statement below (note that ‘#’ denotes a comment line; R ignores it, so there is no immediate need to type that). To execute, press ‘Enter’.

R will execute the command and return the answer back to the console.

```
# Code snippet 2.1: R is a calculator.
1 + 1
```

Results of calculations can be saved into variables, by making use of the assignment operator (“`<-`”). If you type the name of a variable, R returns its value.

```
# Code snippet 2.2: Using <- to declare and set a variable.
N <- 50 + 50
N
#> [1] 100
```

To appreciate why R is such a popular tool for statistical computing, consider the following command, which, in one line, 1) uses the variable `N`, just created, to 2) generate 100 random numbers from the normal distribution, and 3) plot a histogram of these numbers.

```
# Code snippet 2.3: Plotting the histogram of a sample from the normal
# distribution.
hist(rnorm(N))
```

The plot appears in the bottom-right pane, as in Figure 2.1.

2.5 Writing R-scripts

Working in the console is a great way to interactively explore R and data, but what if you want to save a particularly useful chain of statements? For this, you can use a script file.

To create a script file, use the RStudio menu: `File > New File > R Script`. This will open a new tab in the top-left pane of RStudio, where you can edit the script.

- In the script window, type all statements that you have been entering in the console in the previous section.
- Next, select all lines in the script.
- Press `Ctrl+Enter` to run the script.

All commands in the script are executed. The commands are echoed in the console pane, and results are shown immediately, as was the case before, when you typed the commands in the console yourself.

Scripts can also be run line by line. Move the cursor to the line you want to run, and press “`Ctrl+Enter`”. The line is copied to the console and executed, and the cursor in the script will move to the next line, allowing you to walk through the script, step by step.

2.6 Importing your data

Something that confuses new Rstudio users, who are more familiar with SPSS, is that it is not obvious how to import data into RStudio. In SPSS, the data are in plain sight. In R, you first have to import the data.

2.6.1 Using RStudio menu's to import data

One way to load data into R is to use RStudio’s data import wizard. Follow the steps below to see how this works with data stored in a comma-separated-values (csv) format, a common data format to which many programs, including SPSS and Excell, can export data to.

- Download the example csv data file at <https://tinyurl.com/ybfafxxk> (or create a csv-version of one of your own data files).
- In RStudio’s menu, choose `File > Import Dataset > From Text (base)`.

- In the window that appears, click on **Browse** to locate the csv- file on your computer, and click **Import** in the next window (see Figure 2.2).

RStudio shows the data, in tabular view, in the top-left window, ready for analysis. You will also find a new entry in the **Environment**-tab in the top-right pane. When you click the small arrow, at the left of the name, you will see a brief summary of the contents of the data.



Figure 2.2: RStudio’s CSV import wizard.

2.6.2 Using functions to import data

While RStudio’s Data import wizard is useful, you will probably use it less over time. Most likely, you will convert to using the more efficient R commands to import data. For example, it takes only a single line to download and import the example data.

```
# Code snippet 2.4: importing csv-data from the internet.
ESMdata <- read.csv(url("https://tinyurl.com/ybfafxxk"), row.names = NULL)
```

2.6.3 Accessing your data

Since the data is now in the environment (under the name `ESMdata`), you can use it in other R commands. For example, to produce a more detailed summary of the first four columns of `ESMdata`, you type:

```
# Code snippet 2.5: summarising data.
summary(ESMdata)

  dayno        beepno    mood_relaxed    mood_down
Min.   : 1.0   Min.   : 1.00   Min.   :1.000   Min.   :-3.0000
1st Qu.: 61.0  1st Qu.: 3.00   1st Qu.:4.000   1st Qu.: 0.0000
Median :252.0  Median : 5.00   Median :4.000   Median : 0.0000
Mean   :198.9  Mean   : 5.24   Mean   :4.173   Mean   : 0.1784
3rd Qu.:303.0  3rd Qu.: 8.00   3rd Qu.:5.000   3rd Qu.: 0.0000
Max.   :366.0  Max.   :10.00   Max.   :7.000   Max.   : 3.0000
                           NA's   :2

  mood_irritat
Min.   :1.000
1st Qu.:1.000
Median :2.000
```

```
Mean    : 2.241
3rd Qu.: 3.000
Max.    : 7.000
NA's    : 3
```

To inspect the first 6 lines of data, type,

```
# Code snippet 2.6: Show first 6 lines of a data frame.
head(ESMdata)

#>   dayno beepno mood_relaxed mood_down mood_irritat
#> 1    226     1          5        -1          1
#> 2    227     5          4         0          3
#> 3    227     6          4         0          2
#> 4    227     8          4         0          1
#> 5    227     9          4         0          2
#> 6    227    10          5         0          1
```

To view all rows of data in a spreadsheet (as in Figure 2.2, type:

```
# Code snippet 2.7: Show data as spreadsheet.
View(ESMdata)
```

To work with a specific variable in the dataset, use '\$'. For instance, to print the first 20 numbers in the `mood_relaxed` variable, type:

```
# Code snippet 2.8: accessing a single variable in a data frame.
head(ESMdata$mood_relaxed, n = 20)
```

This allows you to apply functions to specific variables. For example, to calculate the mean of scores in `mood_relaxed`, type:

```
# Code snippet 2.19: Calculating the mean of a variable.
mean(ESMdata$mood_relaxed)
#> [1] 4.173442
```

There are many ways in which you can summarise and manipulate your data. At this point, the important milestone is that you imported and accessed data in R.

2.7 Extending R with Packages

R's attractiveness lies in the ease with which it can be extended with new functionality. Through so-called packages, which can be freely downloaded from the internet, specialised functions can be added to your workspace.

2.7.1 Installing R-packages from CRAN

Packages can be found at the CRAN website. To browse through the impressive list of available packages, see https://cran.r-project.org/web/packages/available_packages_by_name.html

If you find a package you like, you can install it via the RStudio menu system, choosing `Tools > packages`. But you can also use the console, via the `install.package` function.

A popular package, `tidyverse`, is used extensively in the examples of this manual. Package `tidyverse` comprises a set of popular packages from the creators of RStudio, that greatly simplify working with R. So, while you are at it, install this package now.

```
# Code snippet 2.10: installing a package from CRAN.
install.package(tidyverse)
```

The tidyverse contains a package called ‘haven’, which allows you to read and write SPSS datafiles (.sav files). This is very convenient. You don’t have to convert all your SPSS data to csv files. See `?read_spss` to learn how to import an SPSS-file (or use the data import wizard, by choosing ‘File > Import Dataset > From SPSS’, in RStudio’s top-right pane).

2.7.2 Installing R-packages from GitHub

Not all packages are at CRAN. Many ‘unofficial’ packages are shared at a site called ‘GitHub’. This book’s companion R package ‘emaph’, for example, which contains specialised EMA functions datasets, is on GitHub. You need package emaph to run many examples in the book, so let’s install this package now.

GitHub packages can be installed via the `install_github` function, which is defined in a package called ‘devtools’. So, to install ‘emaph’, enter the following in the console:

```
# Code snippet 2.11: Install the GitHub 'emaph' package.
install.packages("devtools")
devtools::install_github("jruwaard/emaph")
```

2.7.3 Using packages

To use packages, you have to tell R to load them. You do this with the `library` function. For example, to use package ‘tidyverse’ and ‘emaph’, type:

```
# Code snippet 2.12: Loading packages.
library(tidyverse)
library(emaph)
```

Once loaded, you can use the functions and datasets of the packages. Packge ‘emaph’ provides dataset ‘csd’, which contains the data from the ‘critical slowing down’-study (Kossakowski et al., 2017; Wichers et al., 2016), in which a patient recorded his mood, for 239 days (see also Chapter 13).

To plot the irritation levels of this patient in the first six days, using the `ggplot` function from package ‘ggplot2’ (which is in ‘tidyverse’), type:

```
# Code snippet 2.13: Using ggplot to plot EMA time series.
ggplot(data = subset(csd, dayno <= 6),
       mapping = aes(x = beepno, y = mood_irritat)) +
  geom_point() + geom_step() +
  scale_x_continuous(breaks = 1:10) +
  facet_wrap(~ dayno, nrow = 2)
```

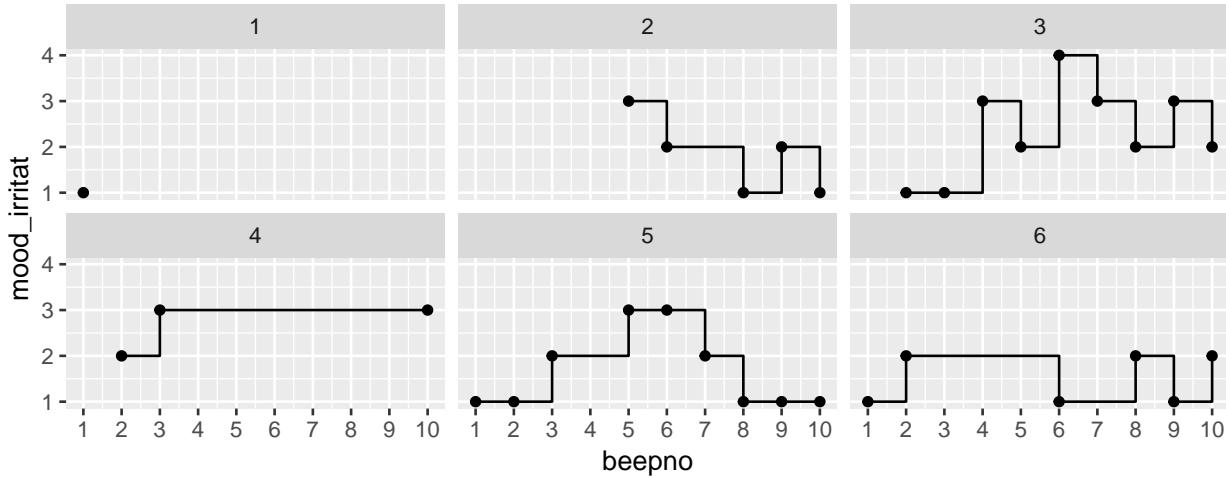


Figure 2.3: Irritation levels of a single patient, in the first six days of an EMA study.

2.8 Getting help

R has no point-and-click menu's that you can browse through to select a statistical procedure. This is a problem for many new users. What if you want, for example, to generate random numbers from a distribution with a mean of 2 and standard deviation of 4? How to tell this to R?

2.8.1 Using ‘?’ to consult the documentation

The good thing is that you already known the name of the function to use, since we used it in the previous section: it is ‘`rnorm`’. To check the documentation of this function, type `?rnorm` in the console.

```
# Code snippet 2.14: Using '?' to find the documentation of a function.
?rnorm
```

This opens the documentation of the `rnorm` function in the ‘Help’-tab, in the bottom right pane, from which you learn that that the `rnorm` function accepts `mean` and `sd` (standard deviation) as additional parameters, which are 0 and 1 default, respectively (which explains why `norm(100)` worked in the previous examples). So, to generate the required numbers, you type:

```
# Code snippet 2.15: Plotting the histogram of a custom random sample
hist(rnorm(1000, mean = 2, sd = 4))
```

All functions in R are documented, and this documentation is shown in RStudio’s Help pane when you prepend `?` to the name of the function in the console.

2.8.2 Using RStudio’s global documentation index search

What if you do not know the name of a function? Suppose you want to run a t-test for independent groups. Does R have a function for that?

At the top-right of the ‘Help’ pane, RStudio has a search input field, which allows you to search through all documentation that is installed on your computer. The search field auto-completes your input. If you type a ‘t’ in this field, you will be presented with a list of functions starting with a ‘t’. In this list, you find a likely candidate: a function called `t.test`. From the documentation of this function (`?t.test`), you learn that, indeed, this is the function you were looking for.

```
# Code snippet 2.16: Running a t-test, on two simulated samples.

# generate two samples (N = 100 per group) from the normal distribution
A <- rnorm(100); B <- rnorm(100)

# the t-test should be non-significant
t.test(A, B)
#>
#> Welch Two Sample t-test
#>
#> data: A and B
#> t = -0.093424, df = 197.63, p-value = 0.9257
#> alternative hypothesis: true difference in means is not equal to 0
#> 95 percent confidence interval:
#> -0.3121253 0.2838895
#> sample estimates:
#> mean of x mean of y
#> 0.03296666 0.04708455
```

2.8.3 Learning from examples

This book contains many R code snippets. By studying these examples, you will become more familiar with R. Some examples will introduce R language constructs and functions that are unknown to you. Learn from these examples, by using `?` on each element that you do not understand.

2.8.4 Google

With Google, you will find many answers to your R questions. Googling for “t-test R”, for example, results in a rich set of online resources. Good resources are:

- RSeek (see <http://rseek.org/>)
- Stackoverflow: (see <https://stackoverflow.com/questions/tagged/r>)
- SearchR (see: <http://search.r-project.org/>)

2.8.5 Read books

This book does not provide a comprehensive tutorial. There is no need for that, since excellent resources are readily available. A selection is presented below.

- Many mental health researchers own a copy of Andy Field’s popular book “Discovering Statistics Using IBM SPSS Statistics” (Field, 2013). For those, Field’s R-version of this book, “Discovering Statistics Using R” (Field et al., 2012) provides a familiar companion in making the transition to R. See <https://www.discoveringstatistics.com/>
- Free manuals can be found at the official CRAN site. The manuals are dry, but complete and authoritative, since the authors are members of the R core development team. See <https://cran.r-project.org/manuals.html> (or type `help.start()` in the console).
- While at CRAN, be sure to browse the ‘contributed documentation’-section. On this page, you will find many freely available manuals contributed by the R community. See <https://cran.r-project.org/other-docs.html>

2.8.6 Online Courses

- DataCamp, an online data science education platform, offers several high-quality interactive courses in R. See <http://www.datacamp.com>
- The Try-R course at the CodeSchool website provides an alternative to DataCamp. See: <http://tryr.codeschool.com/>
- The Quick-R website provides a solid, concise, and rich introduction to R. See <https://www.statmethods.net/>

2.8.7 Learn R, in R

Package ‘swirl’ comprises a set of interactive courses that teach many aspects of the R language. See <http://swirlstats.com>

```
# Code snippet 2.18: starting the interactive swirl-course in R.  
install.packages("swirl")  
library("swirl")  
swirl()
```


Part II

EMA Methods

Chapter 3

Study Design

As with all scientific research, EMA studies start with mindful consideration of the study design. Issues that need to be considered are, for example, the research question(s), the hypotheses, the population of interest, and the nature of the comparison groups (Shiffman et al., 2008).

This chapter highlights key design aspects of EMA studies. Ample information on general study design issues can be found elsewhere (see for example, the APH quality handbook, Amsterdam Public Health, 2018).

3.1 What is the research question?

Given the plethora of new research options that emerged from the rapid development in EMA technologies, it can be tempting to dive straight into explorative data collection, without giving much consideration to the theoretical background of the study. That, however, would be one pitfall of EMA research to avoid. Data mining is no substitute for theory. Asking participants to contribute data without a rationale is unethical. As in all scientific activities, defining the research question should be a first step.

Ask yourself what EMA could bring to your topic of interest. How is it different from traditional assessment methods? What questions does it allow you to address that you could not answer without it? For this, you could use any of the EMA advantages discussed in Chapter 1. Are you interested in real-life behaviour, in individual differences between participants, in potential causal pathways between health-related variables? What relationships do you expect to find, and why? A solid theoretical background, and clearly formulated explicit research questions and hypotheses will help to make the right choices when you have to decide on the other aspects of the study design.

3.2 Who are the prospect participants?

Given the experimental nature of EMA, studies are often piloted in healthy or sub-clinical populations. This is a recommended first step to test the experimental procedures and to avoid unnecessary burden of vulnerable patient populations. You should be aware, though, that results obtained in non-patient populations do not necessarily generalise to patient populations. EMA mood ratings, for example, might be much more variable in patients compared to non-patients. Pilot studies should therefore also be conducted in the target population.

3.3 How are theoretical experimental variables operationalised?

With the study hypotheses in place, experimental constructs can be operationalised into well-defined quantifiable measures.

Precies def wat meten betrouwbaarheid, validiteit, ruwe dat. Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam vehicula augue metus, in tincidunt urna luctus sit amet. Sed ultrices, erat at laoreet semper, sem tellus hendrerit mi, eget pulvinar massa nisl ac dolor. Nunc ac tellus nec tortor interdum porta. Vestibulum hendrerit tempus condimentum. Donec a mollis sem. Aenean lectus nunc, bibendum ut orci vel, tristique pellentesque arcu. Vestibulum id laoreet neque. Phasellus at ex velit. Vestibulum scelerisque nulla ut massa tempor, ac dapibus dui viverra.

What is the data acquisition interface? (Stone and Shiffman, 2002). Opletten wat je koopt aan technologie. Onderbouw keuze. Zie hoofdstuk X. Gevalideerd vs nieuw.

- Technical Reliability of data platform
- Track record of data platform suppliers
- User-friendliness of data device for study participants.
- User-friendliness of data platform for researcher (availability of an administrative back-office).
- Location of data storage
- Costs

For an overview of existing EMA data platforms, see 16.

3.4 Constructing the Sample Plan

An important next step is to define the EMA data sample plan. Questions that need to be answered are:

- How many days will data collection last?
- On each day, how often are participants assessed?
- How and when are participants invited for assessment?

The questions above should be answered as detailed as possible to best serve the research question and the statistical power (see below). In practice, however, it is often necessary to balance between research interests, respondent burden, and practical considerations, such as hardware limitations.

When determining the appropriate sample plan, researchers are advised to start with mapping the expected fluctuation or patterns, based on available knowledge. For example, when an event is rare, it can be sufficient to ask participants to initiate EMA whenever the event occurs, or prompt them with an end-of-day diary. Adding more prompts in this scenario would not lead to more reliable data (Piasecki et al., 2007).

Increasing the assessment frequency and study duration will allow for a more detailed assessment of the outcome of interest. It is tempting to collect often and for a long period of time. However, this may also increase respondent burden, which may affect compliance and accuracy. Measurement reactivity could occur, where the EMA-induced enhanced focus on the outcome of interest causes participants to increase or decrease on this outcome (Hufford et al., 2002; van Ballegooijen et al., 2016).

Issues related to hardware should also be considered. Electronic wearables have limited battery life and memory storage space. Actigraph watches memory space limitations may require participants to visit the research site. GPS-monitoring apps may have a negative impact on the battery life of the smartphone of the participants. These practical issues may result in data loss, through problems with study adherence or even study drop-out.

Once all decisions related to the sampling plan are made, the procedure should be thoroughly tested. As a first step, it can be insightful to simulate the sample plan, as is done below, using the ‘sample_plan’ of package ‘emaph’:

```
# code snippet 3.1: simulating a signal-contingent sample plan
plan <- sample_plan(n_participants = 5,
                     n_days = 2,
                     times = c("09:00-11:00", "12:30", "17:00-19:00"),
                     plot = TRUE)
```

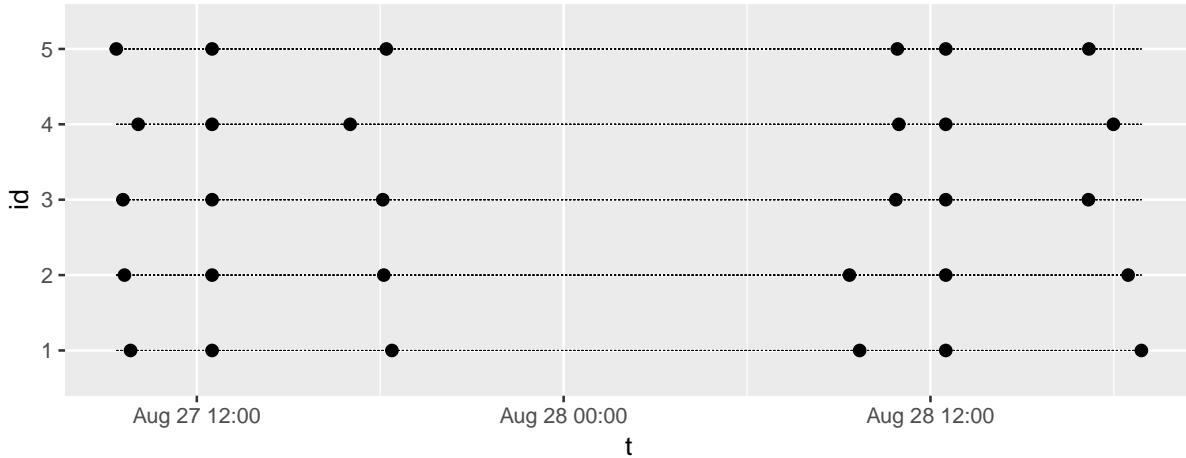


Figure 3.1: Simulated EMA sampling plan

3.5 Power Analysis

The power of a statistical test is the probability that it will detect an effect when this effect, in reality, exists. It is a function of the strength of the effect size, sample size, the significance level (alpha), and the statistical model. Determining the power of the experiment is an important step in the design of any study - EMA studies included. Both underpowered and overpowered studies are a waste of time and resources.

Conducting a power analysis can be easy or very difficult, depending on the complexity of the experimental design and the adopted statistical technique. For simple tests, such as the t-test and ANOVA, straightforward analytical solutions exist, which are implemented in readily available tools. In R, one of those tools is package ‘pwr’.

For example, to use ‘pwr’ to calculate the power of a t.test to detect a moderate effect size ($d = 0.5$), with $n = 30$ per group, and a (two-sided) significance level alpha of .05, type:

```
# code snippet 3.2: Power analysis of a t-test
# (analytical approach)

library(pwr)
pwr.t.test(d = 0.5,
            n = 30,
            sig.level = 0.05,
            type = "two.sample",
            alternative = "two.sided")

#> Two-sample t test power calculation
#>
#>      n = 30
#>      d = 0.5
#>      sig.level = 0.05
```

```
#>           power = 0.4778965
#>   alternative = two.sided
#>
#> NOTE: n is number in *each* group
```

The power is 48% - not even close to the generally adopted standard of 80%. More participants are needed to detect the hypothesised effect.

EMA study designs are often characterised by repeated measures, complex multi-level structures and the application of advanced statistical techniques. You may find that available power calculators are too limited to properly take key aspects of your design into account. If this happens, simulation techniques may help. If power is the probability that a test will detect an effect it exists, it can be determined by noting the proportion of times a statistical test reaches significance, if it is run, many times, on simulated data, in which the hypothesized effect is present. To illustrate how this works, we will calculate the power of the t-test again, through simulation:

```
# code snippet 3.2: Power analysis of a t-test
# (simulation approach)

m1 = 0    # mean in group 1
m2 = 0.5 # mean in group 2
sd = 1    # sd (in both groups)
n = 30    # sample size, per group

# conduct the experiment many times
nsim <- 10000
p <- numeric(nsim)
for (i in 1:nsim) {

  data <- data.frame(
    outcome <- c(
      rnorm(n, m1, sd), # group 1 data
      rnorm(n, m2, sd)  # group 2 data
    ),
    group <- c(
      rep(1, n), # group 1 indicator
      rep(2, n)) # group 2 indicator
  )

  # save significance of test
  p[i] <- t.test(outcome ~ group, data)$p.value
}

# power
sum(p < 0.05) / nsim
#> [1] 0.4784
```

As can be seen, the simulation results are very close to the output of ‘pwr.t.test’.

There was no immediate need to run this simulation. We already knew that the power was 48%. The example illustrates, however, that simulation is a valid option when power calculators are too limited (or too difficult to understand...). Simulating the right data, of course, can be challenging as well, but you will find that R has packages that simplify data simulation. For example, ‘mvtnorm’ in package MASS (Venables and Ripley, 2002) can be used to generate correlated data, and package ‘simstudy’ (Goldfeld, 2018) can be used to generate complex (longitudinal) data.

3.6 Ethical Considerations

When collecting digital data, you should be mindful of the rules and regulations that apply to data collection, storage and sharing. From May 2018 onward, the European Committee has enforced the General Data Protection Regulation (GDPR) (in Dutch, Algemene Verordening Gegevensbescherming (AVG)). The regulation aims to protect the data and privacy of EU citizens.

3.6.1 Privacy Protection

Aliquam vehicula augue metus, in tincidunt urna luctus sit amet. Sed ultrices, erat at laoreet semper, sem tellus hendrerit mi, eget pulvinar massa nisl ac dolor. Nunc ac tellus nec tortor interdum porta. Vestibulum hendrerit tempus condimentum. Donec a mollis sem. Aenean lectus nunc, bibendum ut orci vel, tristique pellentesque arcu. Vestibulum id laoreet neque. Phasellus at ex velit. Vestibulum scelerisque nulla ut massa tempor, ac dapibus dui viverra.

[EMA data sharing is complicated. Indirect identifiability should perhaps be the default assumption. GPS data cannot be fully anonymised.] Vivamus enim turpis, pulvinar volutpat purus nec, lobortis imperdiet diam. Nunc hendrerit cursus eleifend. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Vivamus enim turpis, pulvinar volutpat purus nec, lobortis imperdiet diam.

3.6.2 Medical device

All clinical studies that involve human participants need to be evaluated by a Medical Research and Ethics Committee (MERC; Dutch: ‘METC’). Recently, the committees have also been tasked to determine whether a medical device is used and to evaluate the safety and quality of the device. Researchers are therefore required to add a section in the research protocol, explaining why the software/device is or is not a medical device. This paragraph gives a brief overview of this process.

The official definition of a medical device (Medical Device Act, or ‘Wet Medische Hulpmiddelen’) is as follows:

“Any instrument, apparatus or appliance, any software or material or any other article that is used alone or in combination, including any accessory and the software required for its proper operation, that is intended by the manufacturer to be used specifically for diagnostic or therapeutic purposes, and is intended by the manufacturer to be used for human beings for the purpose of:
- diagnosis, prevention, monitoring, treatment or alleviation of disease - diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap - investigation, replacement or modification of the anatomy or of a physiological process - control of conception, and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.”
(CCMO, 2018)

In short, software can be classified as a medical device if it collects patient-specific data and is specifically intended for one of the above-mentioned objectives. Or in other words, if a health care professional takes this information into account when determining the course of treatment. The law does not differentiate between passive and active EMA.

In practice, the definition of medical devices leaves a lot of room for confusion. Researchers often struggle with the question whether their assessment tools should be considered a medical device or not. For this purpose, flowcharts exist that help to determine whether an app or product should be classified as a medical device (see, e.g., Ekker and van Rest, 2013, and <http://cetool.nl/general/scanAid>). Figure 3.2 shows such a flow-chart.

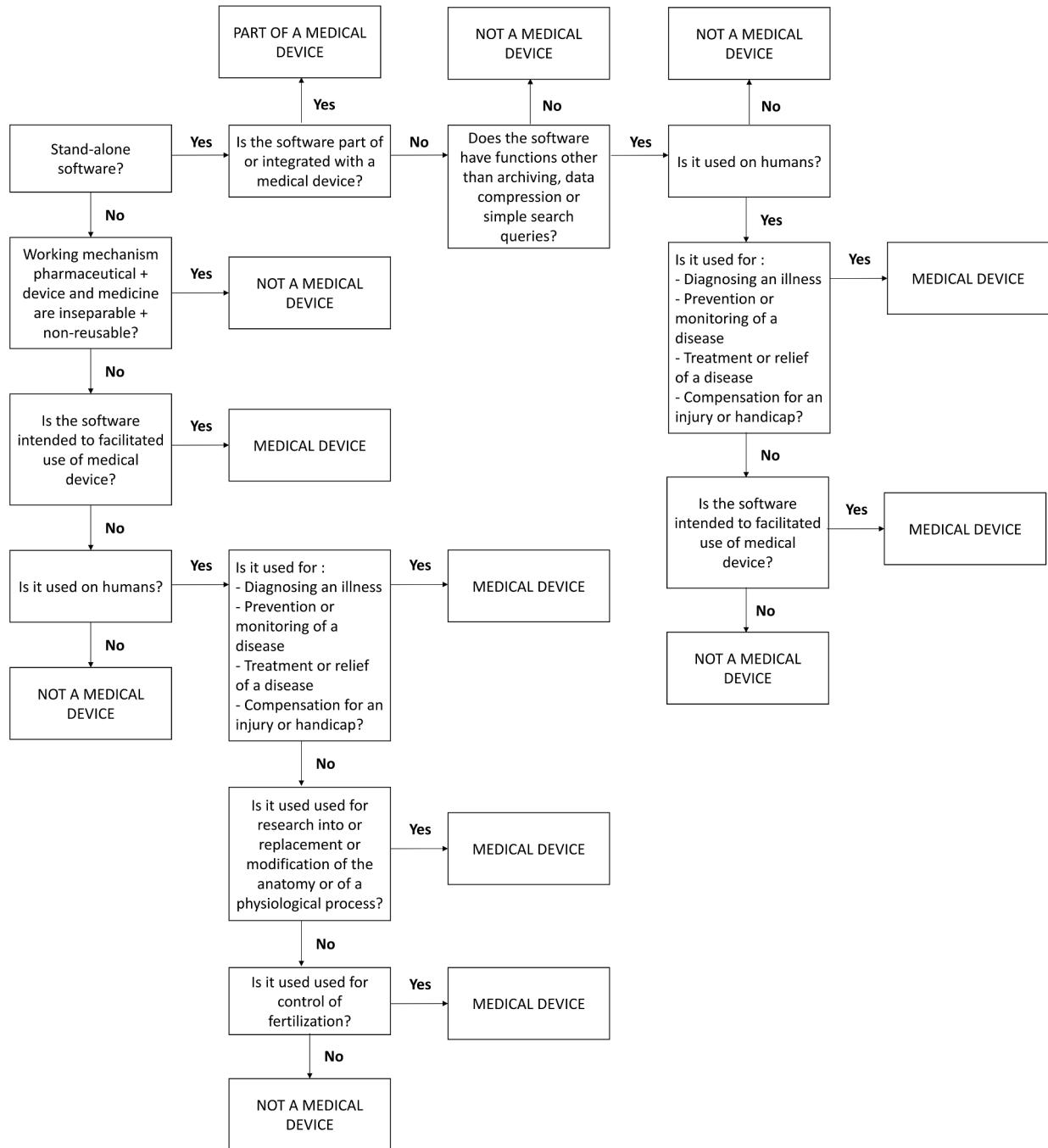


Figure 3.2: Flow-chart medical device.

3.6.3 Data Processing Agreements

When data processing is (partly) outsourced to a third party, a Data Processing Agreement (DPA) should be drafted, that specifies the agreements between the ‘controller’ and ‘processor’. In this context, a controller is the person or organisation that determines the why and how of data collection (for example you as a researcher). The processor processes the data on behalf of the controller, for example by storing the data in a

cloud. Aspects of data processing that need to be addressed in the agreement are for example:

Wie, niet delen anderen, data leaks rap., niet uitbesteden, log toegang binnen organisatie

Context, duration and termination of agreement Processing data Secure data storage Sharing or exporting data Confidentiality Data leaks Liability Data storage period

3.6.3.1 Informed consent

Part of the General Data Protection Regulation is that individuals should provide consent before their data can be collected and processed. The European Union has formulated a number of conditions that need to be met for a consent to be valid:

"it must be freely given; it must be informed; it must be given for a specific purpose; all the reasons for the processing must be clearly stated; it is explicit and given via a positive act (for example an electronic tick-box that the individual has to explicitly check online or a signature on a form); it uses clear and plain language and is clearly visible; it is possible to withdraw consent and that fact is explained (for example an unsubscribe link at the end of an electronic newsletter email)".

The CCMO offers a template that can be used to construct an informed consent form for your specific study [see <http://www.ccmo.nl/en/consent>].

Chapter 4

EMA instruments

General introduction Procedure

Features

Costs new development vs known player Low-tech vs high-tech

Validation, reliability (noise) Is raw data available (genactiv versus fitbit) Dedicated software y/n Back-office (autonomy to define questions and design)

Device limitations (technical considerations) Storage (local, cloud, etc) Data sharing (wifi, usb etc) Server (where, who owns the server/data) Battery life

Pilot (on your own phone) Make sure there is a plan b

4.1 Participant perspective

Social environment participant, stigma Impact Carrying the device (remembering to take it with you)
Charging battery

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam vehicula augue metus, in tincidunt urna luctus sit amet. Sed ultrices, erat at laoreet semper, sem tellus hendrerit mi, eget pulvinar massa nisl ac dolor. Nunc ac tellus nec tortor interdum porta. Vestibulum hendrerit tempus condimentum. Donec a mollis sem. Aenean lectus nunc, bibendum ut orci vel, tristique pellentesque arcu. Vestibulum id laoreet neque. Phasellus at ex velit. Vestibulum scelerisque nulla ut massa tempor, ac dapibus dui viverra.

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4.2 Section

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Donec sed lectus at sem ultrices commodo. Proin a viverra metus, nec scelerisque odio. Morbi viverra tristique libero vel fringilla. Sed at varius erat, id consequat nibh. Ut eget leo blandit orci posuere tincidunt ac sed erat. Aenean metus metus, eleifend ut facilisis a, fringilla ut neque. Nunc hendrerit cursus eleifend. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Vivamus enim turpis, pulvinar volutpat purus nec, lobortis imperdiet diam.

4.3 Section

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Chapter 5

Data management

Modern EMA research generates a lot of data. Repeated self-reports, GPS-data, accelerometer data, background demographic data and traditional questionnaire data quickly add up to hundreds of megabytes of raw data. This raises the importance of proper data management. Without a proper data management plan, the EMA researcher quickly drowns in the data feed.

5.1 Using RStudio-projects to manage EMA data

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“File | New Project...”

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5.2 Project directory structure

```
1 project
2   |--data
3   |   |--source
4   |   |   |--keyfile.csv
5   |   |   |--GPS
6   |   |   |   |--subject1.json
```

```

7   |   |   |   °--subject2.json
8   |   |   |--accelerometer
9   |   |   |   |--subject1.bin
10  |   |   |   °--subject2.bin
11  |   |   °--surveys
12  |   |   |   |--demographics.sav
13  |   |   |   °--survey.sav
14  |   °--pruned
15  |   |   |--GPS.Rda
16  |   |   |--accelerometer.Rda
17  |   |   °--surveys.Rda
18 |--scripts
19   |   |--import
20   |   |   |--import_GPS.R
21   |   |   |--import_accelerometers.R
22   |   |   °--import_surveys.R
23   |   °--analysis
24   |   |   |--explore.R
25   |   |   °--test.R
26 |--output
27   |   °--images
28   |   |   |--figure_1.png
29   |   |   °--figure_2.png
30 °--README

```

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5.3 The keyfile

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Table 5.1: Sample Study Keyfile

ID	Status	SurveyID	Watch ID	App ID
P001	QM01221	192.A102.83A	APC009	
P002	QM01228	192.A102.83B	APC010	

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Store personal data in another location. Aliquam vehicula augue metus, in tincidunt urna luctus sit amet. Sed ultrices, erat at laoreet semper, sem tellus hendrerit mi, eget pulvinar massa nisl ac dolor. Nunc ac tellus nec tortor interdum porta. Vestibulum hendrerit tempus condimentum. Donec a mollis sem. Aenean lectus nunc, bibendum ut orci vel, tristique pellentesque arcu. Vestibulum id laoreet neque. Phasellus at ex velit. Vestibulum scelerisque nulla ut massa tempor, ac dapibus dui viverra.

5.4 Source data

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5.5 Import & Prune

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5.6 Visual Exploration

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5.7 Analysis

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Part III

Analytic Approaches

Chapter 6

Feature Extraction and Selection

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6.1 Feature extraction

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```
# Figure 6a: Features of a timeseries
d <- data.frame(i = 1:100)

d$x <- rnorm(nrow(d), 0, 2)
d$mean <- mean(d$x)
d$variance <- var(d$x)
d$autocorrelation <- cor(d$x, lag(d$x), use = "complete.obs")
d$rolling_mean <- zoo::rollapply(d$x, 10, fill = NA, mean)
d$rolling_variance <- zoo::rollapply(d$x, 10, fill = NA, var)
d$rolling_autocorrelation <- zoo::rollapply(d$x, 10, fill = NA,
                                              function(x) {
                                                cor(x, lag(x), use = "complete.obs")
                                              })

d <- tidyr::gather(d, aspect, value, -i)
d$aspect = factor(
  d$aspect,
```

```
levels = c(
  "x", "mean", "variance", "autocorrelation",
  "rolling_mean", "rolling_variance", "rolling_autocorrelation"))

ggplot(data = d,
       aes(x = i,
           y = value)) +
  geom_point(alpha = .3, size = .8) +
  geom_line() +
  facet_wrap(~ aspect, scales = "free", ncol = 2) +
  theme(axis.title.x=element_blank(),
        axis.text.x=element_blank(),
        axis.ticks.x=element_blank())
```

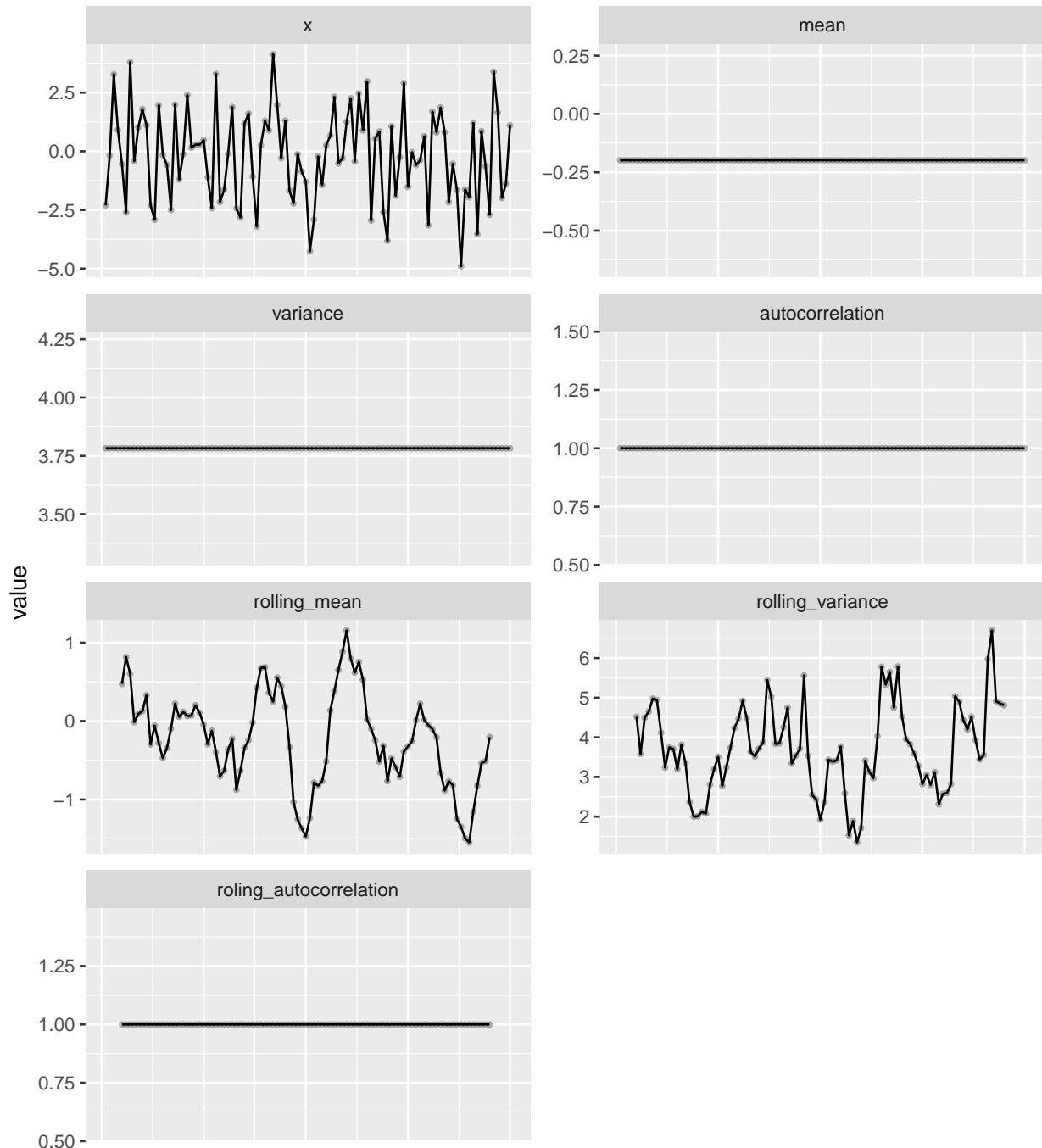


Figure 6.1: features of a series.

6.1.1 Variance

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6.1.2 Autocorrelation

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6.1.3 Rolling statistics

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6.2 Reliability and Validity

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6.3 Feature Selection

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Chapter 7

Mixed Modeling

EMA data are timeseries that are characterised by complex correlational structures, irregular sampling intervals, missing data, and substantive individual differences. Mixed models are well-suited to deal with these data. This chapter provides a brief introduction to conducting mixed models analysis of EMA data in R.

7.1 The Mixed Model

Mixed modeling can be understood as a regression technique in which separate regression functions are estimated for each cluster in the data set. In EMA data, these clusters are defined by the participants. Data from the same participant are expected to be correlated, and one way to honour this correlation is to conceptualise a separate regression for each participant. This idea, in the most simple regression model, can be expressed as:

$$Y_{ij} = \text{intercept}_i + \epsilon_{ij} \quad (7.1)$$

This models the expected value of the j-th measurement of participant i as the mean of all measurements of participant i, plus error. It defines a set of regression functions - one for each participant.

The regression functions are, however, not independent. Mixed models divide the intercepts of the individual participant regression functions into two components: 1) the intercept of the group ($\text{intercept}_{\{g\}}$; the mean intercept of all regression functions), and 2) a participant-specific component $\text{intercept}_{\{p\}}$ (i.e., the difference between the intercept of the participant and the mean intercept), i.e.:

$$\text{intercept}_i = \text{intercept}_g + \text{intercept}_p \quad (7.2)$$

The group intercept is called the ‘fixed’ effect. If we would gather more data from new participants, we would expect to find approximately the same group intercept.

The participant-specific component of the intercept is known as the ‘random’ effect. If we sample new data, we would expect a similar *variance* of the participant-specific intercept components around the group intercept. This “mixing” of fixed and random effects is what gives mixed modeling its name.

7.2 Simulating example data

To understand analysis techniques, it often helps to apply the technique to simulated data, in which parameters of interest are known.

Here, we will use the ‘sim_ema’ function from package ‘emaph’, to simulate EMA mood assessments of 100 participants, who rate their mood, three times per day, for one week. We set the mean mood (intercept_g) to 5, the variance around this mean - var(intercept_i) - to .5., and the average variance around these means within participants - the error - to 1.

As you can learn from the documentation of ‘sim_ema’ (see ‘?sim_ema’), the function expects at least two arguments: the definition of a sample plan (see ‘?sample_plan’), and a specification of the data-generating model, in the form of a list defining fixed effects, the random effects, and residual variance (i.e, the error). From these specifications, a data set is simulated (which is assigned to variable d1).

```
# code snippet 7.1: simulating ema data
library(emaph)
plan <- sample_plan(n_participants = 100,
                     n_days = 7,
                     times = c("10:00-11:00",
                               "13:00-14:00",
                               "16:00-18:00"))

d1 <- sim_ema(plan,
               mm_par = list(fixed  = c(intercept = 5),
                             random = c(intercept = 1),
                             error = .5),
               lim = c(0, 10))
```

Figure 7.1 shows EMA mood ratings of the first 6 participants in the simulated data set. Mean mood ratings of the participants (the red lines) vary around 5 (the grey dashed line), as specified.

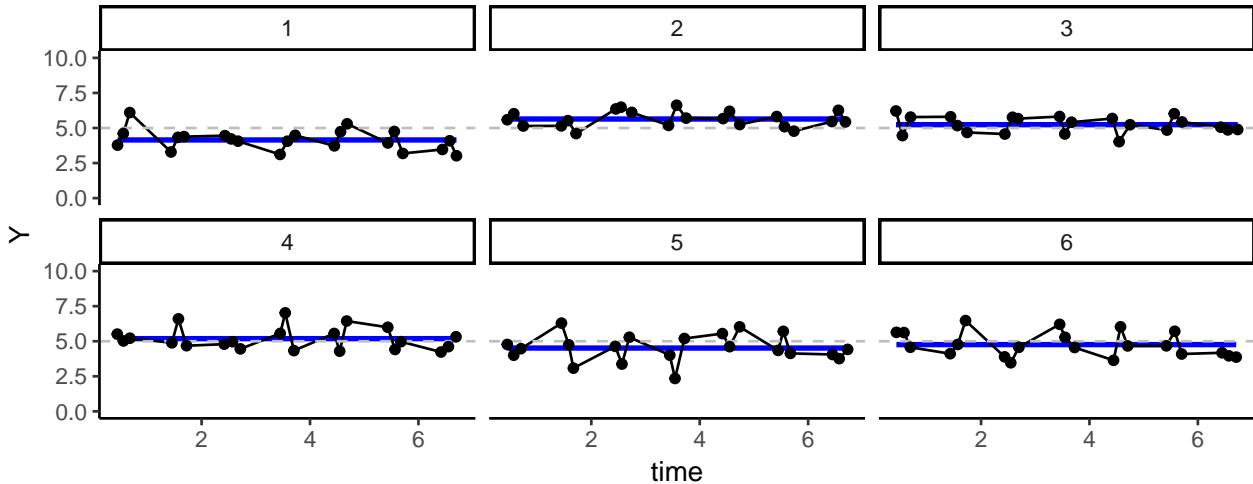


Figure 7.1: Simulated EMA data of Six Participants.

7.3 Fitting a mixed model in R

Now, let’s fit a mixed model to the data, to see whether the simulation parameters are detected. For this, we will use the ‘lme’ function, from package ‘nlme’ (Pinheiro et al., 2018).

The first argument of the `lme` function , ‘`Y ~ 1`’, specifies the fixed ‘effect’ (in this case: the mean intercept). The second argument, ‘`random = ~ 1 | id`’ specifies the random effect: in this model, intercepts are allowed to vary between participants. The fitted model is assigned to variable `fm`.

```
# code snippet 7.1: fitting a mixed model with lme
library(nlme)
fm <- lme(Y ~ 1, random = ~ 1 | id,
            data = d1)
```

We can now extract the fixed effects regression coefficients table, by calling the ‘`summary`’ function on the fitted model. The estimated intercept should be around to 5 (as this is a finite sample, we expect some deviation):

```
# code snippet 7.2: print fixed effects
summary(fm)$tTable
#>           Value Std.Error DF t-value p-value
#> (Intercept) 5.08    0.0974 2000    52.2      0
```

Random effects and residual variance are shown by the ‘`VarCorr`’ function. Again, since we specified the data ourselves in this case, we know the ‘true’ value of these parameters: the random intercept variance should be around .5 and the residual error variance should be close to .2.

```
# code snippet 7.3: fitted random effects
VarCorr(fm)
#> id = pdLogChol(1)
#>          Variance StdDev
#> (Intercept) 0.925    0.962
#> Residual    0.502    0.709
```

It can be instructive to plot the predicted values of the model, to make clear how the model ‘thinks’. As shown by Figure 7.2, the model predicts a series of straight lines, one for each participant, that vary around 5.

```
# code snippet 7.4: saving predicted values
d1$predY <- predict(fm)
```

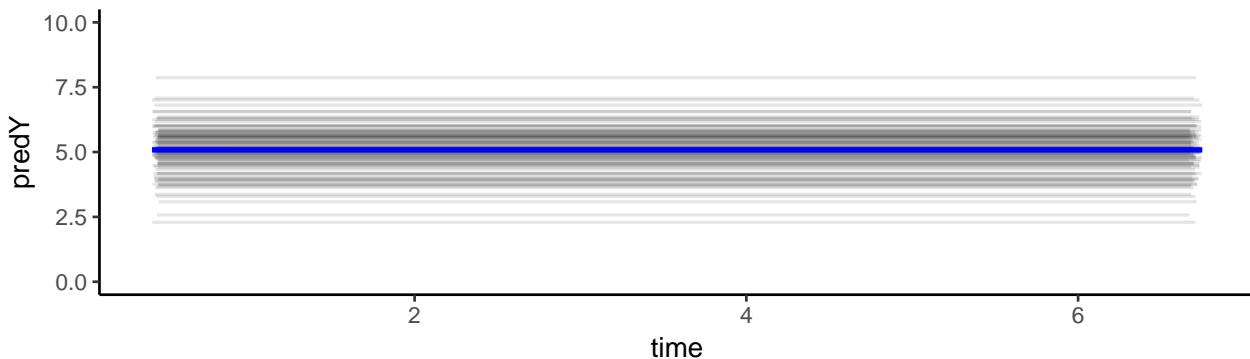


Figure 7.2: EMA ratings, of each participant in the simulated data set, as predicted by the intercept-only mixed linear model.

7.4 Adding time as a predictor

Now that we know how to fit a simple mixed model, we can consider a more complicated scenario. In the first data set, participants’ mood ratings did not change over time. Scores varied around a stable mean during the full week. Hence, there was no need to model a time effect. But suppose we would expect a systematic improvement of mood ratings over time, for instance in response to a mental health intervention?

Let's first call 'sim_ema' again, with parameters that will result in data in which mood rating increase over the course of the week, 0.5 scale points per day. Let's also assume that individual participants will vary in the degree of mood improvement: the mean time effect will be 0.5, but this parameter is allowed to vary between participants, with a variance of 0.05.

```
# code snippet 7.5: simulating ema data (time effect)
d2 <- sim_ema(plan,
               mm_par = list(fixed = c(intercept = 5, time = 0.5),
                             random = c(intercept = 1, time = 0.1),
                             error = .5),
               lim = c(0, 10))
```

Figure 7.3 shows the data of the first six participants in the second data set. Both the intercept and the slope vary across the participants. Some participants improve more over time, and others improve less: the slope in this data set is a random effect.

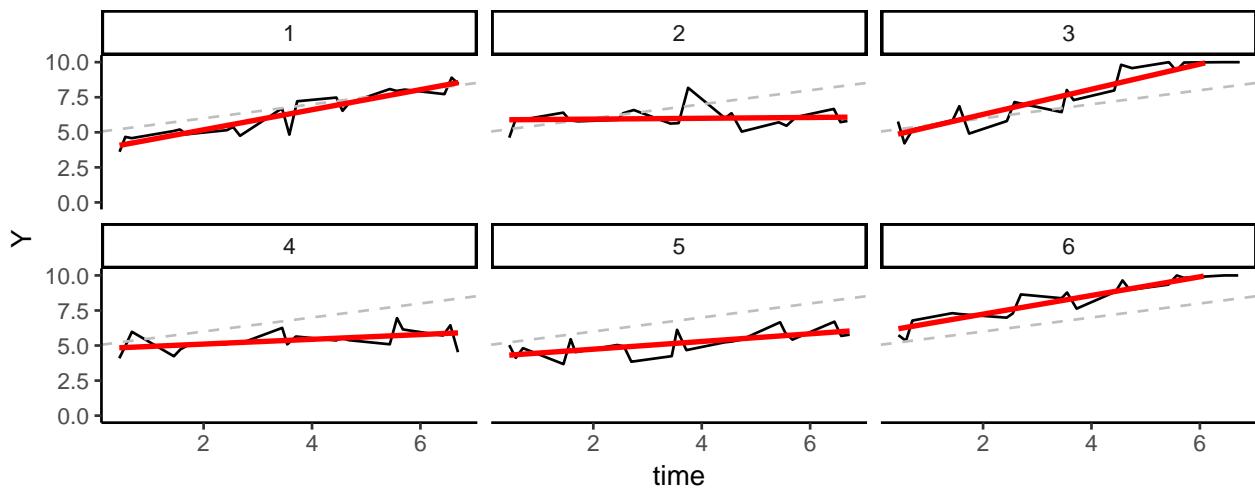


Figure 7.3: Simulated EMA data of Six Participants (Time-varying model).

To fit the extended mixed model, time can simply be added to both the fixed and random arguments of the 'lme' function. Fixed effects estimated of this model should be around 5 and 0.5, since that is how we specified the data. Calling 'summary' on this function, we see that the fixed time effect is significant.

```
# code snippet 7.6: a mixed model, with a random slope
library(nlme)
fm <- lme(Y ~ 1 + time, random = ~ 1 + time | id,
            data = d2)
summary(fm)$tTable
#>           Value Std.Error   DF t-value p-value
#> (Intercept) 5.110    0.1151 1999    44.4 3.04e-300
#> time         0.414    0.0285 1999    14.5  1.45e-45
```

The random effects now has four components: the variance of the intercept, the variance of the slope, the residual error and the correlation between the random intercept and the random slope.

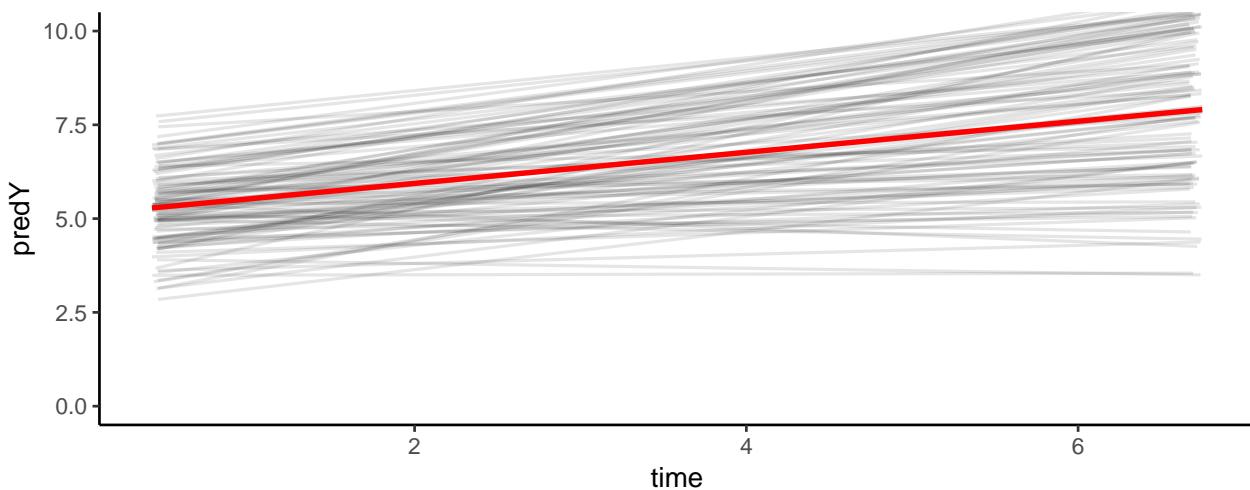
```
# code snippet 7.7: extracting random effects
VarCorr(fm)
#> id = pdLogChol(1 + time)
#>          Variance StdDev Corr
#> (Intercept) 1.2282  1.108 (Intr)
```

```
#> time      0.0755  0.275 -0.167
#> Residual  0.4843  0.696
```

Model predictions clearly show how the mixed model estimated varying intercepts and slopes, that, on average, reflect the fixed effect regression formula ' $Y \sim 5 + 0.5 * \text{time}$ '.

```
d2$predY <- predict(fm)

ggplot(d2, aes(x = time, y = predY, group = id)) +
  geom_line(alpha = .1, size = .6) +
  geom_smooth(aes(group = NULL), method = "lm", color = "red") +
  coord_cartesian(ylim = c(0, 10)) + theme_classic()
```



7.5 Adding a Two-Group Comparison

In data-set 1, mood ratings did not change during the week, while in data-set 2, the mood ratings increased. Suppose the two data-sets reflect the data that you collect in a two-group RCT, in which you compare the effects of a mental health intervention (data-set 2) against a waiting list condition (data-set 1). By combining the two data-sets, we can illustrate how to conduct a group comparison with 'lme'.

Since the two data-sets are already available (in d1 and d2), the new data set can be created with just three lines of code (below). In the first line, the 'rbind' function is used to combine the rows of data-set 1 and 2 into a new variable: data.frame d3. The second line adds a group indicator to d3. The third line updates the id's of the participants in the second group, to explicitly differentiate the participants in the second group from the participants in the first group.

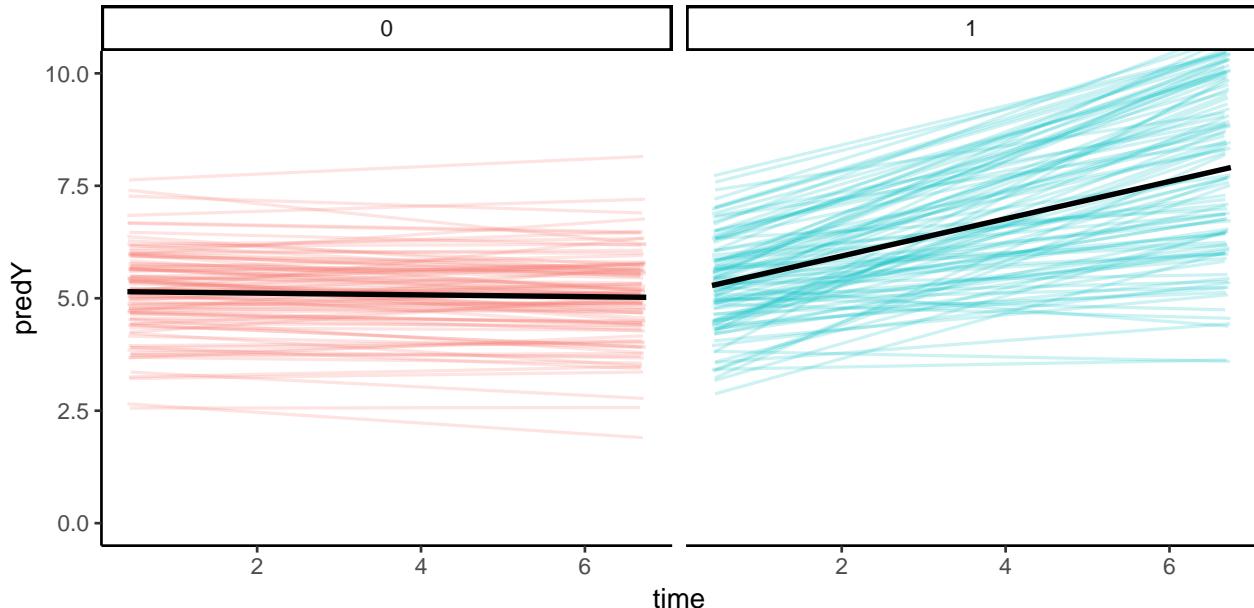
```
# code snippet 7.7: two-group simulation
d3 <- rbind(d1, d2)
d3$group <- factor(c(rep(0, nrow(d1)), rep(1, nrow(d2))))
d3$id[d3$group == 1] <- d3$id[d3$group == 1] + 100
```

The effect of the intervention can be tested by adding a (fixed) 'time * group' interaction effect to the model. This effect, we know, is 0.5, and, as can be seen, this is what the model picks up:

```
# code snippet 7.8: a mixed model, with two groups
library(nlme)
fm <- lme(Y ~ 1 + time * group, random = ~ 1 + time | id,
           data = d3)
```

```
round(summary(fm)$tTable, 2)
#>           Value Std.Error DF t-value p-value
#> (Intercept) 5.15     0.11 3998   46.91    0.00
#> time        -0.02     0.02 3998   -0.93    0.35
#> group1      -0.04     0.16 198    -0.27    0.78
#> time:group1 0.43     0.03 3998   14.63    0.00
```

In Figure ?? below, EMA mood ratings predicted by the fitted model clearly show how the model detects 1) the fixed between-group effect, and 2) the variance in intercepts and slopes in both groups.



7.6 Further reading

In this chapter, we introduced mixed model analysis of EMA data. To do so, we could only touch upon the theoretical foundations of mixed models, and we deliberately used simple examples with clean simulated data. Readers, who consider the application of mixed models, are strongly advised to study additional resources.

The authoritative reference for mixed effect modeling in R is a book by Pinheiro and Bates (2000). To fully appreciate this book, however, a strong background in formal statistics is required. Gentle introductions in the topic can be found in XXX, YYY and ZZZ () .

Chapter 8

Fitting Networks

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8.1 What are Networks?

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8.2 Fitting Networks on Single-Subject Repeated Measures Data

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```
# code snippet 9.1: Fitting symptom networks
library(graphicalVAR)
library(dplyr)

# Simulate model:
set.seed(2)
Mod <- randomGVARmodel(5, probKappaEdge = 0.8, probBetaEdge = 0.8)

# Simulate data:
d <- as.data.frame(graphicalVARsim(50, Mod$beta, Mod$kappa))

e <- tidy::gather(d) %>% group_by(key) %>% mutate(t = 1:n())
ggplot(data = e, aes(x = t, y = value)) +
  geom_point(size=.2) + geom_line() +
  facet_grid(key~.)
```

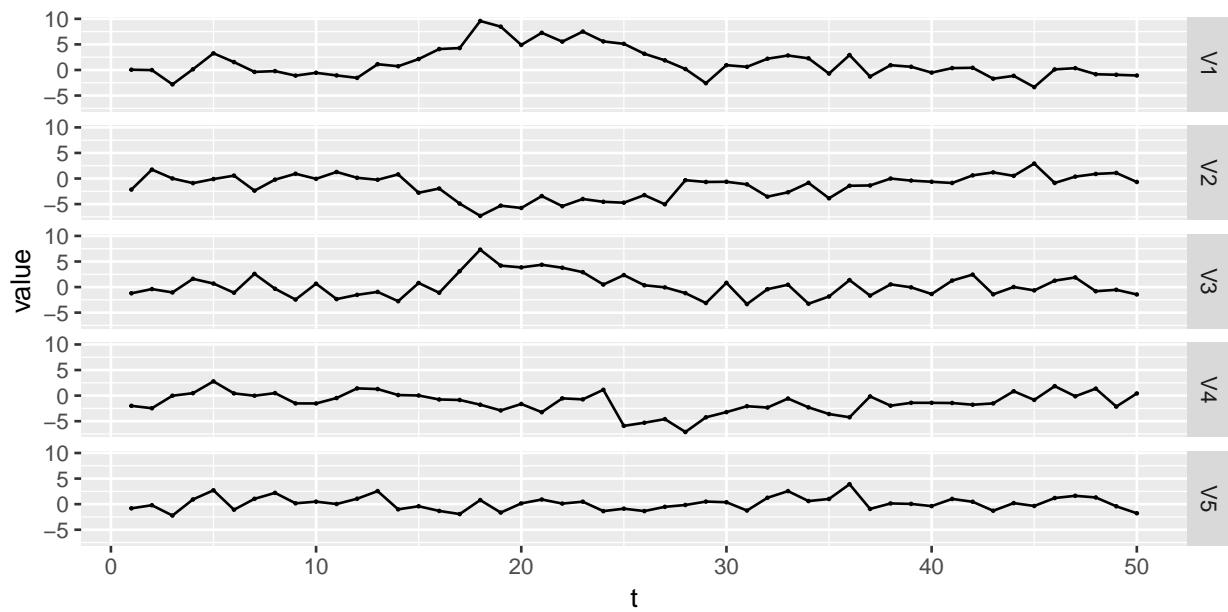


Figure 8.1: Simulated timeseries of 5 variables

8.2.1 Contemporaneous and Directed Correlations

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```
# code snippet 9.2: plotting symptom networks
Res <- graphicalVAR(data = d, gamma = 0,
                      nLambda = 10, verbose = FALSE)

# Show networks
```

```
plot(Res, title = FALSE)
```

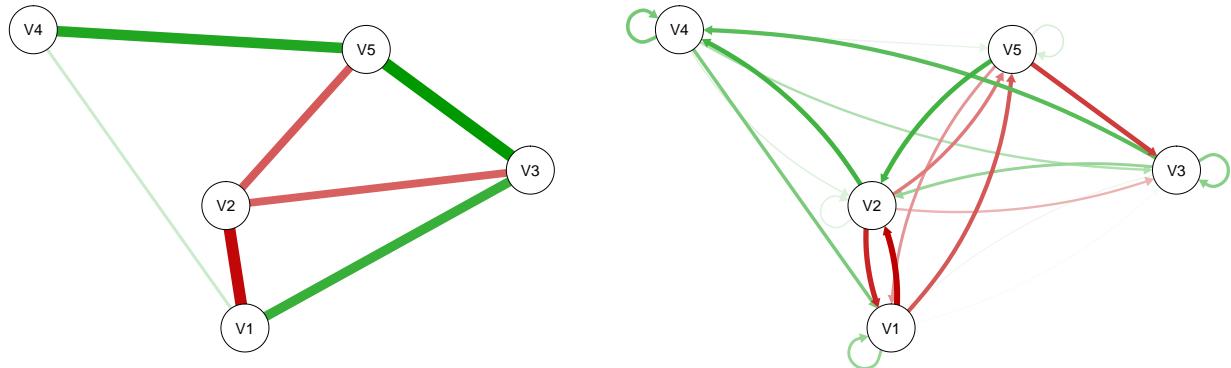


Figure 8.2: Partial Contemporaneous Correlations (left) and Partial Directed Correlations (right).

8.2.2 Node Analysis

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- Betweenness
- Closeness
- Strength

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- InStrength
- Outstrength

```
# code snippet 9.3: Node Centrality plots
library(qgraph)
centralityPlot(qgraph(Res$PCC, DoNotPlot = TRUE))
centralityPlot(qgraph(Res$PDC, DoNotPlot = TRUE))
```

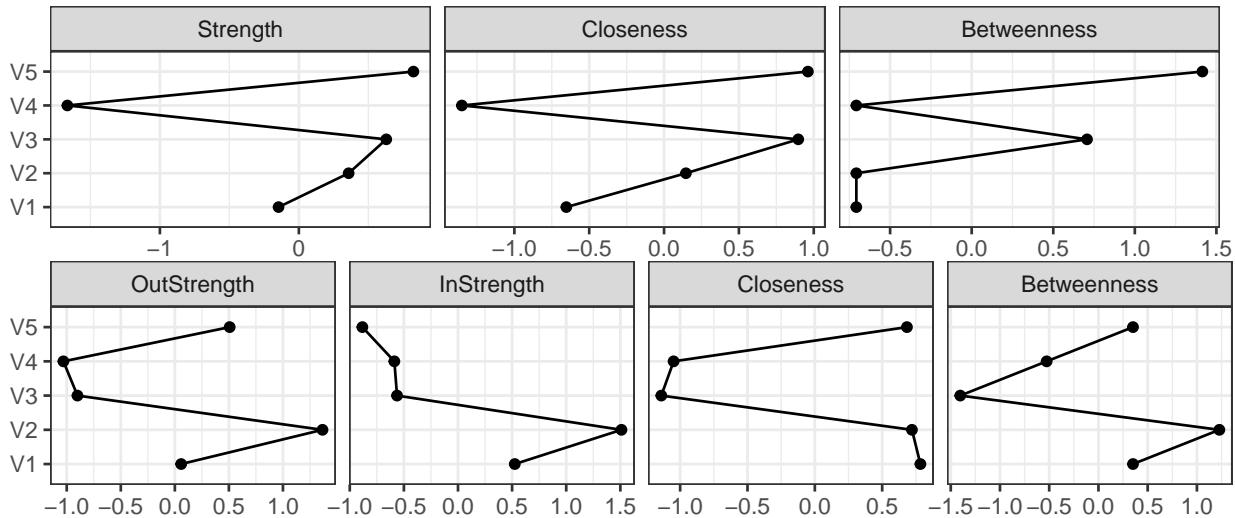


Figure 8.3: Centrality plot of Partial Contemporaneous (top) and Directed (bottom) Correlations.

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8.3 Fitting Networks on Multiple Subjects Repeated Measures Data

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```
# code snippet 9.4: Fitting symptom networks of multiple subjects
library("m1VAR")

Model <- m1VARsim(nPerson = 30, nNode = 5,
                   nTime = 50,    lag = 1)

fit1 <- m1VAR(Model$data,           vars = Model$vars,
               idvar = Model$idvar, verbose = FALSE,
               lags = 1,                 temporal = "correlated")
```

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```
# code snippet 9.5: plotting symptom networks of multiple subjects
layout(matrix(c(1:6), ncol = 2, byrow = TRUE))

plot(Model, "contemporaneous", layout = "circle", verbose = FALSE)
```

```
plot(fit1, "contemporaneous", layout = "circle", verbose = FALSE)

plot(Model, "temporal", layout = "circle", verbose = FALSE)
plot(fit1, "temporal", layout = "circle", verbose = FALSE)

plot(Model, "between", layout = "circle")
plot(fit1, "between", layout = "circle")
```

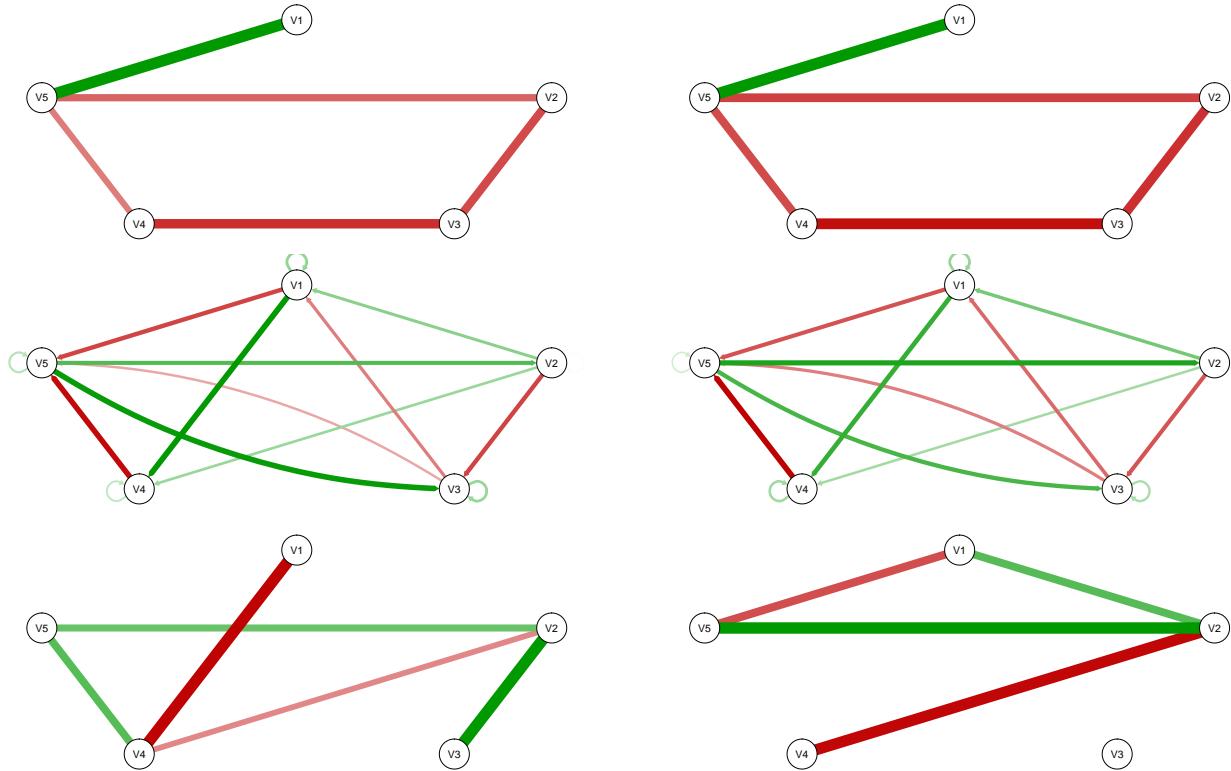


Figure 8.4: True (left) vs estimated (right) contemporaneous (top), temporal (middle) and between-subject relationships (bottom)

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8.4 Discussion

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8.4.1 Pitfalls of Network Analysis

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8.4.2 Subsection

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Part IV

EMA Outcomes

Chapter 9

Mood

Mood is a common outcome in EMA research (Myin-Germeys et al., 2016; Desmet et al., 2016). Having respondents rate their mood during the day allows researchers to assess mood fluctuation over time or reactivity to events and daily-stressors (Wenze and Miller, 2010). Often, it is studied in relation to depressive symptoms and mood disorders (aan het Rot et al., 2012). In addition, mood can be linked to other variables, such as substance abuse (Kirchner and Shiffman, 2013; Serre et al., 2015), somatic health (Engel et al., 2016; Moore et al., 2016) or activity patterns (Dunton, 2017; Marszalek et al., 2014).

The definition of mood varies across studies. Usually the concept refers to a general affective state such as arousal or valence. Following this line of reasoning, a distinction can be made between mood states (e.g. irritable, cheerful, relaxed, etc.) and discrete emotions (e.g. happy, sad, anxious, etc.), where moods are thought to be less specific and more subjective, enduring and related to context (Beedie et al., 2005; Cranford et al., 2006; Desmet et al., 2016).

Depending on the study focus and research questions, mood measurement can be operationalized in several ways. Therefore, it is vital to consider the goal of measuring mood in your own study and to choose an operationalisation that matches your hypothesis and theoretical framework. In this chapter, we will discuss the most commonly used options: 1) unidimensional mood assessment, 2) the ‘bag of items’ approach, and 3) dimensional models, namely the Circumplex model and Negative and Positive affect (NA/PA).

9.1 Unidimensional mood assessment

Perhaps the most seemingly straight-forward method to measure mood is to ask ‘face-valid’ unidimensional questions such as “How is your mood right now” (van Ballegooijen et al., 2016) or “How are you feeling right now” (van de Ven et al., 2017).

Respondents usually rate these questions on a Visual Analogue Scale (VAS), aimed to indicate mood intensity. Typically, VAS scales will range from zero (low or worst mood) to 10 or 100 (good or best mood). Keep in mind that the middle of a VAS scale (e.g. 5 or 50) is generally considered a negative result, and only scores above 6 or 60 are considered acceptable or positive mood states (Groot, 2010). In order to address this issue, some researchers have proposed to use VAS-scales ranging from -1 to 1, with 0 as a neutral centre. However, such a scale implies a mood state that ranges from negative to positive, rather than absent to present. Another alternative is to use Likert scales, where the scale centre often reflects a neutral response.

Plotting data from an unidimensional item in a graph is an easy way to visually inspect within-subject change in general mood:

```
# code snippet 9.1: plotting data over time
library(ggplot2)
library(emaph)
```

```
plotmood_down <- ggplot(csd, aes(x = date, y = as.numeric(mood_down))) +
  geom_smooth(method = "loess", span = .05, se = FALSE, colour="dodgerblue4") +
  geom_point(size = .3, alpha = .3, position = position_jitter(height = .1),
  colour="dodgerblue2") + scale_x_date() + scale_y_continuous(breaks = 1:7) +
  xlab("Time") + ylab("Mood")
print(plotmood_down)
```

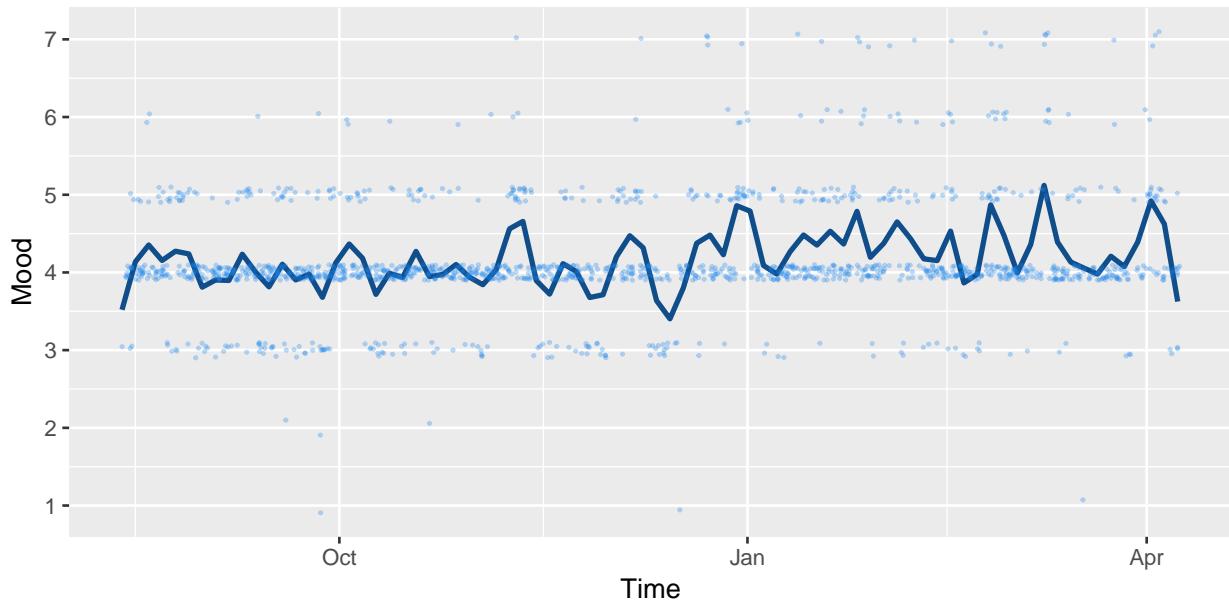


Figure 9.1: 34 weeks of mood data, from a single participant

9.1.1 Bipolar unidimensional items

Another option to assist respondents with the interpretation of single mood items, is to use a bipolar scale. These items place two opposing mood states at each end of the scale, for example by asking “Please rate your current mood on a scale of 0 to 100, on which 0 indicates happy, and 100 indicates sad” (van Rijssbergen et al., 2014). This does assume that the opposing mood states, such as happy and sad, are mutually exclusive and thus cannot occur simultaneously. The bipolar-unidimensional method was shown to be able to predict time to relapse over 5.5 years in recurrently depressed out-patients, with 6.3% of variance in time to relapse explained. This percentage was comparable to that of the HAM-D (Rijssbergen et al., 2012). Also, the scale was able to detect relapse in patients with recurrent Major Depressive Disorder (based on SCID-I interview) at a cut-off score of 55, and outperformed the HAM-D and IDS-SR. However, 47% of patients indicated by the VAS scale did not fulfil formal criteria for relapse (van Rijssbergen et al., 2014).

9.2 Bag-of-Items

In order to make sure all constructs of interest are measured, you can also consider including a number of specific mood items in your EMA questionnaire, rather than one general unipolar item or one bipolar item. For example you can ask respondents “How depressed are you feeling right now” and “How anxious are you feeling right now (Starr and Davila, 2012). This strategy often leads to a ‘bag-of-items’ approach, where single items from various sources, such as existing questionnaires on mood and sleep, are combined into a new EMA questionnaire. A benefit of this approach is that you can select items for which information on

validity and test-retest reliability is available. A downside of the bag-of-items approach is that item scores can only be evaluated separately, rather than providing one overall indication of mood or well-being.

Combining data from multiple items, such as mood and loneliness, in one graph can provide respondents with insight in the interaction between the constructs. In R two variables can easily be plotted together:

```
# code snippet 9.2: Plotting multiple variables in one graph
library(ggplot2)
library(emaph)

combined <- plotmood_down +
  geom_point(data=csd, aes(date, as.numeric(mood_lonely)),
             size = .3, alpha = .3, position = position_jitter(height = .1),
             colour="indianred4") +
  geom_smooth(data=csd, aes(date, as.numeric(mood_lonely)),
              method = "loess", span = .05, se = FALSE, colour="indianred2")
print(combined)
```

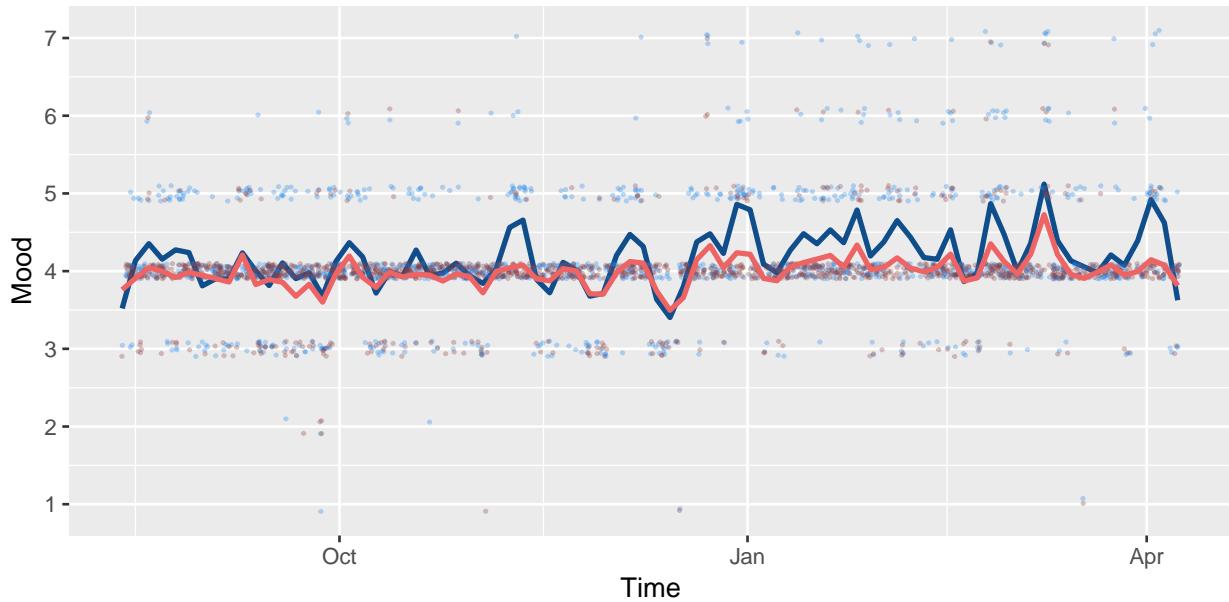


Figure 9.2: 34 weeks of combined mood data, from a single participant

9.3 Multi-dimensional mood assessment

Dimensional models assume that every affective state or emotion should be described by the combined score on (at least) two items, instead of just one. Over the past decades several multi-dimensional models have been specified (for an overview, see Sander and Scherer (2009)). In the context of EMA, researchers most often base their items on the Circumplex model (Russell, 1980) or the Negative/Positive affect (NA/PA) theory (Watson and Tellegen, 1985).

9.3.1 The Circumplex Model

The Circumplex Model of affect (Russell, 1980; Posner et al., 2005) argues that all mood states are a linear combination of two independent, bipolar scales: valence (ranging from low to high arousal) and affect (ranging from unpleasant to pleasant). Combining scores on these scales places the affective states in a circle on one of

four quadrants (9.3). States within one quadrant are believed to be positively correlated, while states in the opposing quadrant are thought to be negatively correlated.

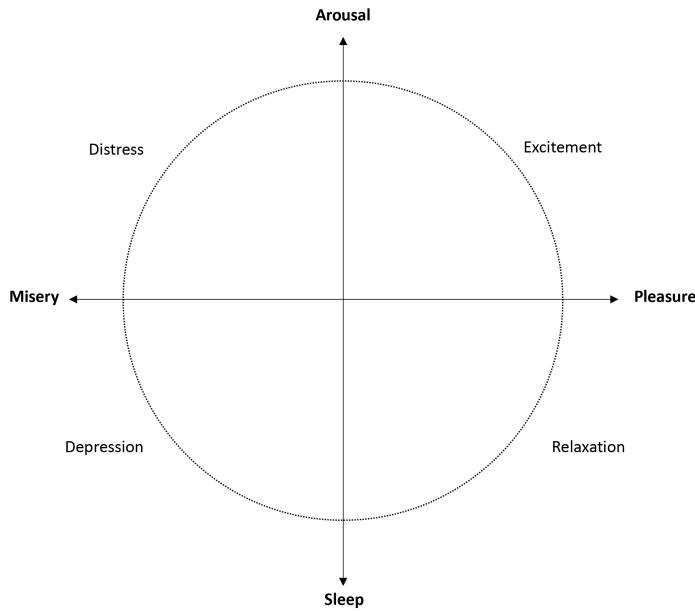


Figure 9.3: Russell's Circumplex model of affect.

There are several options to operationalise the Circumplex model in EMA research. For example, respondents can rate valence and arousal on two VAS scales. The most pragmatic approach is to report both scale scores separately (Asselbergs et al., 2016). Alternatively, scores can be combined to give insight into the quadrant in which respondents' affective states fall:

- Low aroused - unpleasant
- Low aroused - pleasant
- High aroused - unpleasant
- High aroused - pleasant

A downside of the Circumplex model is that the concepts of valence and arousal can be hard to convey to respondents, especially when translated to other languages, such as Dutch. One alternative is to adjust the scale ends, for example using “extreme sleepiness” and “extreme high energy” (Sharar et al., 2016). Another option is to use pictures or emoticons, rather than language. For this purpose, DeSmet and colleagues developed the pick-a-mood scale, which is a pictorial self-report scale. The scale builds on the circumplex model and adds the third dimension “dominance” (level of experienced control over the mood state), rendering eight (instead of four) different mood states and one neutral state (9.4).

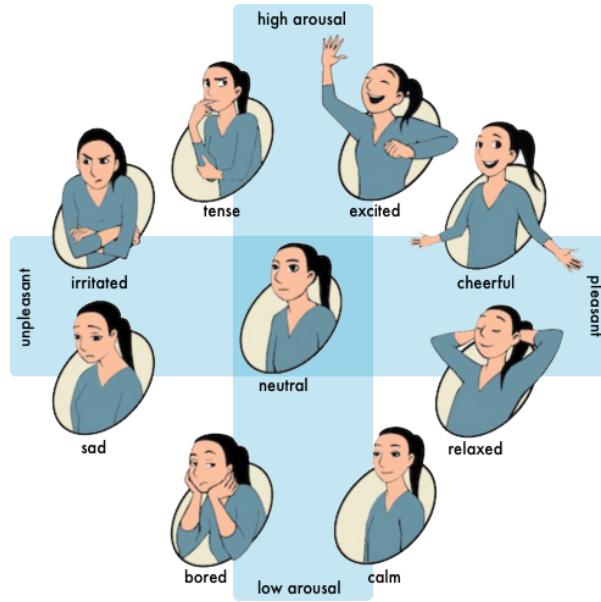


Figure 9.4: The Pick-A-Mood Circle.

9.4 Negative & Positive Affect

Watson and Tellegen (Watson and Tellegen, 1985) also specified the underlying theory of the Circumplex model, arguing that the diagonal quadrants represent Positive and Negative affect (PA/NA) and that these two terms are the main dimensions of affect (Watson and Clark, 1994). PA ranges from sadness to high energy, NA from calmness to distress (Watson et al., 1988). While bipolar-unidimensional assessment assumes that positive and negative affect are mutually exclusive, the PA/NA affect model assumes that these seemingly opposing mood states can occur simultaneously. Watson and Clark (Watson and Clark, 1997) for example, showed a moderate correlation between the two constructs (.32). In order to measure Positive and Negative Affect, a designated Positive and Negative Affect Schedule was developed by Watson, Clark and Tellegen (Watson et al., 1988). Respondents are asked to indicate “to what extent you feel this way right now” on 20 affect items. The scale uses a 5-point Likert-scale, ranging from 1 (very slightly or not at all) to 5 (very) (Watson and Clark, 1994). Items include:

- Negative Affect (10): afraid, scared, nervous, jittery, irritable, hostile, guilty, ashamed, upset, distressed
- Positive Affect (10): active, alert, attentive, determined, enthusiastic, excited, inspired, interested, proud, strong

There are several short-forms available. For example, Wichers and colleagues created a 10-item short-form of the PANAS for their EMA studies. The items were based on the PANAS and their own experience with EMA (Wichers et al., 2012). Using factor analyses, the following 7-point Likert items were chosen for the questionnaire:

- Negative affect (6): insecure, lonely, anxious, low, guilty, suspicious.
- Positive affect (4): cheerful, content, energetic, enthusiastic.

PA and NA were calculated as the average score across all five items and weighted for their factor loadings (Wichers et al., 2012). In R, such a factor analysis can be executed as follows:

```
# code snippet 9.3: Performing a factor analysis
library(dplyr)
library(tibble)
```

```

items <- csd %>%
  select(c(
    "mood_enthus", "mood_cheerf",
    "mood_strong", "mood_satisfi",
    "mood_lonely", "mood_anxious",
    "mood_guilty)) %>%
  scale(.) %>%
  as.tibble(.) %>%
  mutate_all(funs(residuals(stats::arima(., order = c(1,0,0)))))

correlations <- cor(items, use = "complete.obs")
fa = psych::fa(items,
               nfactors = 2,
               rotate = "oblimin",
               fm = "pa",
               scores = "regression")

psych::fa.diagram(fa,
                  simple = TRUE,
                  main = "")

```

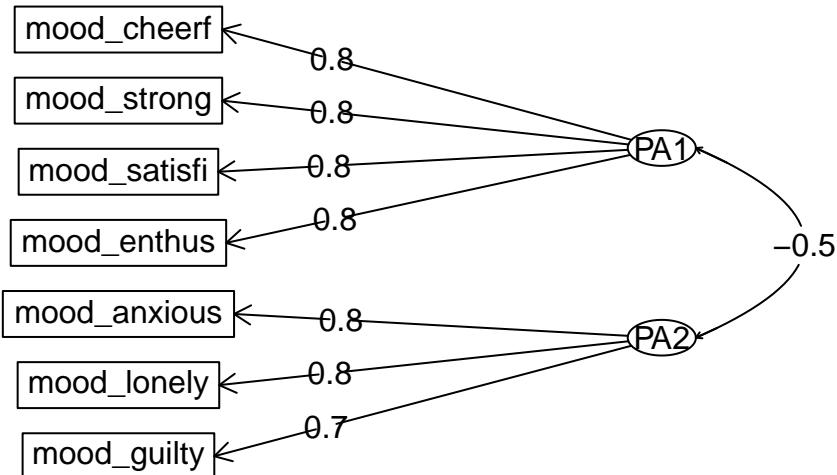


Figure 9.5: Factor analysis of 7 EMA items, revealing two factors: Positive Affect (PA) and Negative Affect (NA).

Chapter 10

Activity

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10.1 Accelerometry

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vertical (Y), horizontal right-left (X) and horizontal front-back axis (Z).

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10.1.1 Data collection

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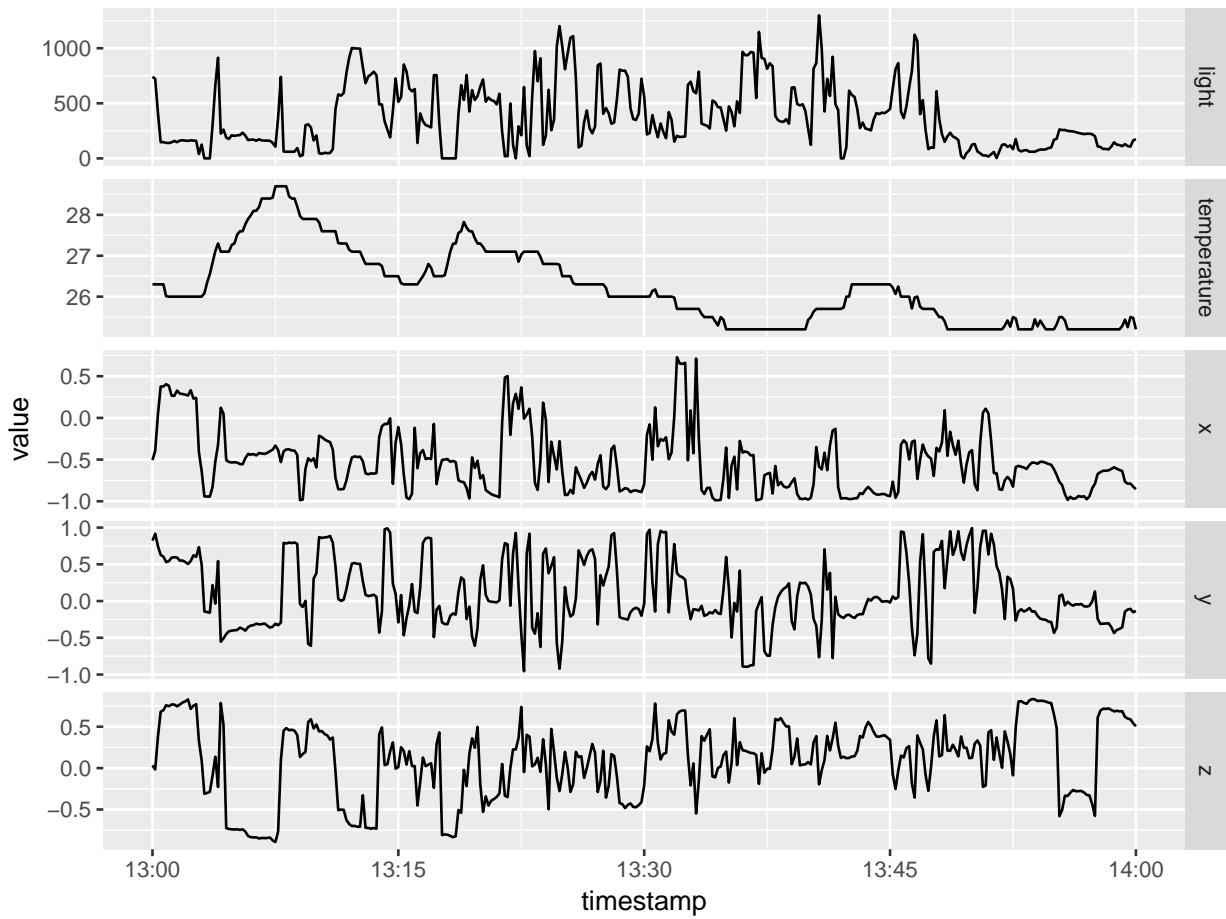


Figure 10.1: One hour of raw data collected with a wrist-worn GENEActive accelerrometer, sub-sampled to 10-seconds epochs (0.1 Hz)

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$$1 \text{ g} = 9.81 \text{ m/s}^2$$

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10.1.2 Data cleaning

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10.1.3 Feature extraction

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signal vector magnitude (svm):

$$\sqrt{x^2 + y^2 + z^2} \quad (10.1)$$

Euclidian Norm minus one (ENMO):

$$\sqrt{x^2 + y^2 + z^2} - g \quad (10.2)$$

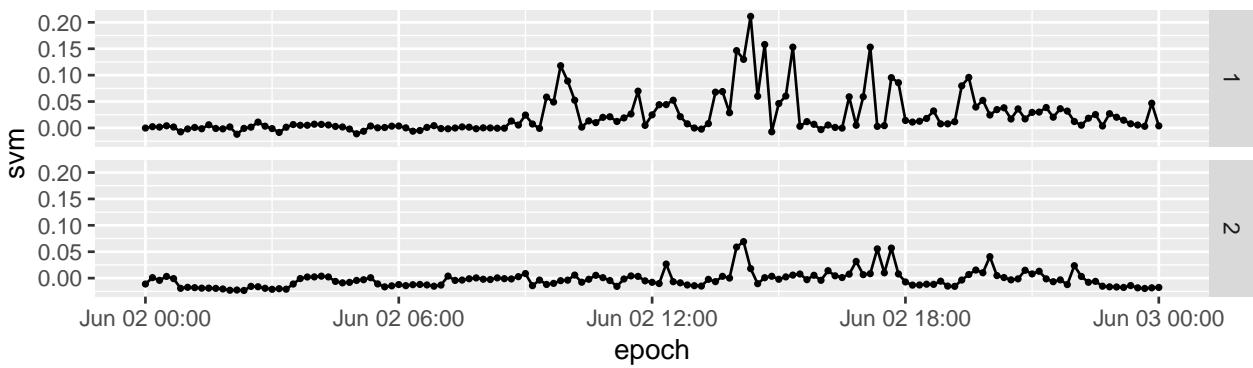


Figure 10.2: One day of data of the two persons in the genea data set, summarised with ENMO, calculated from 15-minute epoch windows

10.1.4 Analysis

Donec sed lectus at sem ultrices commodo. Proin a viverra metus, nec scelerisque odio. Morbi viverra tristique libero vel fringilla. Sed at varius erat, id consequat nibh. Ut eget leo blandit orci posuere tincidunt ac sed erat. Aenean metus metus, eleifend ut facilisis a, fringilla ut neque. Nunc hendrerit cursus eleifend. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Vivamus enim turpis, pulvinar volutpat purus nec, lobortis imperdiet diam.

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10.2 Location analysis

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10.2.1 Global Positioning Systems (GPS)

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```
library(emaph)
library(ggplot2)

d <- subset(locations,
             accuracy <= 100 &
               lon >= 4.80 & lon <= 5.00 &
               lat >= 52.25 & lat <= 52.50)

ggplot(d, aes(lon, lat)) +
  geom_point(alpha = .1, shape = 21, size = 3) +
  facet_wrap(~ id)
```

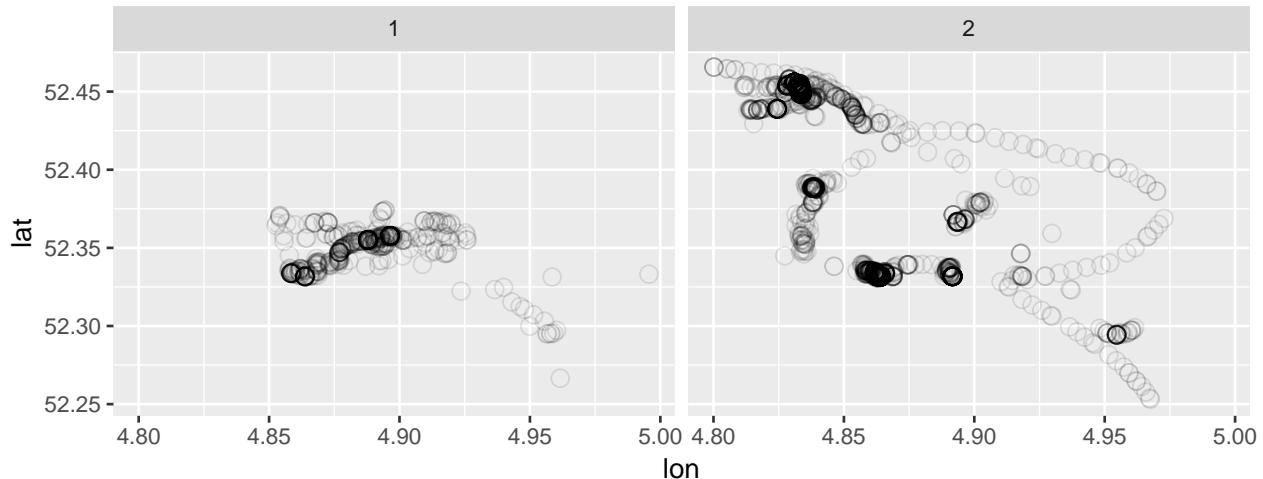


Figure 10.3: Four-week Location history of two people, collected with Google Timeline

10.2.2 Features

Table 10.1: Features of a GPS data set (Saeb et al., 2015).

Name	Formula	Description
Total Distance		Total distance between locations
	$\sum (distance((lat_t, lon_t), (lat_{t-1}, lon_{t-1}))$	
Location variance		Variability of location visits
	$\sigma_{lon}^2 + \sigma_{lat}^2$	
N Places	k-means(loc, lat)	Location clusters
Location Entropy	$-\sum_i p_i * log(p_i)$	Variability in location cluster visits
Normalized Entropy	$\sigma_{lon}^2 + \sigma_{lat}^2$	Entropy, controlled for number of clusters
Home Stay		Percentage of time spent at home
	$Entropy \log(N)$	
Circadian Movement	lomb_scargle(lat / lon)	Consistency of location schedule based on a 24-hour period.

Part V

EMA Case Studies

Chapter 11

Early Warning Signs of Depression

One of the promises of EMA is that it might detect signs of mental health deterioration in an early stage. Subtle changes in time series of mood variables, for example, might signal a depression relapse. If we can detect these changes, preventive interventions can be triggered to avoid the relapse.

But what changes, exactly, should we look for? What are these early warning signs?

11.1 Critical Slowing Down

Critical Slowing Down (CSD) is a concept from dynamic systems theory. In dynamic systems, state transitions are preceded by a change in which the system reacts to disturbances. In a stable state, the system quickly recovers from disturbances. Prior to a transition to a new state, however, the system takes more and more time to recover back to its current state: the variance and auto-correlation of the system increases (Scheffer et al., 2009; Dakos et al., 2008).

In this chapter, we re-analyze data from a study that aimed to demonstrate CSD in EMA-data of a single patient with a history of major depression (Groot, 2010, Kossakowski et al. (2017); Wichers et al., 2016). The patient, a 57-year old male, used EMA to monitor himself during a 239-day single-case double-blind medication reduction trial. During the experiment, he experienced a relapse, and Wichers and colleagues showed how variance and auto-correlation in the EMA data increased, several weeks prior to this relapse. The transition appeared to be preceded by CSD.

We will try to reconstruct the finding, using an alternative analysis strategy. One of the limitations of the Wicherts et al analysis is that autocorrelation was analysed at lag 1 only (i.e., only the correlation between t and $t-1$ was considered). With another analysis technique, called ‘Detrended Fluctuation Analysis’, all lags can be considered.

To conduct the analysis, we need three R packages:

- Raw EMA data of this study were published in the public domain (Kossakowski et al., 2017). We included the data in the emaph package.
- To manipulate the raw data and reconstruct the plots of the article, we are going to use several functions from the tidyverse.
- DFA is implemented in package ‘nonlinearTseries’, so we will need that as well.

```
# Code snippet 13.1: required libraries for the CSD-study re-analysis.  
library(emaph)  
library(tidyverse)  
library(nonlinearTseries)
```

11.2 Plotting the course of depression

Let's take a look at the development of the depressive symptoms of the patient first. These were tapped with weekly assessments of the depression scale of the 'Symptom Checklist-90-Revised' (SCL-90-R; Derogatis, 1994), a well-established self-report questionnaire.

The code below reconstructs Figure 1 of the Wichers et al article. It plots the SCL90-R depression scale score over the time. Around day 120, the depression score increased considerable: the patient experienced a relapse.

```
# Code snippet 13.2: Plot depression score
dep <- csd %>% select(dayno, scl90r_dep) %>%
  filter(!is.na(scl90r_dep)) %>% unique

# plot dep + change point (day 120 in our data)
ggplot(dep, aes(x = dayno, y = scl90r_dep, group = 1)) +
  geom_step() + scale_colour_manual(values = c("black", "red")) +
  xlab("Days") + ylab("SCL-90-R Depression")
```

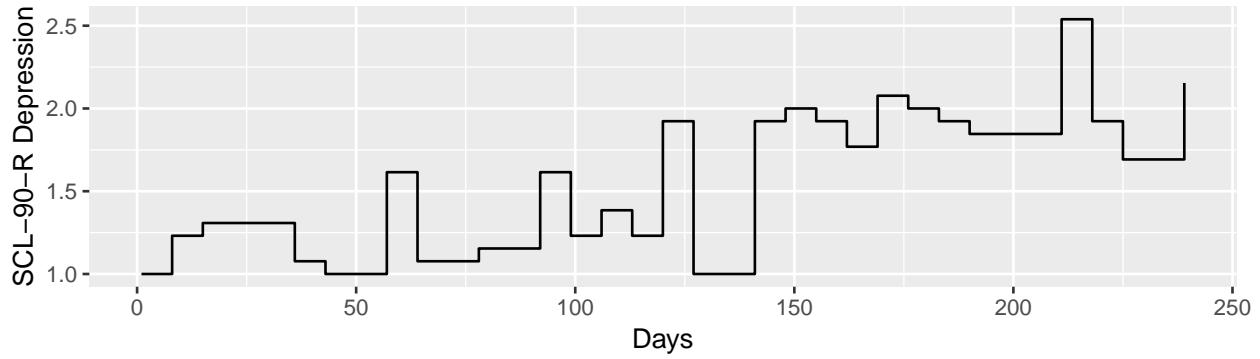


Figure 11.1: SCL-90 depression score, over the study period

11.3 Mental state EMA items

Wichers and colleagues selected 13 items from the full EMA dataset, which they grouped in 5 factors: positive affect (pa; 4 items), negative affect (na; 4 items), mental unrest (mu; 3 items), suspiciousness (su; 1 item), and worrying (wo; 1 item). From these factors, an overall mental state sum score can be calculated.

```
# Code snippet 13.3: mood states calculation

# positive affect
pa_items <- c("mood_enthus", "mood_cheerf",
             "mood_strong", "mood_satisfi")

csd$pa <- csd %>%
  select(pa_items) %>%
  rowMeans(., na.rm = TRUE)
csd$pa <- -csd$pa

# negative affect
na_items <- c("mood_lonely", "mood_anxious",
             "mood_guilty", "mood_doubt")
```

```

csd$na <- csd %>%
  select(na_items) %>%
  rowMeans(., na.rm = TRUE)

# mental unrest
mu_items <- c("mood_irritat", "pat_restl",
              "pat_agitate")
csd$mu <- csd %>%
  select(mu_items) %>%
  rowMeans(., na.rm = TRUE)

# 'single-item' states
csd$su <- csd$mood_suspic
csd$wo <- csd$pat_worry

# global mental state score
csd$ms <- rowSums(csd[c("pa", "na", "mu", "su", "wo")])

```

Rows, in which one or more of the factors have missing values, are removed from the analysis. In a full analysis, options to impute the missing values could and should be considered. However, since only 3 of the 1476 rows have missing item scores, not much is probably lost by running a simple complete-case analysis.

Code snippet 13.3: missing value removal

```

# count number of items with missing items, per row
csd$nna <- csd %>%
  select(matches("mood_")) %>%
  is.na(.) %>% rowSums

# drop rows with missing values
csd <- csd %>% filter(nna == 0)

```

11.4 Running the DFA

```

# code snippet #13c: Running the DFA

# prepare result rows: one row for each day
d <- NULL
d <- csd %>%
  group_by(dayno) %>%
  summarise(ms = mean(ms))

d$ms_dfa = NA

# determine DFA, in a moving window of 32 days,
# in steps of 7 days
window <- 32
for (i in seq(window, max(csd$dayno), 7)) {

  # get the sliding window data
  w <- subset(csd, dayno > (i - window) & dayno <= i)

```

```
# dfa: ms
dfa.analysis <- dfa(time.series = w$ms,
                      npoints = 30,
                      window.size.range = c(10, nrow(w)),
                      do.plot = FALSE)

fgn.estimation <- estimate(dfa.analysis,
                             do.plot = FALSE,
                             fit.col = "blue", fit.lwd = 2, fit.lty = 2,
                             main = "Fitting DFA to fGn")

d$ms_dfa[d$dayno == i] <- fgn.estimation
}
```

11.5 Results

We can now plot the DFA indicator over time, to see whether it peaks prior to the onset of the relapse. As can be seen, the DFA-indicator clearly peaks prior to the onset of the relapse, around day 110. Interestingly, a second peak is reached at the end of the experiment, around day 239, possibly to indicate a recovery from the relapse.

```
# Code snippet 13.8: Plot DFA results
```

```
ggplot(na.omit(d),
       aes(x = dayno, y = ms_dfa,
            colour = factor(dayno < 120),
            group = 1)) +
  geom_point() +
  geom_line() +
  ylab("dfa (60-day window)") +
  xlim(c(0, 250)) +
  guides(color = FALSE)
```

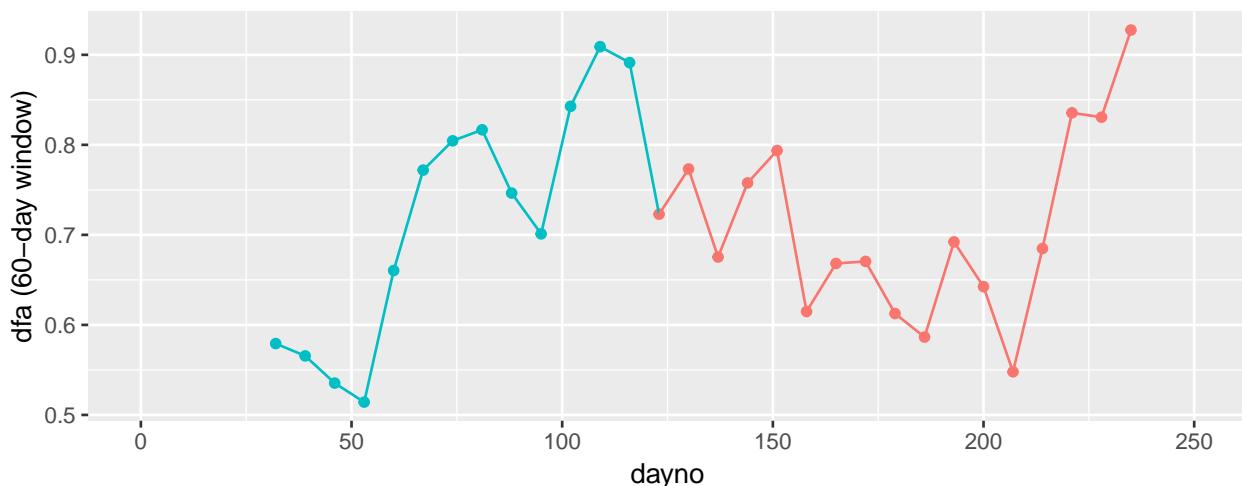


Figure 11.2: Results of the DFA analysis.

11.6 Discussion

Our re-analysis replicates the main finding of the Wichers et al article ((Wichers et al., 2016)): several weeks prior to a depression relapse, as predicted by complex systems theory, the variance and autocorrelation in EMA mood ratings increased.

One swallow does not make summer. Yes, in this case, the DFA-indicator peaked prior to the relapse. This could be a mere coincidence. The predictive power of CSD needs to be confirmed in larger samples. Given the theoretical background, successful applications of CSD in other domains, and the present finding, these studies seem warranted.

Important additional questions remain to be answered. When it predicts a state change, what is the expected delay between this prediction and the change? Does a critical DFA-value exist? Given that critical value, are false positive and false negative rates of this prediction acceptable? These are important questions that should be answered before any clinical application of DFA can be considered.

Re-analysis of data from completed clinical studies, in which EMA data were collected, may be a first step to further explore the value of CSD. One option, for example, would be to re-analyse data from the E-COMPARED study (Kleiboer et al., 2016). In this trial, patients, who were treated for major depression, completed weekly self-report questionnaires (the Patient Health Questionnaire; PHQ-8, Kroenke et al., 2009) and daily EMA mood ratings throughout treatment, which lasted up to 16-week. Since CSD is an indicator of *any* state change (i.e., irrespective of whether the change is clinically “good” or “bad”), theory would predict a (lagged) relationship between CSD (i.e., the DFA-score) and clinically significant changes in PHQ-scores (Jacobson and Truax, 1991).

Potential clinical applications, of course, are clear. If clinically relevant changes can be predicted algorithmically from EMA ratings, automated patient feedback systems could help to prevent pending deterioration or consolidate the path towards recovery.

Chapter 12

CASPAR

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12.1 Section

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```

library(nlme)
library(dplyr)

#
d <- subset(caspar, substr(item, 1, 3) == "PHQ")
d <- d %>% group_by(id) %>%
  mutate(t = difftime(timestamp, timestamp[1], units = "days")) %>%
  mutate(t = as.numeric(t)) %>%
  mutate(t = round(t, 2))

fm1 <- nlme::lme(score ~ t, data = d, random = ~ 1 | id)
summary(fm1)
#> Linear mixed-effects model fit by REML
#> Data: d
#>      AIC      BIC    logLik
#> 5803.774 5824.967 -2897.887
#>
#> Random effects:
#> Formula: ~1 | id
#>          (Intercept) Residual
#> StdDev:     1.142463 1.615498
#>
#> Fixed effects: score ~ t
#>             Value Std.Error DF t-value p-value
#> (Intercept) -0.8725024 0.16003972 1409 -5.451787 0.0000
#> t            -0.0283811 0.01060745 1409 -2.675578 0.0075
#> Correlation:
#>   (Intr)
#> t -0.443
#>
#> Standardized Within-Group Residuals:
#>      Min       Q1       Med       Q3       Max
#> -2.8123009 -0.6657001 -0.2083093  0.6800873  2.9925857
#>
#> Number of Observations: 1480
#> Number of Groups: 70

```

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Chapter 13

Homerange Estimation

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Part VI

EMA Catalogues

Chapter 14

EMA Research Groups within APH

This chapter summarises ongoing EMA research projects within the APH mental health consortium, as a guide to other researchers looking for nearby EMA-expertise and research collaboration.

Chapter 15

Overview

Table 15.1: Overview of APH EMA research groups.

Name	Focus	URL	Organisation
Bockting group	Depression	claudibockting.com	AMC
CASPAR	Suicide	ilumivu.com	VU
Chronic Fatigue	Chronic Fatigue	—	AMC
FAntasTIGUE	Fatigue	tinyurl.com/ybb7up87	AMC
van der Gaag group	Psychotic symptoms	—	VU
TEMSTEM	Auditory hallucinations	tinyurl.com/ybac6flo	VU
VRETp	Psychotic disorders	psymate.eu	VU
Huibers group	Depression	—	VU
IMPACT	Heart failure	impactonderzoek.nl	AMC
MERITS	Type 1 diabetes	-	VuMC
Moodbuster/ E-COMPARED	Depression	ict4depression.eu	VU
NESDA	Depression	nesda.nl	VuMC / GGz InGeest
Psychosystems	Symptom Networks	psychosystems.org	UvA
RADAR-CNS	Depression	radar-cns.org	VuMC / Ggz InGeest
van Someren group	Sleep	https://herseninstituut.nl/onderzoek/onderzoeksgroepen/van-someren-groep/vu-ams.nl	AMC
VU-AMS	Stress & emotion	—	VU

15.1 The Bockting group

Prof. dr. Claudi Bockting is a professor in clinical psychology at the psychiatry department of the AMC location of Amsterdam UMC and the Rijksuniversiteit Groningen. Her group focuses on treatment and relapse prevention of (severe) depressive disorder and related common mental health disorders.

Aspect	Description
Project team	Claudi Bockting, PhD; Yvonne Stikkelbroek, PhD; Gerard van Rijsbergen, PhD
APH site	AMC, Rijksuniversiteit Groningen
Topic	Depression
Status	Ongoing
Target populations	Adults with depression, remitted recurrently depressed individuals
Platforms used	Psymate, Roqua, 'Imagine your mood' app (TEMPEST software)
EMA active	<p>1) Imagine your mood study (2012-2017): The randomised controlled study aimed to evaluate relapse in remitted depressed patients who either continue or taper antidepressant medication with or without preventative cognitive therapy (three conditions). Participants were prompted 10 times per day, 3 days a week, for 8 weeks. Prompts were sent randomly within fixed time-intervals. EMA items were scored on VAS scales (0-100) and include mood, positive affect (PA, 5 items) and negative affect (NA, 9 items) 0 to 100 VAS scales (average score for PA and NA) and mental imagery (2 items).</p> <p>2) StayFine study (ongoing, http://stayfine.nl): the randomised controlled study aims to prevent relapse in young people (12-23) with remitted anxiety or depression. The app contains a monitoring function (diaries), which is used for 3 weeks at each assessment (0,3,6,12,24 and 36 months). Half of participants will also gain access to an EMI function, with tailored content (based on Preventive Cognitive Therapy) and a chat-function with peers, guided by an expert patient counsellor.</p>
EMA passive	In the StayFine study, wristwatches (Polar) will be used to measure activity.
Data management	How is data stored (cloud, server, locally), under an ID or actual patient name, who moderates the server, how much time do patients have to answer the prompts (in minutes)
Project goals	Prevent relapse of anxiety and depression, and improve quality of life.
Results	The VAS mood scale that was used in the imagine your mood study ('Please rate your current mood on a scale of 0 to 100', on which 0 indicates 'happy', and 100 indicates 'sad') (van Rijsbergen et al., 2014), was shown to have a high positive predictive value without any false negatives at a cut-off score of 55. Compared to the HAM-D17 and the IDS-SR, the VAS also was a better predictor of current relapse status, as measured by the SCID-1 interview (variance explained for VAS: 60%; HAM-D17: 49%; IDS-SR: 34%).
Lessons learned	<p>1) Roqua proved not to be the preferred EMA method in adolescents, because SMS messages (prompts) were not noticed due to infrequent use of SMS. In addition, adolescent participants preferred using designated apps to websites. 2) It is important to evaluate the value of EMA data more thoroughly (usability, reliability, specificity). For many self-report EMA items it remains unclear which construct is measured. 3) There is a need for scientific research examining existing applications. 4) APH should consider joining forces to develop a shared system (website and mobile application) that has a back-office, so that it can be adapted to fit the requirements of different projects.</p>
Website	www.stayfine.org ZonMw summary claudibockting.com

15.2 The CASPAR Project

The Continuous Assessment for Suicide Prevention And Research (CASPAR) study (2016-2010) aims to evaluate the feasibility of mobile safety planning and daily mobile self-monitoring in routine care treatment

for suicidal patients, and to conduct fundamental research on suicidal processes (Nuij et al., 2018).

Aspect	Description
Project team	Wouter van Ballegooijen, PhD; Chani Nuij, MSc.; Ad Kerkhof, PhD; Jan Smit, PhD; Heleen Riper, PhD
APH site	Vrije Universiteit Amsterdam, VUmc, GGZ inGeest
Full title	Continuous Assessment for Suicide Prevention and Research
Topic	Smartphone-enabled safety planning, self-monitoring, suicide
Status	Ongoing, 2016 - 2020
Target population	Adult suicidal patients (N = 80) with major depression or dysthymia and suicide risk in mental health care
Platform used	Ilumivu (https://ilumivu.com)
EMA active	Participants are prompted 3 times a day to answer 8 self-report items (e.g. 'I feel sad'). Items are based on existing questionnaires, such as the Patient Health Questionnaire (PHQ-9) and are rated on a 7-point Likert-scale, ranging from 'Not at all' to 'Very much'. Measured concepts include mood, rumination, hopelessness, defeat, entrapment, burdensomeness, belongingness, impulsiveness, suicidal imagery and suicidal ideation. Results are presented to patients in separate graphs.
EMA passive	Location data are gathered to indicate movement patterns and daily rhythm. Planned variables include accelerometer and smartphone usage patterns. These data are not visible to patients.
Data management	Patients receive a unique code to log in to the app. No names, phone numbers or other contact information are stored on the Ilumivu server. Patients are encouraged to show their graphs to their clinicians during treatment sessions.
Project goals	The primary objective of the CASPAR study is to test the feasibility of smartphone-based safety planning and real-time self-monitoring for patients with major depression or dysthymia and suicide risk in mental health care. Feasibility will be operationalised in terms of uptake, usage, acceptability, usability and patient satisfaction. EMA data will be used to: (a) empirically validate hypothesised psychological processes and stages of suicide pathways (b) identify individual pathways to suicidal behaviour (c) profile types of suicidal individuals.
Results	An interactive safety plan that patients can access 24/7, increased disease awareness of patients due to self-monitoring, and input for the national and international field of mental health care by sharing our results and our data, ultimately contributing to more personalised interventions according to precision medicine principles, and more effective suicide prevention.
Lessons learned	Constructing the right EMA items takes time. The constructs that you need to measure should be based on theory. Translate these concepts to momentary items in collaboration with EMA experts. Then test extensively among your target group
Website	ZonMw summary

15.3 Study on Chronic Fatigue Syndrome

The Study on Chronic Fatigue Syndrome (CFS) focusses on CFS patients that are treated at the Expert Centre for Chronic Fatigue (ECCF). The study aims to examine determinants of chronic fatigue.

Aspect	Description
Project team	Margreet Worm-Smeitink, MSc; Judith Rosmalen, PhD; Anne van Gils, MSc; Rei Monden, PhD; Hans Knoop, PhD
APH site	AMC
Topic	Time series study on patients with chronic fatigue syndrome
Status	Completed (Period of data collection: October 2015 - April 2016)
Target population	New patients attending the Expert Centre for Chronic Fatigue for diagnosis of chronic fatigue syndrome (ECCF, n = 102)
Platform used	RoQua (https://www.roqua.nl)
EMA active	Participants were asked to complete an e-diary, 5 times a day for 2 weeks. The times were fixed in consultation with the participant, with a 3-hour break in between each assessment. The e-diary assessed concepts such as fatigue, pain, anxiety, depression, activity (physical, mental, social), focus on fatigue, fatigue catastrophising, self-efficacy, fear avoidance, and social incomprehension. Items were scored a 5-point Likert scale.
EMA passive	Participants wore an actometer (actigraphy) during the period when the self-reports were collected.
Data management	Participants received a link to the (web-based) e-diary via an SMS to their smartphone. Participants needed to have internet/wifi access to log in to complete the questionnaire.
Project goals	The objective of this study was to conduct time series analyses on fatigue, namely to investigate whether there are differences in perpetuators of fatigue between individual patients.
Statistical methods	The R auto-var package was used to conduct network analyses
Results	Results are forthcoming. Determinants of fatigue will be identified with the aim of personalizing treatment of fatigue in patients with CFS.
Lessons learned	Think carefully beforehand which variables to include in EMA, as assessing too many variables will make it difficult to determine which variables to include in the model. This also makes interpretation of results difficult.

Try to relate EMA to other (traditional) clinical parameters to determine relevance of the new type of assessment. Prepare a clear and detailed guideline/handbook for colleagues who will assist in including participants and be aware of potential problems with the EMA app. Clear guidelines will ensure that colleagues stay motivated to include participants in the study. No METC approval was required, as this type of EMA studies do not fall under the scope of Medical Research Involving Human Subjects (WMO). It was not feasible for all participants to have access to the internet at all times that the Roqua questionnaire needed to be filled-in. This caused some data to be missing. |

15.4 Moodbuster and E-COMPARED (EU)

E-COMPARED is a European study (EU CIP), executed in nine countries, comparing the costs and effects of blended treatment (combined internet, mobile and face-to-face treatment) with Cognitive Behavioural Therapy (CBT) in routine and specialised mental healthcare for depression. Within the project, the Moodbuster application was used to gather EMA data on patient variables, such as depression and sleep. Patients were presented personalised reports on their mental and physical health over time (Kleiboer et al., 2016).

Aspect	Description
Project team	Heleen Riper, PhD; Jan Smit, PhD; Jeroen Ruwaard, PhD; Stasja Draisma, PhD.; Lise Kemmeren, MSc.
APH site	Vrije Universiteit Amsterdam, GGZ inGeest

Aspect	Description
Full title	Moodbuster
Project	Developed within the European FP7 project “ICT4Depression” Applied in Horizon 2020 FP7 EU-project “European COMPARative Effectiveness research on blended Depression treatment versus treatment-as-usual” (E-COMPARED)
Topic	Ecological Momentary Assessment alongside formal depression treatment
Status	Data collection completed (2012 – 2018)
Target population	Patients with Major Depressive Disorder in primary and specialised mental health care
Platform used	Moodbuster [http://www.ict4depression.eu/moodbuster/]. The platform is currently available in five languages: English, Dutch, German, Polish and French
Moodbuster	The original Moodbuster platform aimed to provide unguided self-help treatment to people with depressive symptoms. ICT4depression had 4 components: 1) physiological sensors aimed ad acceleration data and sympathetic nervous system responses (chest strap and glove), 2) a medication adherence monitor, 3) a website with treatment modules, automated feedback messages and tools (calendar, mood graph, sensor chart, ratings), and 4) Moodbuster (Android) app for access to treatment modules and mood ratings, location and activity tracking, and aggregation of physiological sensors
E-COMPARED	Within the E-COMPARED study, the Moodbuster website and application were used. A therapist portal was added, in order to allow therapists to monitor patients' progress and send feedback messages.
EMA active	Patients rated 7 items on a visual analogue scale (VAS), ranging from 0 (low) to 10 (high). Concepts that were measured, included: sleep, mood, worrying, self-esteem, activities (2 items) and social contacts. Items focused on current state, for example by asking “How is your mood right now”. Mood was assessed once a day, for the duration of treatment. Prompts were sent at a random time point between 10:00 and 22:00. At the beginning and during the final phase of treatment, patients received two additional prompts per day for one week. In the morning (around 10:00), sleep, worrying and self-esteem items were assessed. In the evening (around 22:00), these questions were repeated, along with the activity and social interaction items.
EMI	The platform sent out automated reminders for scheduled activities and therapist appointments, and sent tailored automated motivational text messages. The aim of EMI was to keep patients engaged with Moodbuster (rate mood and log in on platform).
Data management	Patient data was stored on a server under a unique participant ID number. Patients with an iPhone were offered an android phone for the duration of EMA. Participants had a 60-minute window per assessment to complete the items. Patients and therapists accessed the platform with a personalised log-in. On the platform, they could access an interactive graph displaying mood ratings over time.
Results	Results are forthcoming. Patients (n=193, in NL, FR, DE and PL) on average rated their mood for 14 weeks during treatment (use of mobile application). The total number of mood ratings was 95 on average (range 40-148).
Lessons learned	Make sure to extensively pilot the application before the start of actual data collection. Not all prompts were received by patients. Reasons for this are still unclear, most likely it was caused by updates of the application.
Website	http://www.ict4depression.eu/ Final evaluation report https://www.e-compared.eu/

15.5 FAntasTIGUE

The FAntasTIGUE study examines fatigue in patients with COPD, by evaluating the course of fatigue, precipitating/perpetuating factors and hospitalisation. A secondary aim is to identify diurnal differences in fatigue by using EMA (Goërtz et al., 2018).

Aspect	Description
Project team	Yvonne Goërtz, MSc; Zjala Ebadi (from July 2018), MSc; Melissa Thong, PhD; Daisy Janssen, MD, PhD; Jeanette Peters, PhD; Jan Vercoulen, PhD; Chris Burtin, MSc; Yvonne Meertens-Kerris; Arnold Coors; Jean Muris, MD, PhD; Emiel Wouters, MD, PhD; Judith Prins, PhD; Mirjam Sprangers, PhD Martijn Spruit, PhD
APH site	AMC (in collaboration with Ciro-Horn, Maastricht UMC, Radboud UMC, and Hasselt University)
Full title	Fatigue in patients with chronic obstructive pulmonary disease: FAntasTIGUE study
Topic	Management of fatigue in patients with COPD
Status	Ongoing, 2017-2020
Target population	Patients with clinically stable chronic obstructive pulmonary disease (proposed: n=60)
Platform used	Psymate (https://psymate.eu)
Study design	Longitudinal with 4 data collection periods (baseline, 4, 8, 12 months)
EMA active	For each data collection period, participants are prompted 8 times a day at random moments between 7.30am and 22.30pm, for 5 consecutive days, to answer 19 items (including 9 contextual items). Measured concepts include fatigue, relaxed feeling, breathlessness, agitation, uncertainty, irritation, satisfaction, anxiety, feeling energetic, and feeling mentally fit. Items are rated on a 7-point Likert-scale, ranging from ‘Not at all’ to ‘Very much’. In addition, participants are asked to complete a morning questionnaire soon after they awaken to assess the quality of their sleep the previous night. Participants also complete an evening questionnaire assessing the general perception of their day just before going to bed.
Data management	During the data collection period, patients are provided with iPods installed with the EMA application.
Project goals	To capture possible diurnal fluctuations in fatigue.
Results	Future results will guide the development of interventions for the management of fatigue in this patient group.
Lessons learned	The experience with Psymate is generally positive. Queries are promptly answered and we could also tap into the wealth of experience Psymate has in conducting EMA.
Protocol paper	http://bmjopen.bmj.com/content/8/4/e021745.long

15.6 The van der Gaag group

15.6.0.1 TemStem

The TemStem project focusses on people who suffer from hearing voices and are obstructed by them in their daily life. Study participants install an app that contains both an EMI and EMA function, aiming to reduce distress and dysfunction caused by auditory verbal hallucinations (Jongeneel et al., 2018).

Aspect	Description
Topics	Psychosis, auditory hallucinations, social participation in people with schizophrenia.
Project title	Temstem
Project team	Mark van der Gaag, PhD; Alyssa Jongeneel, MSc; David van den Berg, PhD; Dorien Scheffers, MSc
APH site	Vrije Universiteit Amsterdam, VUmc, GGZ inGeest, Parnassia Psychiatric Institute
Status	Ongoing, March 2016- July 2018
Target population	People who suffer from hearing voices and are obstructed by them in their daily life
Platform	Temstem application. Developed by Reframing Studio, in collaboration with Parnassia Psychiatric Institute and TU Delft. Available for IOS and Android
EMI	Mobile application (Temstem) focuses on reducing distress and dysfunction caused by auditory verbal hallucinations (AVH). Components: 1) coping: addressing verbal working memory phonological loop with a language task, thereby blocking the hearing of voices, 2) positive reinforcement: decreasing self-reported negative self-esteem themes, 3) treatment: reducing emotional response to memories associated with voices by taxing the auditory working memory during recall of negative auditory memories (as in EMDR therapy).
EMA active	Users are encouraged to fill-in 9 self-report items on a daily basis. Outcomes include: 1) hearing voices: 6 items (e.g. "Today, the voices were disturbing"), 2) mood, 3) self-esteem, 4) the use of Temstem ("I used Temstem today"). Items are rated on a 7-point Likert-scale. Items are based on existing EMA questionnaires. Results are presented to users in separate graphs, in order to support users in gaining insight in the pattern of AVH over time, or after use of Temstem.
Project goals	Examine the effect of the app on distress and dysfunction in a RCT. Investigate the effect of Temstem on frequency and severity of AVH, to determine working mechanisms, to identify predictors and mediators of effects, and to test the usability of Temstem.
Results	Reduce distress and dysfunction caused by auditory verbal hallucinations
Data management	Data is stored on a server hosted by Service Heroes (via Reframing Studio), under users' unique download numbers. Stored variables include, among others, scores of vividness of AVH pre and post use of Temstem, data on application use (duration), used function (e.g. 'Silencing' function which focuses on coping, or 'Challenging' function which is based on dual tasking), and how users feel when they hear voices. Users can choose to provide additional information on age, gender, which county in the Netherlands they are currently located, how they found the app, and why they want to use it (e.g. because they hear voices, because they are a clinician and they want to learn more about the app to support clients, etc.). Clinicians cannot access user data or graphs. Researchers can, but only in big data files. To see users' personal data (e.g. how many times they used the app, how vivid the voices were before and after the use of Temstem, etc.) researchers need the users' unique download number.
Lessons learned	Users need internet to use the app, because it works on an online platform. However, not all our users have wireless internet. If we had known this in time, we would have chosen to run it offline. Other lessons we have learned are that you have to resolve bugs as soon as possible, because otherwise it may take a long time before it is fixed. Be very explicit in what you want and expect from the app developers, even when you think that it is quite logic and clear.
Website	https://www.parnassiagroep.nl/hoe-wij-helpen/online-hulp/temstem

15.6.0.2 VRETp trial

The VRETp trial examined virtual-reality-based cognitive behavioural therapy for patients with a psychotic disorder, aiming to improve social functioning and reducing paranoid ideation. EMA was used to measure change in these outcomes (Pot-Kolder et al., 2016).

Aspect	Description
Project	Effect of virtual reality exposure therapy on social participation in people with a psychotic disorder (VRETp)
Project team	Mark van der Gaag, PhD; Roos Pot-Kolder, MSc; Wim Veiling; Chris Geraets
APH site	Vrije Universiteit Amsterdam, VUmc, UMC Groningen
Status	Completed, 2013-2016
Target population	Patients (n = 116) with psychotic disorders who fear social situations.
Platform	PsyMate (http://www.psymate.eu/)
Study information	EMA data was collected as part of a RCT comparing treatment as usual plus virtual reality therapy (VR-CBT) to treatment as usual for outpatients suffering from a psychotic disorder and paranoid ideation. EMA was used to assess the primary outcome social participation.
EMA active	1) Anxiety (1 item, e.g. "I feel anxious"), 2) Perceived social threat (4 items, e.g. "In this company, I feel accepted"), 3) Paranoia (3 items, e.g. "I feel suspicious"), and 4) Time spent with others (max. 3 multiple choice items inquiring about type of company (nobody, family, non-family, etc.). Patients were prompted 10 times a day, during 6 days. Anxiety, threat and paranoia Items were rated on a 7-point Likert scale, ranging from 1 ("not at all") to 7 ("very"). Reports had to be completed within 15 min of the beep. EMA items were used in previous studies (Collip et al., 2010).
Data management	To be included in the analysis, participants had to complete diary entries for at least one-third of the beeps (i.e., a minimum of 20 measurements). Because the PsyMate application was not finished at the time of the trial, participants were provided with a small palmtop device for the duration of EMA. Data was extracted with 4D software. Time spent with others was defined as the percentage of time participants were in company of others (excluding mental health care professionals). Other EMA measurements were only used when a participant reported being in a social situation. Information was stored on the PsyMate server, under a user-specific PsyMate-ID number. Researchers had access to a file matching study-ID to PsyMate-ID numbers, which allowed matching of information acquired via EMA with information acquired with regular self-report measures during the RCT study.
Project goals	Testing the effects of virtual-reality-based cognitive behavioural therapy (VR-CBT) on paranoid thoughts and social participation via momentary assessment
Results	All 116 participants completed EMA measurements at baseline (mean number of completed self-assessments 46.1, SD 13.3), 96 participants completed the post-treatment assessment sufficiently (43.1, SD 10.1), and 87 participants completed the follow-up (43.2, SD 11.1). The trial results suggest that the addition of VR-CBT to standard treatment can reduce paranoid ideation and momentary anxiety in patients with a psychotic disorder.
Lessons learned	Participants reported not wanting to explain to others why they were using the palmtop (a small black hand-held computer) as a reason for non-compliance with EMA. This directly interfered with the primary aim, namely assessing social context. An app facilitates measurement without the participant having to explain to others what they are doing

15.7 The IMPACT project

The IMPACT project studies state and trait quality of life in patients with cardiac diseases who have multiple somatic co-morbidities. The project aims to improve the conceptualisation of QoL and enhance the sensitivity and comprehensiveness of its measurement by taking the trait-state distinction and response shift into account (<http://www.impactonderzoek.nl/>).

Aspect	Description
Project team	Iris Hartog, MSc; Justine Netjes (until 2017), MSc; Tom Ooreel (since 2017), MSc; Pythia Nieuwkerk, PhD; Michael Scherer-Rath, PhD; José Henriques, MD, PhD; Hanneke van Laarhoven, MD, PhD; Mirjam Sprangers, PhD
APH site	AMC
Full title	Improving the conceptualisation and measurement of quality of life of patients with multiple chronic morbidities, exemplified by patients with cardiac disease undergoing cardiac intervention
Topic	Quality of life in patients with cardiac disease after undergoing a cardiac intervention
Status	Ongoing, 2016-2010
Target population	Cardiac patients with comorbidities who were scheduled for elective percutaneous coronary intervention (PCI) or elective coronary artery bypass graft (CABG) (N= 37 EMA /320 total)
Platform used	Psymate (https://psymate.eu)
Study design	Longitudinal with three EMA data collection periods: 1. pre-treatment, 2. two weeks after treatment for PCI patients or 3 months post-treatment for CABG patients, and 3. six months post-treatment
EMA active	Participants are prompted to answer nine general and one evening questionnaire per day for seven consecutive days. During the day, patients are beeped randomly between 7.30 and 22.30 hours to complete the general questionnaire. The general questionnaire contains 19 items, including 5 contextual items. Concepts measured include: positive mood (feeling energetic, relaxed feeling, cheerfulness, happy), negative mood (anxiety, sadness, irritation, worry), coronary artery disease symptoms (chest pain, tightness in chest, oppressive feeling on the chest), and general symptoms (tiredness, other types of pain, shortness of breath). Items are rated on a 7-point Likert-scale, ranging from 'Not at all' to 'Very much'. Patients are asked to complete the evening questionnaire just before they go to bed. The evening questionnaire had, besides the general questionnaire, an additional set of questions from the EQ-5D, and the health state of that day. The last item is rated on a visual analogue scale from 0 (worst) to 100 (best).
Data management	Participants were provided with iPods installed with the EMA application during data collection. Or if they preferred, patients could use their own device.
Project goals	The project aims to get a better understanding of the moment-to-moment changes in quality of life and how this compares with changes found in retrospective QoL measurements. The project aims to compare QoL collected retrospectively through online or paper surveys with that collected via EMA. Data collected through EMA can also inform possible changes in daily QoL, taking contextual situations into account.
Statistics	Data will be analysed using vector autoregressive models using R.
METC	METC approval was waived as EMA was not considered a WMO study.
Results	Work in progress, currently exploring the data using network analysis.

Aspect	Description
Lessons learned	To maintain response during follow-ups, it is important to maintain contact with patients between follow-ups. The development and testing of the app can take a significant amount of time, and during the study, updates of the smartphone operating system may lead to new bugs in the app. Due to the amount of data collected via EMA, data cleaning can take up a significant amount of time. The quality of EMA data can be low due to significant amount of missing data. Besides missing data, lack of variation in answers from day-to-day (through use of a Likert scale) could also be an issue. Possible solution is the use of continuous rating scales instead of 7-point Likert scales. Both missing data and lack of variation can be a problem if planning to estimate vector autoregressive models.

15.8 MERITS

The Momentary assessment of patient Experiences in Real life of Insulin Glargine 300 in Type 1 diabetes (MERITS) Study aims to 1) evaluate whether blood glucose variability is associated with changes in wellbeing (mood) during waking time, and 2) assess whether there are individual differences (profiles) with regard to this association.

Aspect	Description
Project team	Frank J. Snoek, PhD; Maartje de Wit, PhD; Daniel van Raalte, MD, PhD; Erik Serné, MD, PhD; Cati Racca, MD; L. Muijs, MSc
APH site	VUMc, AMC
Full title	MERITS - Momentary assessment of patient Experiences in Real life of Insulin Glargine 300 in Type 1 diabetes Study
Topic	Type 1 diabetes, relationship between blood glucose variability (continuous glucose measurement) and changes in mood and energy.
Status	Ongoing proof-of-concept study, 2018 - 2020
Target population	Adult patients (N=70) with type 1 diabetes
Platform used	Illumivu
EMA	Currently under development. Participants will be (randomly) prompted to answer questions on mood (based on POMS questionnaire), diabetes distress, fear of hypoglycaemia and sleep.
Project goals	Explore whether a) blood glucose variability (SD and CV) is related to changes in wellbeing (mood) during waking time, b) if switching to U-300 results in less glucose variability and translates into improved mood over time within patients, c) explore if individual differences (profiles) can be distinguished with regard to the (strength of the) association between glucose variability and changes in mood.

15.9 NESDA EMA Diary Study

The main aim of NESDA (the Netherlands study of Depression and Anxiety) is to examine the long-term (eight-year) course and prognosis and co-morbidity of anxiety and depression in order to improve quality of care and prevent chronicity (Penninx et al., 2008) (<https://www.nesda.nl/>). Within the 9-year follow-up of the NESDA study, EMA was used to assess a variety of research questions, concerning topics such as the dynamic interplay between cognitions, emotions, behaviour and environment in daily life of individuals, the feasibility of EMA in participants with affective disorders, and chronotype and diurnal patterns of activity in depressed versus non-depressed participants.

Aspect	Description
Project team	Femke Lamers, PhD, Brenda Penninx, PhD (VUmc); Hariette Riese (UMCG)
APH site	VUmc, GGZ inGeest
Full title	the Netherlands Study of Depression and Anxiety (NESDA), Wave 6 diary study
Topic	Momentary assessment of people with depressive and anxiety symptoms
Status	Completed, 2015 - 2017
Target population	Selected sample of NESDA participants with symptoms of depression and healthy controls (n=384)
Platform used	RoQua (https://www.roqua.nl/). Participants were prompted with a SMS, which contained a link to the EMA questions
EMA active	The self-report questionnaire contained circa 31 items. Items were rated on a 7-point Likert scale, ranging from 'not [at all]' to 'very'. Participants were prompted five times a day, for two weeks. Constructs of interest were 1) valance (unpleasant to pleasant) and arousal (calm to excited), 2) current state, symptoms of depression/anxiety, physical condition, 3) social context, 4) sleep, 5) daily uplifts/hassles, 6) activities, and 7) substance use. Examples of items were: "I feel down", "I feel cheerful" and "Where are you now" (e.g. at the neighbour's house). In addition, there was an addendum questionnaire with one item inquiring about questionnaire burden and an open-ended question for general comments on circumstances that might influence answers.
Origin of items	The items on valance, arousal and current state have been used in a previous study; the Uncovering the Positive Potential of Emotional Reactivity (UPPER) study (Bennik (2015)). The other items are inspired on earlier EMA studies, such as the work by Mehl and colleagues (Mehl and Conner (2012)), van Os and colleagues (Wichers et al. (2012)) and studies performed at the Interdisciplinary Center of Psychopathology and Emotion regulation (ICPE), such as the Mood and Movement in Daily life (MOOVD) study (Booij (2015))
EMA passive	In order to record the amount of physical activity during EMA monitoring, participants (n=370) were asked to wear an accelerometer (GENEActiv, 30Hz) on their non-dominant wrist 24 hours a day for two weeks. Recording started on the evening prior to the first EMA assessment and continued until the morning after the last assessment. After data collection, participants mailed their watch to the research centre. Data was extracted via a USB with GENEActiv software. EMA started within 31 days after the regular NESDA assessments (face-to-face interview and self-report measures). Participants could use their own smartphone if they had sufficient data, or access to WiFi for at least 80% of the two-week time period. If participants did not have a smartphone, they could borrow one. Patients were briefed on the EMA study during a face-to-face session with a research assistant. Participants were asked to fill in the questionnaire within 15 minutes after the SMS. After 30 minutes a reminder was sent, and after 60 minutes the link would become inactive. Participants needed to answer all questions before the questionnaire could be send to the secured server. Participants received a personalised mood fluctuation report after the data collection period, in order to motivate them to adhere to EMA. Reports were sent via e-mail in a password protected document. Research assistants actively monitored data collection and contacted participants if they missed three consecutive questionnaires. Data were stored in a secured web-environment of the University Medical Centre Groningen (UMCG)
Data management	
Results	EMA data will be used to assess a variety of research questions, concerning topics such as the dynamic interplay between cognitions, emotions, behaviour and environment in daily life of individuals, the feasibility of EMA in participants with affective disorders, chronotype and diurnal patterns of activity in depressed versus non-depressed participants, and MDD subtypes.

Aspect	Description
Website	https://www.nesda.nl/

15.10 The Psycho-systems group

The Psycho-systems group is an UvA based initiative, led by Prof. Dr. Denny Borsboom, focusing on “the development of new methodologies for psychological research using complex systems theory and network models” (<http://psychosystems.org/>).

Aspect	Description
Senior project team	UvA: Denny Borsboom, PhD; Lourens Waldorp, PhD; Han van der Maas, PhD; Sascha Epskamp, PhD; Claudia van Borkulo, PhD; Donald Robinaugh, PhD
APH site	Universiteit van Amsterdam (UvA)
Topic	Complex systems theory and network models
Status	Ongoing, founded in 2013
Aims	Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam
Results	(Epskamp et al., 2018c,) “temporal and contemporaneous relationships should not be overinterpreted, as these merely show predictive effects and can at most only highlight potential causal pathways.” Reproducibility Project: Psychology
Website	http://psychosystems.org/

15.11 Project RADAR-CNS (EU)

The European (EU H2020-IMI) RADAR-CNS project (Remote Assessment of Disease and Relapse - Central Nervous System) aims to study the potential of wearable devices and smartphone technology to help prevent and treat depression, multiple sclerosis and epilepsy (<https://www.radar-cns.org/>). The Dutch research site (VUmc/GGZ inGeest) will focus on depression (RADAR-MDD).

Aspect	Description
Dutch project team	Femke Lamers, PhD; Brenda Penninx, PhD; Sonia Difrancesco, MSc
APH site	VUmc, GGZ inGeest
Context	RADAR-CNS is jointly led by King's College London (KCL) and Janssen Pharmaceutica NV. The project is funded by the Innovative Medicines Initiative, a Public Private Partnership set up between the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the European Union). It includes 23 organizations from across Europe and the US. The RADAR-MDD study is coordinated by KCL.
Full title	RADAR-CNS: Remote Assessment of Disease and Relapse - Central Nervous System
Topic	Wearable devices to monitor and prevent and treat depression, multiple sclerosis and epilepsy
Status	Ongoing, 2016
Target populations	Patients with major depressive disorder, epilepsy or multiple sclerosis (MS)
Platform	RMT application (http://thehyve.nl/cases/radar-cns/), https://github.com/RADAR-base/RADAR-aRMT-protocols

Aspect	Description
Project goals	Examine how remote measurement technologies can monitor and improve quality of life and psychological well-being for people with depression, epilepsy, or multiple sclerosis
Technical goals	1) Build an end-to-end system with generalised data aggregation capabilities. The platform focuses on classes of data rather than specific devices, to enhance modularity and adaptability as new devices become available. The platform is delivered under an Apache 2 open source license, 2) Big data solutions.
Clinical goals	1) Feasibility of continuous monitoring of patients, 2) predicting disease onset or relapse (prevention and risk assessment)
EMA active	aRMT application: Outcomes include variability in sleep quality, levels of activity, social interactions, mood, cognitive performance and stress as possible predictors of clinical course. The questionnaire for EMA was developed by prof. I. Myin-Germeys (Leuven), one of the consortium members.
EMA passive	pRMT application: 1) Location and movement (GPS) 2) Mood: voice recognition 3) Social interaction (call and message logs), and 4) App interaction and app usage.
Wearables	Skin temperature, heart rate (-variability), actigraphy (3-axis accelerometer, gyroscope), galvanic skin conductance (Empatica E4 Wristband, Pebble 2 Smartwatch, Biovotion VSM, Faros 180, and Fitbit devices). In the depression study a Fitbit Charge 2 will be used to measure sleep and activity.
Data management	Participants are requested to install three apps on their Android smartphone. Data is collected during a 2-year period. Active EMA will be activated every 6 weeks for 6 consecutive days. Four times per year a non-EMA follow-up is conducted, which contains (qualitative) interviews and self-report questionnaires. Log in is facilitated with token-based authentication and authorization. A dashboard app allows for live monitoring of results. Data is streamed and analysed live.
Results	VUmc Psychiatry will participate in the depression study as a research site. Data will be used to assess if RMT data can help predict relapse.
Lessons learned	When measuring over such a long timespan, extra attention should be paid to the possible burden for participants. Continuous monitoring via a Smartphone can severely impact battery life. Participants prefer consumer devices (such as FitBit) to research devices (such as GenActiv), because of stigma. Carrying a research device will prompt questions.
More information	Presentation RADAR

15.12 The van Someren group

Eus van Someren is head of the department of sleep and cognition, which is part of the Netherlands Institute for Neuroscience and is situated at the Amsterdam Academic Medical Center. The group focusses on studying healthy and disturbed sleep. The department has a fully equipped sleep-lab and combines various research methods, such as neuro-imaging, actigraphy and EMA.

Aspect	Description
Project team	Eus van Someren, PhD (departement head); Tessa Blanken, MSc; Michele Colombo, MSc; Kim Dekker, MSc; Jeanne Leerssen, MSc; Bart te Lindert, MSc; Wisse van der Meijden, MSc; Rick Wassing, Phd
APH site	AMC and GGZ inGeest
Projects that involve EMA	

Aspect	Description
Sleep and light	Wisse van der Meijden studies, among other things, the interplay between light, vigilance, post-illumination pupil response (PIPR) and sleep by combining information from a) a questionnaire on habitual lights-out time, sleep onset latency, and final wake-up time (Munich Chronotype Questionnaire), a one-week sleep diary on actual wake/sleep times and actigraphy.
EMA passive	Actigraphy data was obtained using either a Philips Actiwatch Spectrum or a microelectromechanical accelerometer (Move II, Movisens GmbH). Data collection was set to 30hz.
Data management	Sleep onset and final wake-up time were estimated using an algorithm that is implemented in Matlab (https://github.com/btlindert/actant-1).
Results	Participants (adolescents and young adults, n=71) with a later sleep timing had a stronger responsiveness to blue light. The mid-sleep timing estimates from sleep diaries and actigraphy shared 94.5% of their interindividual variance (Van Der Meijden et al., 2016).
Sleep and context	Bart te Lindert studies the relation between context and sleep, for example by measuring light, body temperature and posture, and psychological variables. A recent study focused on Insomnia, light intensity and Liking, Wanting and mood. Prompts were sent eight times a day for one week. Prompts were timed at quasi-random intervals between 8:00 and 22:00. In addition, participants provided input after waking up and before bedtime. The interval between prompts ranged between 16 minutes and 3 hours. EMA consisted of 22 items. Liking and Wanting (6 items each), focused on taste or smell, bodily sensation, watching or listening, interactions with other, physical activity or being busy, and receiving something. Participants indicated whether they enjoyed and wanted these categories on a 0-100 VAS scale (ranging from not to very much). Mood items were derived from the Daytime Insomnia Symptom Scale (DISS, Buysse et al. (2007)), which was developed specifically for EMA. Items focused on positive mood (5 items; relaxed, energetic, calm, happy, and efficient) and negative mood (5 items; anxious, stressed, tense, sad, and irritable). Items were scored on a 0-20 VAS-scale (ranging from very little to very much).
EMA active	Participants wore two light sensors (Dimesimeter), one on their indoor clothes and one on their jacket. A build-in accelerometer indicated at what times the outdoor clothing was used. Light was sampled every minute for one week.
Data management	Participants received a designated Android smartphone for the duration of EMA. Detailed information on data processing and analysis can be found in Te Lindert et al. (2018).
Results	On average, 80% of the prompts contained valid data. People with insomnia disorder (n=17) had significantly lower subjective Liking and Wanting than matched controls without sleep complaints (n=18). This was most apparent at low environmental light intensity. There were no overall differences between groups in Positive mood and Negative mood. Participants with insomnia did have a different diurnal profile of Positive mood and Negative mood (Te Lindert et al., 2018).

Aspect	Description
Lessons learned	The one-item Karolinska sleepiness scale is advised as a simple way to measure sleepiness in EMA. The item was validated against performance and EEG variables (Kaida et al., 2006). A 30hz frequency is an acceptable sampling frequency for actigraphy, and is generally considered the gold standard. Higher frequencies lead to shorter battery life, while not improving estimations. Asking participants to keep a sleep diary parallel to wearing an accelerometer/actigraph is vital in order to determine lights-out time and wake-up time. When actigraph data and the sleep diary do not overlap, the information from the diary should be used.

15.13 VU-AMS

The VU University Ambulatory Monitoring System (VU-AMS) is a non-invasive wearable device that is used for continuous ambulatory measurement of the autonomic nervous system. The device was developed by the department of Biological Psychology of the Vrije Universiteit Amsterdam and is used worldwide by many research groups to study stress and emotion in both laboratory and naturalistic settings (<http://www.vu-ams.nl/vu-ams/>).

Aspect	Description
Project team	Eco de Geus, PhD; Gonke Willemse, PhD; Martin Gevonden, PhD; Denise van der Mee, MSc, Mandy Tjew-A-Sin, MSc; Cor Stoof, MSc
APH site	Vrije Universiteit Amsterdam
Full title	VU University Ambulatory Monitoring System (VU-AMS)
Topic	Wearable for continuous (non-invasive) ambulatory measurement of the autonomic nervous system for research purposes
Status	Ongoing (1990 - present)
Target population	Various target populations. The VU-AMS device has been used to study the effects of ADHD, aggression, anxiety and depressive disorders, mental, social and work-related stress, circadian rhythms, hyperventilation, migraine, sleep, and in studies linking the autonomic nervous system to metabolic and immunological risk factors
EMA passive	The VU-AMS device is a battery powered wearable that can record 24 to 48 hours of data (4GB storage). It measures the electrocardiogram, the impedance cardiogram, and skin conductance. The VU-AMS data can be used to compute the following outcomes:
Heart	Heart Rate / Inter beat Interval (IBI), Heart Rate Variability (SDNN, RMSSD, IBI power spectrum: HF, LF), Respiratory Sinus Arrhythmia (RSA), Pre-Ejection Period (PEP), T-wave amplitude (TWA), Left Ventricular Ejection Time (LVET), Stroke Volume (SV) and Cardiac Output (CO)
Respiration	Respiration Rate (RR)
Skin conductance	Skin Conductance Level (SCL) and Skin Conductance Responses (SCRs)
Movement	Hip-worn tri-axial accelerometer signals (g)
Data management	The freely available Data Analysis and Management System (DAMS) package is used for data extraction and processing (http://www.vu-ams.nl/support/downloads/software/) . The DAMS tool offers options for data inspection (visual inspection of raw data), automated detection of R-peaks in raw ECG signal and visual inspection of final IBI time series, event/diary-based data labelling, IBI spectral power calculation, automated scoring of RR, RSA, and PEP from the combined ECG and impedance cardiogram signals, and data export per label (to EXCEL or ASCII).

Aspect	Description
Current VU-AMS projects	<p>1) Validation of a wristwatch-based technology, developed by Philips, to measure skin conductance responses in a laboratory (~2.5 h) and ambulatory (~22h, including the night) setting on a total of 100 subjects (van der Mee et al., ongoing, 2017 - 2021). The goal is to test whether wrist based (Philips) and palm based (VU-AMS) measured skin conductance responses accord, how these measures relate to the heart based measured pre-ejection period (PEP, VU-AMS) and whether it can be related to positive and negative affect (hourly diary prompts). The end goal for the wrist based technology is to detect sympathetic nervous system activity (measured as skin conductance responses) and present this information to the person's as an index of the current stress level, alongside a one-hour prediction of changes in stress level and cognitive functioning (Cognitive Zone Changes; http://www.ip.philips.com/licensing/program/121)</p> <p>2) Ambulatory study on self-regulation among youth (Tjew A Sin et al., 2018-2019). This study is conducted at the schools as part of the neurolab project. A total of 50 students, will wear the VU-AMS device for approximately 22 hours. Autonomic nervous system activity is collected continuously over the course of a regular school day (including the night and morning thereafter) and will be related to multiple components of self-regulation, including emotion-regulation, cognitive functioning, impulsivity and inhibition</p>
Results	VU-AMS is considered by many to be the golden standard in ambulatory assessment (de Geus and van Doornen, 1996). For more information on publications go to http://www.vu-ams.nl/research/publications/
Lessons learned	The autonomic nervous system is almost entirely governed by homeostatic control over cardiovascular function, meaning that posture and physical activity changes will dominate ambulatory recordings. Without appropriate attention to these confounding factors (e.g. by selecting only sedentary fragments, or by deconvolution of the physiological outcomes by parallel registration of posture and activity, location of the accelerometer, robustness of the measure) erroneous conclusions will be drawn. It is therefore of importance that a clear research question is formulated before data collection is started. With regard to measuring behaviour or affect during an ambulatory study you have to clearly think about the medium you want to use. Thus far no clear consensus is present on a particular medium/diary application that is best suited and/or mostly used by either the department or in combination with the VU-AMS. This may lead to researchers each creating their own diary application which has not been previously validated. In addition, comparing results from studies with similar end goals, but who used different mediums, becomes much more difficult

Chapter 16

EMA Instruments Catalogue

To conduct EMA studies, a variety apps, online applications and wearable devices are on the market. In this chapter, we list a (small) selection of instruments that we found to be in use in scientific studies within the APH consortium.

Table 16.1: EMA Instruments.

Name	Manufacturer	URL	Description
GENEActive	activinsights	activinsights.com	Wrist-worn accelerometer
Illumivu	Illumivu	ilumivu.com	Android / iOS EMA app
MoodBuster	ICT4D Consortium	moodbuster.eu	Android EMA app
Movisense	MoviSence	movisense.org	Android EMA app
PsyMate	PsyMate	psymate.eu	Android EMA app
RoQua	RoQua	roqua.nl	SMS / Browser-based EMA
VU-AMS	VU	www.vu-ams.nl	Wearable for autonomic nervous system measurement

16.1 GENEActive

GENEActive, sold by UK-based company Activinsights (activinsights.com), is a waterproof wrist-worn device with a high-precision, configurable 3-axial accelerometer (range: +/- 8g), an ambient light sensor, a (near-body) temperature sensor, and an event logger (a button that users can press to mark a targeted event). GENEActive was developed to accurately assess human activity in scientific studies. The device has a storage capacity of 0.5GB of raw data. At 10Hz, the device can log activity up to one month. July 2018, the price for one unit is approximately 250 euro.

GENEActive is used in a growing number of clinical studies to measure activity and sleep-wake cycles, in natural conditions, over longer periods of time. Dedicated R-packages to pre-process and analyse the raw data exist (see, e.g., Chapter 17). Note, however, that no accompanying app exists with which study participants can be provided feedback about their activity. This might negatively affect wear-time and study compliance in research participants, who are accustomed to consumer activity-sampling devices, such as Fitbit, where many options for real-time feedback exist.



Figure 16.1: The GENEActiv Accelerometer

16.2 Illumivu

Illumivu (see <https://illumivu.com/>) is an American commercial company specialized in mobile EMA application development. It offers a cross-platform (Android and IOS) smartphone app (mEMA) that researchers can use to collect data from study participants. Researchers can define the assessment plan of their study in an online backoffice (i.e., without any assistance from Illumivu staff).

The Illumivu EMA toolbox library includes a rather complete set of survey elements, survey logic branching tools, and survey scheduling options. Passive EMA options include GPS tagging (of survey responses), GEO-fencing (triggering surveys at specific locations) and smartphone sensor logging (light and noise level, screen brightness, screen locked/unlocked, humidity, ambient temperature, barometric pressure, phone/SMS activity log, and basic device information). A limited number of smartwatch devices can optionally be linked to the Illumivu app for further passive data collection. With the online backoffice, researchers can invite participants, monitor study compliance and download data (in common data formats such as CSV). The company is open for custom development, when studies require features that are not included in the default app.

Current (July 2018) subscription plans range from 3.375 dollar (basic features) to 12.000 dollar (all features), per year. Researchers, who are interested in purchasing a licence of the service, are advised to the ‘Grant Writer’s Guide’ of Illumivu, which can be downloaded from the site of the company (at <https://illumivu.com/pricing/writing-a-grant/>).

Illumivu’s competitive advantage is that it has multi-platform support. It is, however, not the cheapest EMA product on the market. Being an American company, researchers should also consider EU regulations relating to personal data privacy protection, since regulations are more strict when personal data of EU citizens leave the EU.

16.3 MoodBuster

MoodBuster (<http://www.moodbuster.eu/>) is a web-based treatment platform with an integrated (Android) EMA app. The platform was developed by an international non-profit research consortium, including VU, VUmc and GGZ InGeest, in two major EU-funded research projects: ICT4Depression (see ICT4Depression.eu) and E-COMPARED (see <http://e-compared.eu>).

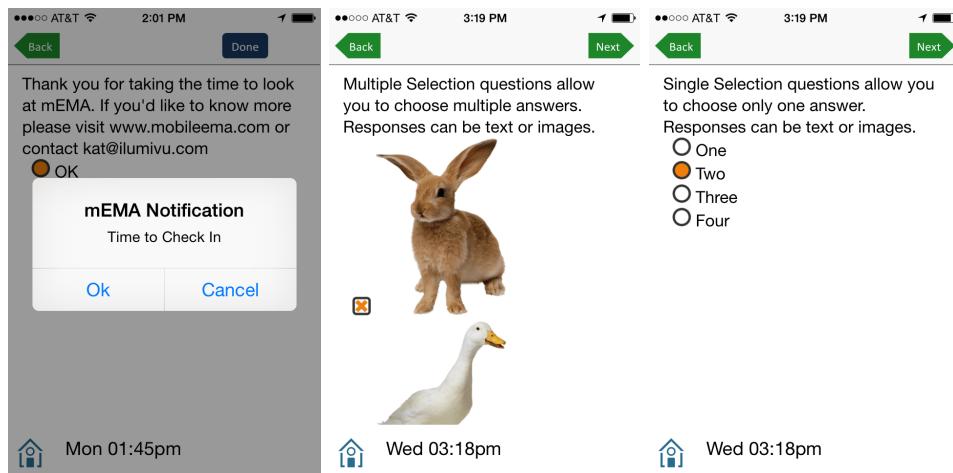


Figure 16.2: Ilumivu App Screenshots

In the E-COMPARED trial, MoodBuster was used, in five EU-countries, to test blended treatment of major depression (Kleiboer et al., 2016). In this study, participants used the smartphone app to rate mood and various other depression-related variables, in the context of their treatment, over a period of up to 20 weeks. In addition, the EMA app was used in a satellite study designed to assess the effects of long-term EMA (van Ballegooijen et al., 2016). MoodBuster will also be used in the EU ImplementAll project (<http://www.implementall.eu>) and in several other clinical trials that are in preparation.

Currently, EMA assessment protocols are hard-coded in the app. New EMA assessments protocols can be implemented in collaboration with the MoodBuster development team. An online backoffice is in development. While this can be advantage, as researchers have more options for custom development, it may take longer before an EMA-study can be started (depending on the specific requirements of the study). Another limitation is that only an Android version of the app is currently available. However, experimental cross-platform versions of the app have been tested in Portugal.

More information on MoodBuster can be requested from Dr. Jiska Aardoom (j.j.aardoom@vu.nl), or prof. dr. Heleen Riper (h.riper@vu.nl).

16.4 Movisens

Movisens (<http://www.movisens.com>) is a German company that is specialised in the development of hard-and software solutions for mobile sensing. The company sells small wearable devices that contain several high-precision sensors, including an accelerometer, gyroscope, barometer and thermometer. In addition, the company has developed an (Android) app, called MovisensXS, which can be used for active EMA research. The app can optionally be configured for smartphone logging (e.g., to log music that a study participant listens to). The wearable sensor can also be linked to the app, so that EMA questionnaires can be triggered based on targeted activity or energy expenditure patterns, such as extended periods of sedentary behaviour. Specialised software to import, pre-process and analyse raw sensor data is available for download.

Like Ilumivi, researchers can define EMA sample schedules for their study in a web-based backoffice (<https://xs.movisens.com>), using an online graphical editor. Once defined, participants can be invited to the study, through the backoffice, to download the freely available Movisens App from Google Play store. The backoffice also allows researchers to monitor study compliance and download data.

MoviSensXS EMA licence costs vary from 500 to 10.000 euro's per year, depending on the required number of 'credits' which are linked to the number of EMA responses. Prospect users can test platform, without



Figure 16.3: MoodBuster App Screenshots

functional restrictions, with a free test account. An EMA test-study can thus be set up and started in less than a day.

A major limitation of Movisens is the lack of an iOS version of the EMA app. Study participants who own an iPhone have to be excluded from studies, or will have to be provided with an Android phone.

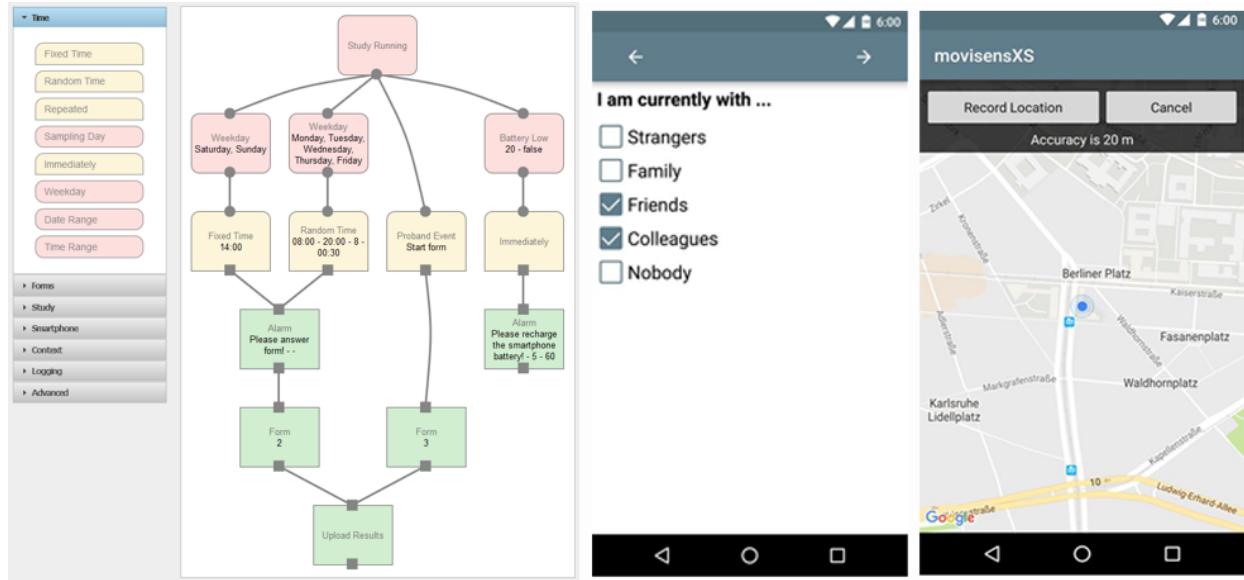


Figure 16.4: Movisens Sample scheme editor (left) and App Screenshots (right)

16.4.1 PsyMate

The PsyMate™ app (www.psymate.eu) was developed by the Department of Psychiatry and Psychology at Maastricht University in the Netherlands to assess psychological problems in daily life. The app has been

validated for use in depression, bipolar disorder, and psychosis, with new scales currently being developed for a range of diseases including Parkinson's disease, pain, cardiology, hypertension, diabetes and Irritable Bowel Syndrome. It is currently used in a EU-funded project to study gene-environment interaction in schizophrenia (<http://www.eu-gei.eu/about-the-project/psymate>).

The app is free to download for iOS and Android devices on Apple and Google play stores. Uses for the app include self-monitoring of mood states, for professional support during treatment, or for research purposes. The app can be customized to address specific client needs or research projects with expertise from the Psymate back office, which includes a working group that meets regularly to discuss and advise new projects.

Researchers have access to the raw data without having to go through the Psymate back office. A disadvantage of the Psymate app is that technical problems could arise when there are either iOS or Android updates. Communication from the Psymate back office to researchers about updates and assistance with technical problems could be a point for consideration for using this platform.

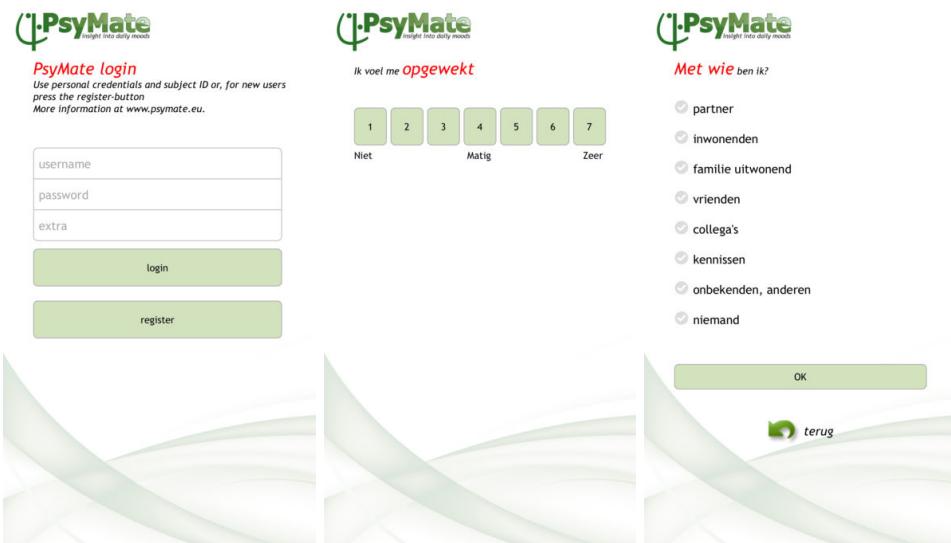


Figure 16.5: PsyMate App Screenshots

16.5 RoQua

RoQua (<http://www.roqua.nl/>) is a web-based Routine Outcome Monitoring system, developed and maintained by a Dutch non-profit development and service organization that is funded by several northern GGZ organisations and the Department of Psychiatry, University Medical Center Groningen. RoQUA has a sophisticated and user-friendly online backoffice portal, with which researchers can define assessment protocols and invite study participants - through e-mail or SMS - to complete questionnaires online (on desktop or mobile devices). By inviting study participants several times a day to complete a questionnaire via the standard web browser of their mobile phone, active EMA can be implemented. This approach is taken in several large-scale studies, including 'NESDA' (nesda.nl) and 'HowNutsAreTheDutch' (www.hoegekis.nl; see (Van Der Krieke et al., 2017; Krieke et al., 2016)).

At present, RoQua does not support the collection of passive EMA data. However, preliminary results have been reported with a system called 'Physiqual' (Blaauw et al., 2016), with which EMA data, collected with RoQUA, can be automatically combined with wearable sensor data.



Figure 16.6: Screenshots of the participant feedback web-page of the 'HowNutsAreTheDutch' project, in which data is collected by the RoQUA system

16.5.1 VU-AMS

The VU University Ambulatory Monitoring System (VU-AMS; <http://www.vu-ams.nl/>), developed by the department of Biological Psychology and the Technical Department (ITM) of the Faculty of Psychology and Education, allows ambulant recording of autonomic and cardiovascular activity. VU-AMS measures heart rate, heart rate variability, Respiratory Sinus Arrhythmia, Pre-Ejection Period, Left Ventricular Ejection Time, Respiration Rate, Stroke Volume (SV) and Cardiac Output, Skin Conductance Level (SCL) and Skin Conductance Responses (SCRs) and Tri-Axial Accelerometry (of Body Movement). For the processing of VU-AMS data, a dedicated software suite called the 'Data Analysis and Management Software' (VU-DAMS) is available (for Windows and Mac).

16.5.2 Points to consider

- Internet access - whether company has an app or is notification for completion of survey via an email or SMS.
- Use of participants' own device (fitness device, tablet, smartphone) or designated device – issues of software updates, compatibility issues if using participants device, issues of storage capacity of device if data has to be stored locally (because of lack of internet access) before it can be uploaded to central system.
- Issue of "stigma" of participating in an EMA study e.g. need to explain the carrying/wearing of a device that might not complement participants' look/lifestyle.

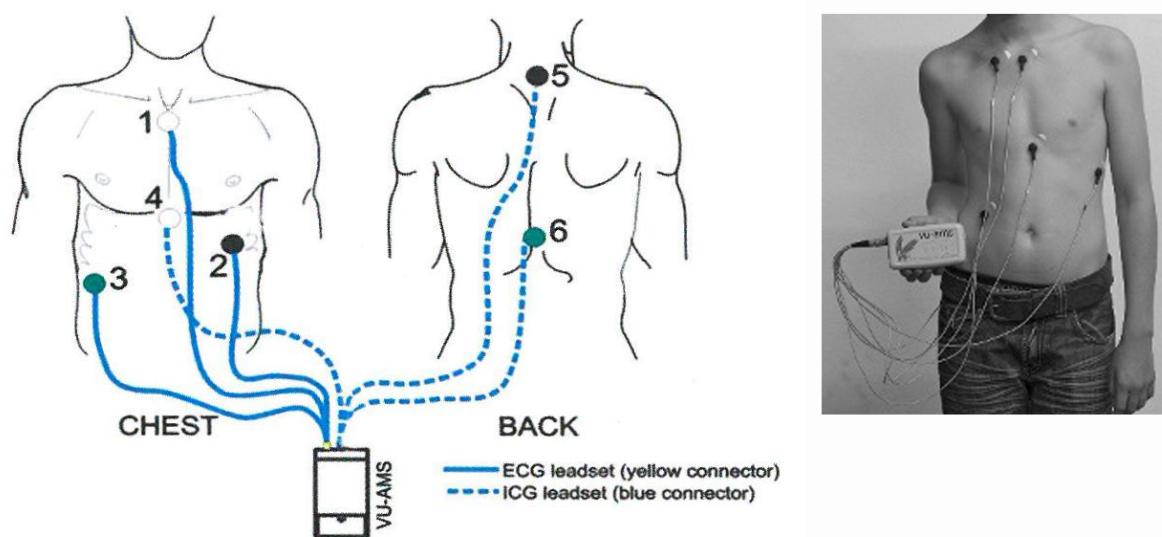


Figure 16.7: VU-AMS device

Chapter 17

R packages for EMA research

Many R packages exist that can help you in the management and analysis of EMA data. In this chapter, a selection of these packages are discussed. For each, we provide a summary description, a code example code, and pointers to further documentation, to give you a head start in using the packages for your work.

Table 17.1: List of R packages that are useful in EMA research.

Category	Package	Description
Accelerometry	GENEActive	Import GENEActive data into R
	GGIR	Pre-proces and analyse raw multi-day multi-day accelerometer data.
Data Management & Visual Exploration	PhysicalActivity	Analyse Actigraph accelerometer data.
	dplyr	Data transformation
Mixed-effects Modeling	ggplot2	Create graphs
	haven	Import and export SPSS data files
	lubridate	Manipulate date and time variables
	lme4	Fit linear and nonlinear mixed-effects models. Fast alternative to package ‘nlme’.
Power Analysis	nlme	Fit linear and nonlinear mixed effects models. Pre-dates package ‘lme4’, but is still used because it provides more advanced options to model correlational structures in the data.
	simr	Simulation-based power calculations for mixed models.
Simulation	simstudy	Simulate study data.
Spatio-temporal analysis	adehabitatHR	Developed for home range estimation of wild animals from GPS data. Useful for human data as well (see Chapter 13).
Symptom Networks	autovarCore	Automate the construction of vector autoregressive models.
	bootnet	Assess the stability of symptom networks.
Time series analysis	qgraph	Estimate and plot symptom networks.
	lomb	Calculate the Lomb-Scargle Periodogram for unevenly sampled time series.

17.1 Accelerometry

Accelerometer data need considerable pre-processing before final analyses can be run. Raw data have to be read in from a variety of brand-specific file formats, data have to re-calibrated on a per-device basis, non-wear periods have to be detected, and summarizing measures, such as activity counts and energy-expenditure measures, have to be calculated from imputed tri-axial (x, y, z) data, often in several time windows (i.e., epochs).

17.1.1 Package GENERead

GENEActive, sold by Activinsights, is a wrist-worn tri-axial accelerometer that is often used in clinical research studies. With package ***GENERead*** (Fang et al., 2018), raw data can be imported into R for further processing, as illustrated below.

```
library(GENERead)
library(tidyverse)

dat <- read.bin(system.file("binfile/TESTfile.bin", package = "GENERead"),
                 verbose = FALSE, downsample = 20)
#> Processing took: 0.031 secs .
#> Loaded 1560 records (Approx 0 MB of RAM)
#> 12-05-23 16:47:50.000 (Wed) to 12-05-23 16:53:01.799 (Wed)

d <- as.data.frame(dat$data.out)
d <- gather(d, key = "sensor", value = "value", -timestamp)
d$timestamp <- as.POSIXct(d$timestamp,
                           origin = "1970-01-01",
                           tz = "UTC")

ggplot(d, aes(x = timestamp, y = value)) +
  geom_line() +
  facet_wrap(~sensor, scales = "free_y")
```

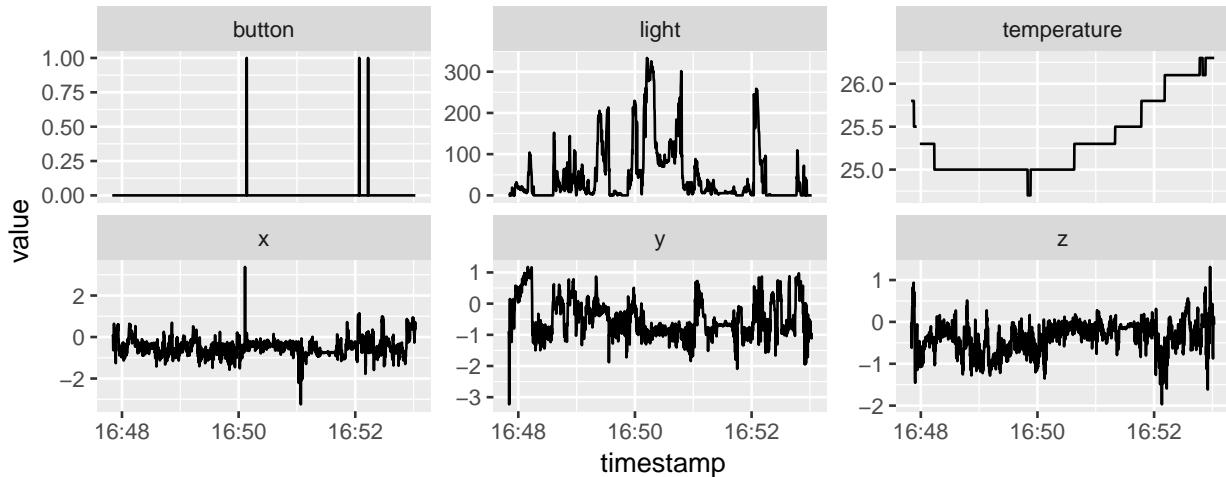


Figure 17.1: Raw sensor data of a GENEActive wrist-worn tri-axial accelerometer (down-sampled from 100Hz to 5Hz).

17.1.2 Package ‘GGIR’

Package *GGIR* (van Hees et al., 2018) is a packages to pre-process raw accelerometry data from three brands of wearables that are widely used in sleep and physical activity research: GENEActiv, ActiGraph and Axivity.

17.1.3 Package ‘PhysicalActivity’

Package ‘*PhysicalActivity*’ (Choi et al., 2018) provides an alternative to package ‘GGIR’, when ActiGraph data are available.

```
library(PhysicalActivity)
library(ggplot2)

data(dataSec)

d <- dataCollapser(dataSec, TS = "TimeStamp", col = "counts", by = 300)

ggplot(d, aes(x = as.POSIXct(TimeStamp), y = counts)) +
  geom_line(size = .5, alpha = .5) +
  xlab("Time") + ylab("Activity Counts")
```

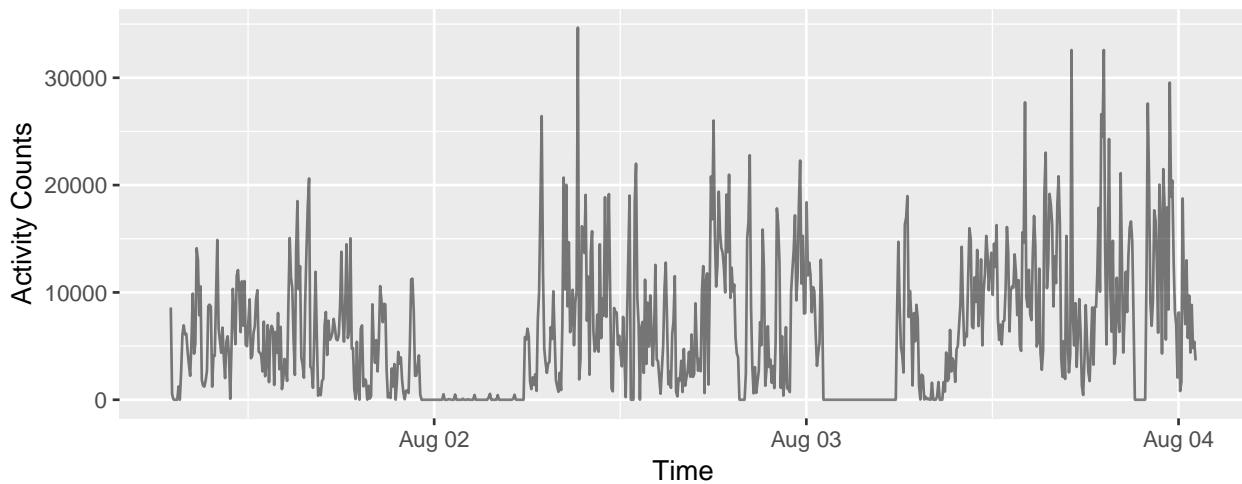


Figure 17.2: Activity Counts (5-minute windows), in a Three-day Accelerometer data set.

17.2 Data management & Visual Exploration

The tidyverse is a collection of well-designed packages, authored by the team behind RStudio, that together add a consistent, modern, and efficient extension of base R functionalities. The tidyverse includes popular packages such as “ggplot2” (for plotting), “haven” (to read SPSS files), “dplyr” (for data manipulation), and many more (see: <http://tidyverse.org> for a full list).

17.2.1 Package dplyr

Package ‘*dplyr*’ (Wickham et al., 2018) implements the ‘split-apply-combine’-strategy. With ‘*dplyr*’, elementary data manipulations can be e chained (using the pipe operator ‘%>%’) to elegantly implement complex data transformations.

```
# code snippet 18.3: aggregate data by ID, through a 'pipe'
require(dplyr)

d <- data.frame(
  c = factor(rep(1:5, each = 10)),
  score = rnorm(50)
)

b <- as_tibble(d) %>%
  group_by(c) %>%
  summarize(mean_score = mean(score))
```

A good introduction to dplyr can be found in the book ‘R for Data Science’ (Wickham and Grolemund, 2016), which can be freely accessed online (<http://r4ds.had.co.nz/>).

17.2.2 Package ‘ggplot2’

Package ***‘ggplot2*** (Wickham, 2016) provides a collection of high-level plotting commands with which graphs can be build up in layers. It is based on ‘The Grammar of Graphics’ (Wilkinson, 2006), an influential analysis of the structure of scientific graphs. Systematic introductions are available on the the tidyverse website, and in the book ‘ggplot2: Elegant Graphics for Data Analysis’ (Wickham, 2016).

The example below illustrates how graphs are layered. In the first step, a coordinate system is set up. In step 2, all time/scores points are plotted. In step 3, a smoothed line is fitted through these points. Finally, in step 4, the graph is split on a variable ID (a subject identifier), to show individual trajectories.

```
# code snippet 18.2: simple ggplot example
library(ggplot2)

# simulate example data
d = data.frame(
  ID      = rep(1:4, each = 25),
  time   = rep(1:25, 4),
  score  = rnorm(100, 0, 2))

# step 1: initialise the coordinate system
g <- ggplot(d, aes(x = time, y = score)); g

# step 2: add scatterplot
g <- g + geom_point(); g

# step 3: fit a smoothed line
g <- g + geom_smooth(); g

# step 4: split plot by ID
g + facet_wrap(~ ID)
```

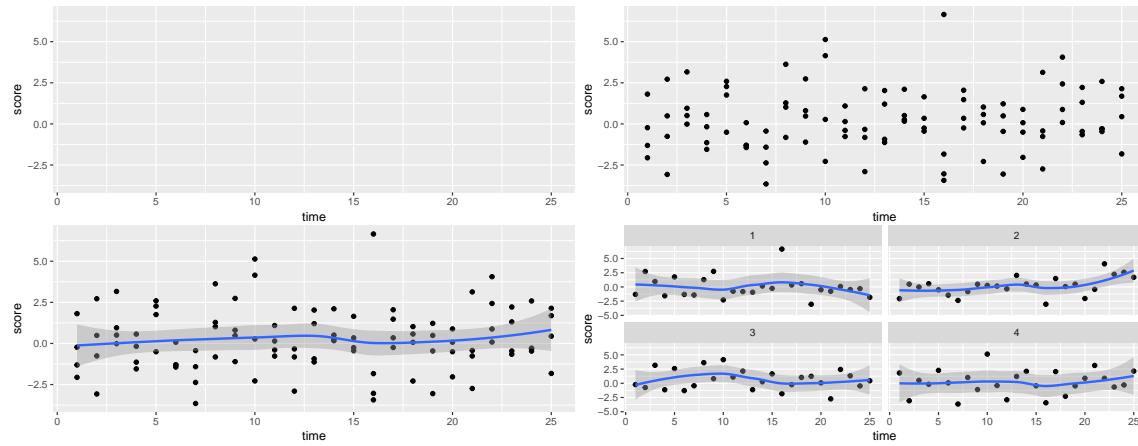


Figure 17.3: Plotting layers with ggplot2

17.2.3 Package ‘haven’

With package **haven** (Wickham and Miller, 2018), SPSS, STATA and SAS files can be read into R.

```
library(haven)

path <- system.file("examples", "iris.sav", package = "haven")
d <- read_sav(path)

attributes(d$Species)
#> $format.spss
#> [1] "F8.0"
#>
#> $class
#> [1] "labelled"
#>
#> $labels
#>      setosa versicolor  virginica
#>      1          2          3
```

17.2.4 Package ‘lubridate’

EMA data analyses frequently require manipulations of datetime variables. For this, package **lubridate** (Gromelund and Wickham, 2011), which provides many functions for common date and datetime operations, can be very useful.

In the code snippet below, for example, the ‘round_date’ function is used to calculate the ENMO value from raw tri-axial accelerometer data, in 15-minute epoch windows.

```
library(emaph)
library(lubridate)
library(ggplot2)
library(dplyr)

d <- subset(genea,
            timestamp > "2018-06-02 12:00" &
            timestamp < "2018-06-02 18:00")
```

```
d$epoch <- round_date(d$timestamp, "minute")

d <- d %>% group_by(id, epoch) %>%
  summarise(svm = sum(sqrt(x^2 + y^2 + z^2) - 1) / length(x))
```

id	epoch	svm
1	2018-06-02 12:00:00	-0.0009766
1	2018-06-02 12:01:00	0.0072235
1	2018-06-02 12:02:00	0.0023875
1	2018-06-02 12:03:00	0.0070644
1	2018-06-02 12:04:00	0.0265187
1	2018-06-02 12:05:00	0.0969168

To learn more about handling dates and times with ‘lubridate’, Chapter 16 of the book ‘R for Data Science’ (Wickham and Grolemund, 2016) provides a good introduction.

17.3 Mixed-effects modeling

Several R-packages for mixed-effects modelling exist. The most popular are package **nlme** (Pinheiro et al., 2018) and package ***lme4** (Bates et al., 2015). Both packages are actively used, as both provide unique functionalities.

17.3.1 nlme

Package **nlme** is introduced in chapter 7. It is an older package (in comparison to package lme4), that is still used a lot because it provides options to model correlational structures that are not implemented (yet) in lme4.

```
# code snippet 18.4: fit a linear mixed model, with lme
library(nlme)
fm <- lme(distance ~ age + Sex, data = Orthodont, random = ~ 1)

fixef(fm)
#> (Intercept)      age   SexFemale
#>  17.7067130   0.6601852 -2.3210227
```

17.3.2 lme4

Package **lme4** (Bates et al., 2015) is a faster R-reimplementation of the mixed-effects model. With large data sets and complex hierarchical models, this package should probably be preferred. As can be seen below, models specifications in ‘lmer’ are different from model specifications in ‘lme’.

```
# code snippet 18.4: fit a linear mixed model, with lme
library(lme4)
fm <- lmer(distance ~ age + Sex + (1 | Subject), data = Orthodont)
fixef(fm)
#> (Intercept)      age   SexFemale
#>  17.7067130   0.6601852 -2.3210227
```

17.4 Power analysis

17.4.1 Package ‘simr’

With package ‘simr’ (Green and MacLeod, 2016), power of mixed-effects models can be determined via simulation. As illustrated below, the procedure requires the researcher to define the “true” parameters of a mixed model, and a single data set. Then, function ‘simPower’ can be used to simulate new datasets and tests (of a specified parameter in the model), to determine the power of the test.

```
# code snippet 3.3: Power analysis of a two-group repeated measures design
# (simulation approach)
library(simr)

# construct design matrix
t <- 1:24
s <- 1:40
X <- expand.grid(t = t, s = s)
X$g <- c(rep(0, 24), rep(1, 24))

# fixed intercept and slope
b <- c(2, -0.1, 0, -0.5)

# random intercept variance
V1 <- 0.5

# random intercept and slope variance-covariance matrix
V2 <- matrix(c(0.5, 0.05, 0.05, 0.1), 2)

# residual standard deviation
s <- 1

model1 <- makeLmer(y ~ t * g + (1 + t | s),
                     fixef = b,
                     VarCorr = V2,
                     sigma = s,
                     data = X)

powerSim(model1,
          fixed("t:g", "lr"),
          nsim = 10,
          progress = FALSE)
#> Power for predictor 't:g', (95% confidence interval):
#>     100.0% (69.15, 100.0)
#>
#> Test: Likelihood ratio
#>     Effect size for t:g is -0.50
#>
#> Based on 10 simulations, (0 warnings, 0 errors)
#> alpha = 0.05, nrow = 960
#>
#> Time elapsed: 0 h 0 m 2 s
```

17.5 Spatio-temporal analysis:

17.5.1 GPS data: Package `adehabitatHR`

Package **adehabitatHR** (Calenge, 2006) was created for the study of the habitat of wild animals, using accelerometer and GPS data. Defined procedures can be used for the analysis of human data as well.

```
library(adehabitatHR)
```

17.6 Symptom Network Analysis

When EMA is used to tap various symptoms, network analysis can reveal the dynamic interplay between these symptoms (see Chapter 8). Various packages exist to fit these networks in R. With these packages, it is relatively easy to fit a graphical network on multivariate data sets. If you are interested in conducting a network analysis, be sure to visit the Psycho-systems website, at <http://psychosystems.org>.

17.6.1 Package 'autovarCore'

Vector autoregressive (VAR) models can be used to detect lagged relationships between multiple timeseries. In VAR, each variable is modelled as a linear function of past values (lags) of itself and of present and past values of other variables. When EMA is used to capture multiple phenomena over time, VAR can provide insight in how these phenomena interact. One challenge in VAR modelling is that many alternative models potentially exist, Package '**autovarCore**' (Emerencia, 2018) was developed to help researchers to find the VAR model with the best fit to a given timeseries data set.

In the (unrealistic) example below, function 'autovar' is used to detect that changes in depression are positively related to past (lag 1) values of activity, in a simulated data set:

```
library(autovarCore)

# simulate data
N = 100
depression <- rnorm(N)
activity <- rnorm(N)
activity_lag1 <- c(NA, activity[1:(N -1)])

depression <- depression + 0.5 * activity_lag1
d <- data.frame(depression, activity)

models_found <- autovarCore::autovar(d, selected_column_names = c('activity', 'depression'))

# Show details for the best model found
summary(models_found[[1]]$varest$varresult$depression)
#>
#> Call:
#> lm(formula = y ~ -1 + ., data = datamat)
#>
#> Residuals:
#>      Min       1Q   Median       3Q      Max
#> -2.76035 -0.54376 -0.00777  0.52714  1.90877
#>
#> Coefficients:
```

```
#>           Estimate Std. Error t value Pr(>|t|) 
#> activity.l1    0.41685   0.09449  4.411 2.76e-05 ***
#> depression.l1   0.01318   0.08995  0.147  0.88378
#> const          -0.06272   0.09165 -0.684  0.49546
#> outlier_32     -0.28850   0.90584 -0.318  0.75083
#> outlier_39     -2.75860   0.92363 -2.987  0.00361 ** 
#> outlier_78      0.96705   0.89644  1.079  0.28348
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
#>
#> Residual standard error: 0.8901 on 93 degrees of freedom
#> Multiple R-squared:  0.2907, Adjusted R-squared:  0.2526 
#> F-statistic: 7.624 on 5 and 93 DF,  p-value: 4.855e-06
```

AutovarCore is a simplified version of a more extensive package *autovar* [@(Emerencia, 2018), which was used in several publications (van der Krieke et al., 2015, Emerencia et al. (2016)). Further information can be found on <http://autovar.nl> and <http://autovarcore.nl>

17.6.2 Package 'qgraph'

Package *qgraph* (Epskamp et al., 2012) can be used to fit, visualise and analyse graphical networks.

In the example below, qgraph is used to fit a network on the ‘Critical Slowing Down’ (CSD) data set, which is included in package ‘emaph’ (see ?csd and Chapter 8).

```
library(qgraph)
library(emaph)

# get mood_ scores from csd data set
d <- subset(csd,
             subset = phase == "exp: db: no change",
             select = grep("mood_", names(csd))[1:5])

# Fit and plot regularized partial correlation network
g <- qgraph(cor_auto(d, detectOrdinal = FALSE),
            graph = "glasso", sampleSize = nrow(d),
            nodeNames = names(d),
            label.scale = FALSE, label.cex = .8,
            legend = TRUE, legend.cex = .5,
            layout = "spring")
```

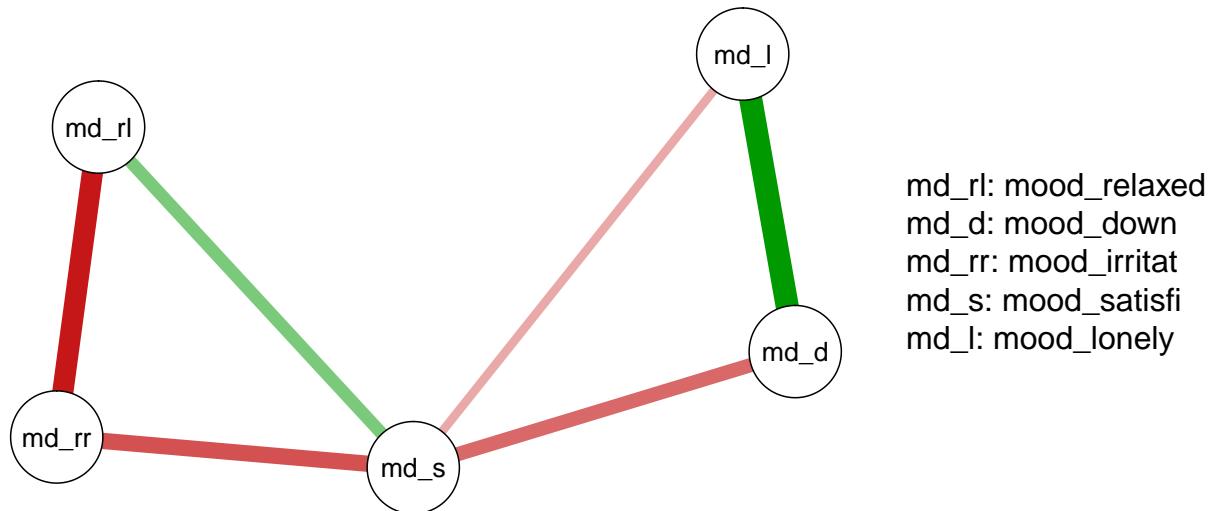


Figure 17.4: Network of mood items from CSD data set

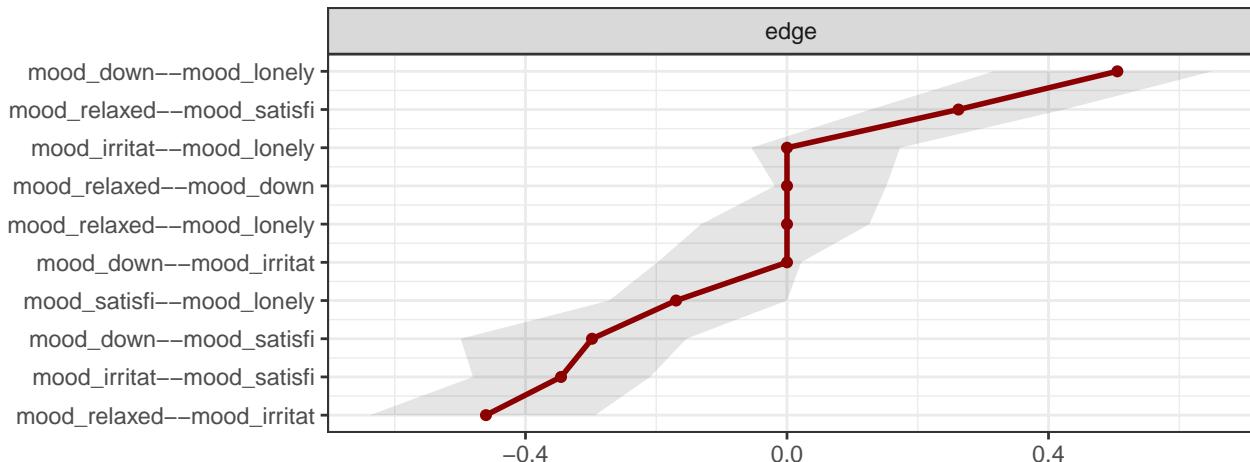
17.6.3 Package ‘bootnet’

In the interpretation of fitted network plots, it is important to take the stability of the network into account. Intuitively, networks that are fit on small sample data sets will be less stable than networks based on large data sets. One solution is to fit a large number of networks on subsets of the original data, through bootstrapping. In stable networks, the variance edges estimations will be small, while in unstable networks, the variance will be high. This idea is implemented in package **bootnet** (Epskamp et al., 2018a).

Below, the stability of the network that was fit in the previous example is examined with bootnet: fifty networks are fit, based on fifty bootstrapped samples. In the results plot, the red line marks the strength of the edges in the full sample, while grey confidence intervals mark the distribution of the edge weights in the bootstraps.

```
library/bootnet)

g <- estimateNetwork(d, default = "EBICglasso",
                      corArgs = list(detectOrdinal = FALSE))
results <- bootnet(g, nBoots = 50, verbose = FALSE)
plot(results, order = "mean")
```

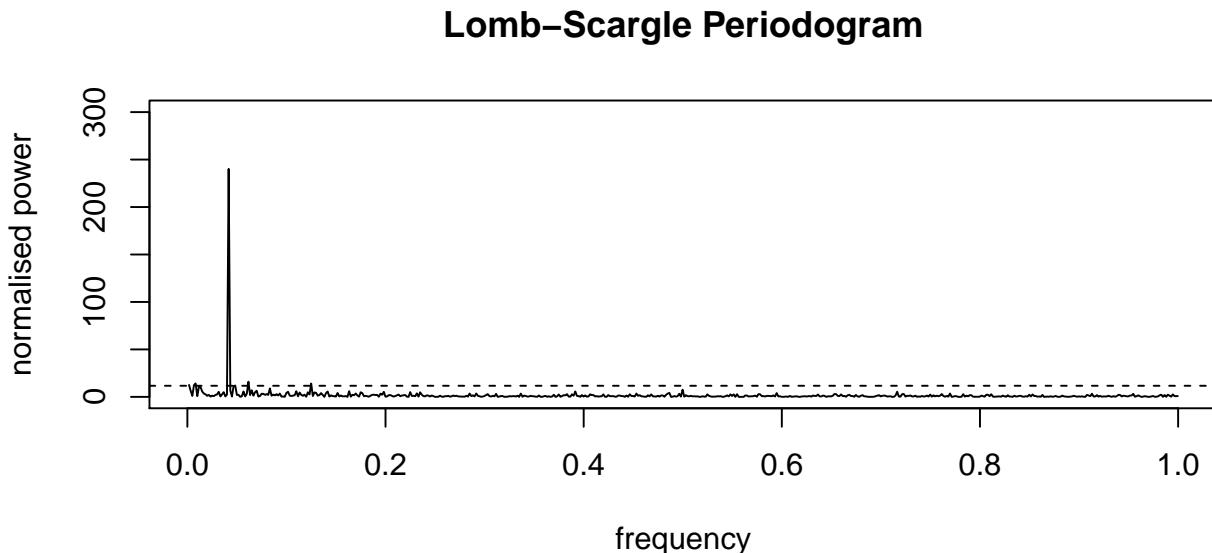


17.7 Timeseries analysis

17.7.1 Package ‘lomb’

Disturbances in circadian rhythms have been related to depressive symptoms (see, e.g., Saeb et al., 2015). With so-called periodograms, these circadian rhythms can be detected in EMA data. Standard analysis techniques, however, expect regular timeseries, in which data are sampled at equidistant intervals. EMA data, typically, are not equidistant. One solution to this problem is to use the Lomb-Scargle periodogram procedure (Lomb, 1976), which can be applied to unevenly-sampled timeseries as well. Package ***lomb*** (Ruf, 1999) implements this procedure.

```
# code snippet 18.5: calculating a Lomb-Scargle periodogram
data(ibex, package = "lomb")
lomb::lsp(ibex[2:3])
```



Part VII

Closing Matters

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Jeroen Ruwaard, Lisa Kooistra & Melissa Thong



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