

Préparée à l'Institut Curie

THÈSE DE DOCTORAT
DE L'UNIVERSITÉ PSL

**From mechanistic modelling of cancer to clinical interpretation and
impact evaluation**

Soutenue par

Jonas BEAL

Le 15/09/2020

École doctorale n°515

Complexité du Vivant

Spécialité

Génomique

Composition du jury :

| | |
|--|-------------------------------|
| Test NOM | |
| Titre, Établissement | <i>Président</i> |
| Test NOM | |
| Titre, Établissement | <i>Rapporteur</i> |
| Test NOM | |
| Titre, Établissement | <i>Examineur</i> |
| Test NOM | |
| Titre, Établissement | <i>Examineur</i> |
| Emmanuel BARILLOT | |
| Institut Curie, INSERM, Mines ParisTech, PSL | <i>Directeur de thèse</i> |
| Aurélien LATOUCHE | |
| Institut Curie, Cnam | <i>Directeur de thèse</i> |
| Laurence CALZONE | |
| Institut Curie, INSERM, Mines ParisTech, PSL | <i>Co-encadrante de thèse</i> |

Abstract

Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliquip ex ea commodo consequat.

Duis aute irure dolor in reprehenderit in voluptate velit esse cillum dolore eu fugiat nulla pariatur. Excepteur sint occaecat cupidatat non proident, sunt in culpa qui officia deserunt mollit anim id est laborum

Key-words:

Résumé

Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliquip ex ea commodo consequat. Duis aute irure dolor in reprehenderit in voluptate velit esse cillum dolore eu fugiat nulla pariatur.

Excepteur sint occaecat cupidatat non proident, sunt in culpa qui officia deserunt mollit anim id est laborum

Mots-clés:

Acknowledgements

Many persons to thanks. Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliquip ex ea commodo consequat.

Duis aute irure dolor in reprehenderit in voluptate velit esse cillum dolore eu fugiat nulla pariatur. Excepteur sint occaecat cupidatat non proident, sunt in culpa qui officia deserunt mollit anim id est laborum

Table of contents

| | Page |
|--------------------------|-----------|
| List of Tables | viii |
| List of Figures | ix |
| I Introduction | 1 |
| 1 What is a model | 3 |
| 1.1 Abc | 3 |
| 1.2 Cde | 4 |
| 2 What is cancer | 5 |
| 2.1 Abc | 5 |
| 3 Test part | 9 |
| 3.1 Abc | 9 |
| Bibliography | 11 |

List of Tables

| Table | Page |
|-------|------|
|-------|------|

List of Figures

| Figure | Page |
|--------------------------------------|------|
| 3.1 Here is a nice figure! | 10 |
| 3.2 Example pic | 10 |

Part I

Introduction

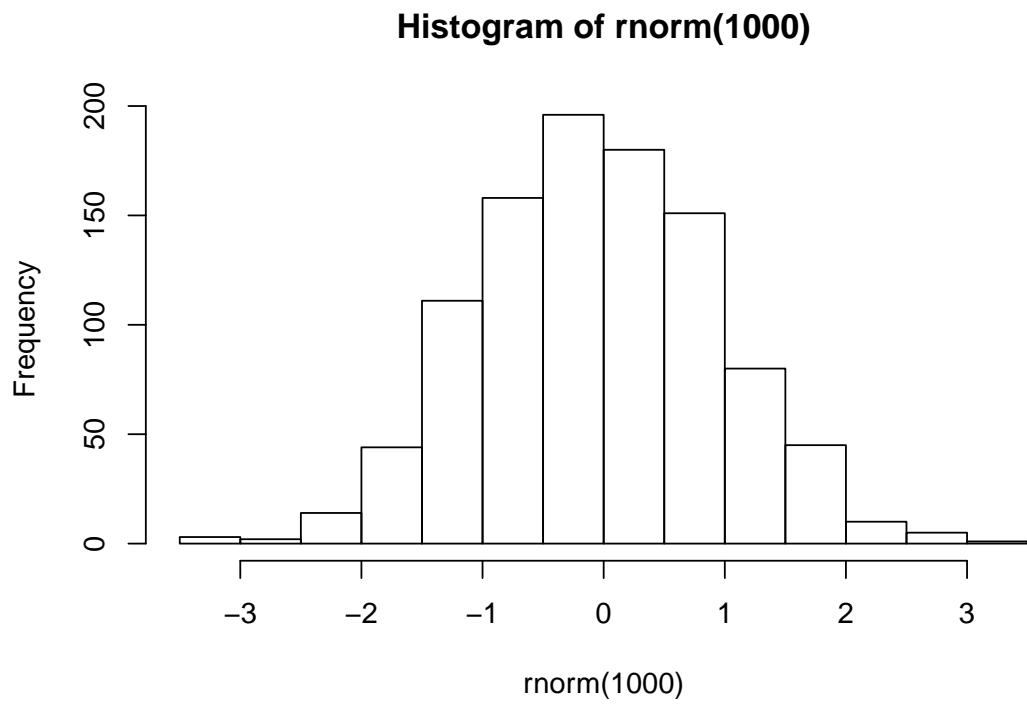
What is a model

"Inner speech is nothing but speech to oneself"
Sokolov, A. N. (1972)

This is a test

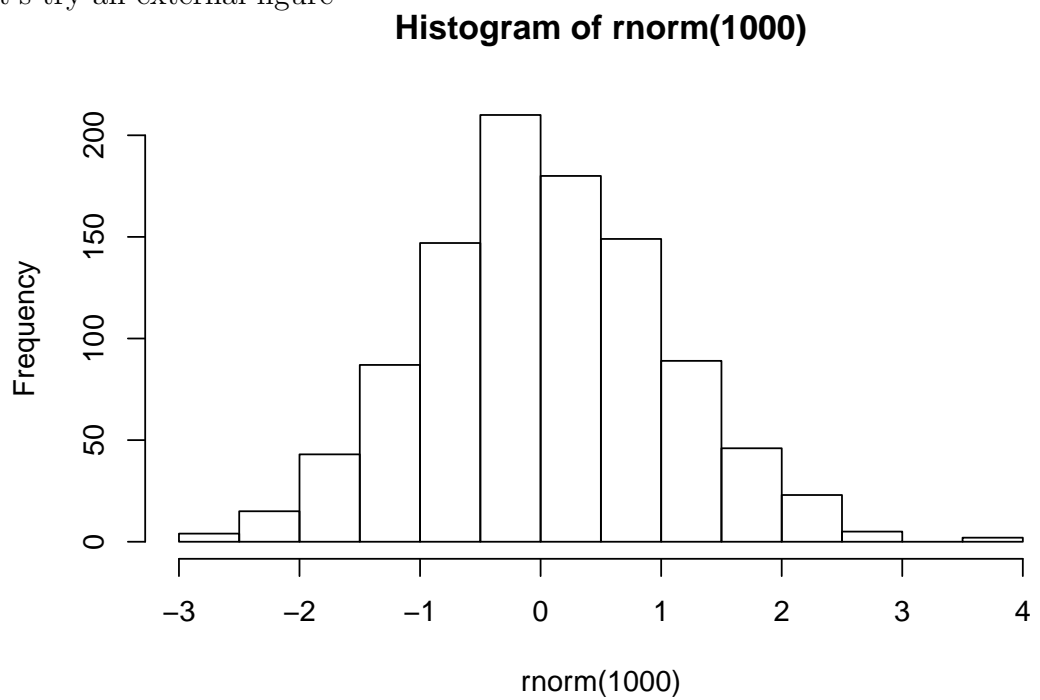
1.1 Abc

Bla bla is



1.2 Cde

Let's try an external figure



CHAPTER 2

What is cancer

This is a test

2.1 Abc

Bla bla

The LaTeX environment `tiny` is only generated for LaTeX output.

CHAPTER 2. WHAT IS CANCER

| | mpg | cyl | disp | hp | drat | wt | qsec | vs | am | gear | carb |
|---------------------|------|-----|-------|-----|------|-------|-------|----|----|------|------|
| Mazda RX4 | 21.0 | 6 | 160.0 | 110 | 3.90 | 2.620 | 16.46 | 0 | 1 | 4 | 4 |
| Mazda RX4 Wag | 21.0 | 6 | 160.0 | 110 | 3.90 | 2.875 | 17.02 | 0 | 1 | 4 | 4 |
| Datsun 710 | 22.8 | 4 | 108.0 | 93 | 3.85 | 2.320 | 18.61 | 1 | 1 | 4 | 1 |
| Hornet 4 Drive | 21.4 | 6 | 258.0 | 110 | 3.08 | 3.215 | 19.44 | 1 | 0 | 3 | 1 |
| Hornet Sportabout | 18.7 | 8 | 360.0 | 175 | 3.15 | 3.440 | 17.02 | 0 | 0 | 3 | 2 |
| Valiant | 18.1 | 6 | 225.0 | 105 | 2.76 | 3.460 | 20.22 | 1 | 0 | 3 | 1 |
| Duster 360 | 14.3 | 8 | 360.0 | 245 | 3.21 | 3.570 | 15.84 | 0 | 0 | 3 | 4 |
| Merc 240D | 24.4 | 4 | 146.7 | 62 | 3.69 | 3.190 | 20.00 | 1 | 0 | 4 | 2 |
| Merc 230 | 22.8 | 4 | 140.8 | 95 | 3.92 | 3.150 | 22.90 | 1 | 0 | 4 | 2 |
| Merc 280 | 19.2 | 6 | 167.6 | 123 | 3.92 | 3.440 | 18.30 | 1 | 0 | 4 | 4 |
| Merc 280C | 17.8 | 6 | 167.6 | 123 | 3.92 | 3.440 | 18.90 | 1 | 0 | 4 | 4 |
| Merc 450SE | 16.4 | 8 | 275.8 | 180 | 3.07 | 4.070 | 17.40 | 0 | 0 | 3 | 3 |
| Merc 450SL | 17.3 | 8 | 275.8 | 180 | 3.07 | 3.730 | 17.60 | 0 | 0 | 3 | 3 |
| Merc 450SLC | 15.2 | 8 | 275.8 | 180 | 3.07 | 3.780 | 18.00 | 0 | 0 | 3 | 3 |
| Cadillac Fleetwood | 10.4 | 8 | 472.0 | 205 | 2.93 | 5.250 | 17.98 | 0 | 0 | 3 | 4 |
| Lincoln Continental | 10.4 | 8 | 460.0 | 215 | 3.00 | 5.424 | 17.82 | 0 | 0 | 3 | 4 |
| Chrysler Imperial | 14.7 | 8 | 440.0 | 230 | 3.23 | 5.345 | 17.42 | 0 | 0 | 3 | 4 |
| Fiat 128 | 32.4 | 4 | 78.7 | 66 | 4.08 | 2.200 | 19.47 | 1 | 1 | 4 | 1 |
| Honda Civic | 30.4 | 4 | 75.7 | 52 | 4.93 | 1.615 | 18.52 | 1 | 1 | 4 | 2 |
| Toyota Corolla | 33.9 | 4 | 71.1 | 65 | 4.22 | 1.835 | 19.90 | 1 | 1 | 4 | 1 |
| Toyota Corona | 21.5 | 4 | 120.1 | 97 | 3.70 | 2.465 | 20.01 | 1 | 0 | 3 | 1 |
| Dodge Challenger | 15.5 | 8 | 318.0 | 150 | 2.76 | 3.520 | 16.87 | 0 | 0 | 3 | 2 |
| AMC Javelin | 15.2 | 8 | 304.0 | 150 | 3.15 | 3.435 | 17.30 | 0 | 0 | 3 | 2 |
| Camaro Z28 | 13.3 | 8 | 350.0 | 245 | 3.73 | 3.840 | 15.41 | 0 | 0 | 3 | 4 |
| Pontiac Firebird | 19.2 | 8 | 400.0 | 175 | 3.08 | 3.845 | 17.05 | 0 | 0 | 3 | 2 |
| Fiat X1-9 | 27.3 | 4 | 79.0 | 66 | 4.08 | 1.935 | 18.90 | 1 | 1 | 4 | 1 |
| Porsche 914-2 | 26.0 | 4 | 120.3 | 91 | 4.43 | 2.140 | 16.70 | 0 | 1 | 5 | 2 |
| Lotus Europa | 30.4 | 4 | 95.1 | 113 | 3.77 | 1.513 | 16.90 | 1 | 1 | 5 | 2 |
| Ford Pantera L | 15.8 | 8 | 351.0 | 264 | 4.22 | 3.170 | 14.50 | 0 | 1 | 5 | 4 |
| Ferrari Dino | 19.7 | 6 | 145.0 | 175 | 3.62 | 2.770 | 15.50 | 0 | 1 | 5 | 6 |
| Maserati Bora | 15.0 | 8 | 301.0 | 335 | 3.54 | 3.570 | 14.60 | 0 | 1 | 5 | 8 |
| Volvo 142E | 21.4 | 4 | 121.0 | 109 | 4.11 | 2.780 | 18.60 | 1 | 1 | 4 | 2 |

By comparison, below is the table with the normal font size.

2.1. ABC

| | mpg | cyl | disp | hp | drat | wt | qsec | vs | am | gear | carb |
|---------------------|------|-----|-------|-----|------|-------|-------|----|----|------|------|
| Mazda RX4 | 21.0 | 6 | 160.0 | 110 | 3.90 | 2.620 | 16.46 | 0 | 1 | 4 | 4 |
| Mazda RX4 Wag | 21.0 | 6 | 160.0 | 110 | 3.90 | 2.875 | 17.02 | 0 | 1 | 4 | 4 |
| Datsun 710 | 22.8 | 4 | 108.0 | 93 | 3.85 | 2.320 | 18.61 | 1 | 1 | 4 | 1 |
| Hornet 4 Drive | 21.4 | 6 | 258.0 | 110 | 3.08 | 3.215 | 19.44 | 1 | 0 | 3 | 1 |
| Hornet Sportabout | 18.7 | 8 | 360.0 | 175 | 3.15 | 3.440 | 17.02 | 0 | 0 | 3 | 2 |
| Valiant | 18.1 | 6 | 225.0 | 105 | 2.76 | 3.460 | 20.22 | 1 | 0 | 3 | 1 |
| Duster 360 | 14.3 | 8 | 360.0 | 245 | 3.21 | 3.570 | 15.84 | 0 | 0 | 3 | 4 |
| Merc 240D | 24.4 | 4 | 146.7 | 62 | 3.69 | 3.190 | 20.00 | 1 | 0 | 4 | 2 |
| Merc 230 | 22.8 | 4 | 140.8 | 95 | 3.92 | 3.150 | 22.90 | 1 | 0 | 4 | 2 |
| Merc 280 | 19.2 | 6 | 167.6 | 123 | 3.92 | 3.440 | 18.30 | 1 | 0 | 4 | 4 |
| Merc 280C | 17.8 | 6 | 167.6 | 123 | 3.92 | 3.440 | 18.90 | 1 | 0 | 4 | 4 |
| Merc 450SE | 16.4 | 8 | 275.8 | 180 | 3.07 | 4.070 | 17.40 | 0 | 0 | 3 | 3 |
| Merc 450SL | 17.3 | 8 | 275.8 | 180 | 3.07 | 3.730 | 17.60 | 0 | 0 | 3 | 3 |
| Merc 450SLC | 15.2 | 8 | 275.8 | 180 | 3.07 | 3.780 | 18.00 | 0 | 0 | 3 | 3 |
| Cadillac Fleetwood | 10.4 | 8 | 472.0 | 205 | 2.93 | 5.250 | 17.98 | 0 | 0 | 3 | 4 |
| Lincoln Continental | 10.4 | 8 | 460.0 | 215 | 3.00 | 5.424 | 17.82 | 0 | 0 | 3 | 4 |
| Chrysler Imperial | 14.7 | 8 | 440.0 | 230 | 3.23 | 5.345 | 17.42 | 0 | 0 | 3 | 4 |
| Fiat 128 | 32.4 | 4 | 78.7 | 66 | 4.08 | 2.200 | 19.47 | 1 | 1 | 4 | 1 |
| Honda Civic | 30.4 | 4 | 75.7 | 52 | 4.93 | 1.615 | 18.52 | 1 | 1 | 4 | 2 |
| Toyota Corolla | 33.9 | 4 | 71.1 | 65 | 4.22 | 1.835 | 19.90 | 1 | 1 | 4 | 1 |
| Toyota Corona | 21.5 | 4 | 120.1 | 97 | 3.70 | 2.465 | 20.01 | 1 | 0 | 3 | 1 |
| Dodge Challenger | 15.5 | 8 | 318.0 | 150 | 2.76 | 3.520 | 16.87 | 0 | 0 | 3 | 2 |
| AMC Javelin | 15.2 | 8 | 304.0 | 150 | 3.15 | 3.435 | 17.30 | 0 | 0 | 3 | 2 |
| Camaro Z28 | 13.3 | 8 | 350.0 | 245 | 3.73 | 3.840 | 15.41 | 0 | 0 | 3 | 4 |
| Pontiac Firebird | 19.2 | 8 | 400.0 | 175 | 3.08 | 3.845 | 17.05 | 0 | 0 | 3 | 2 |
| Fiat X1-9 | 27.3 | 4 | 79.0 | 66 | 4.08 | 1.935 | 18.90 | 1 | 1 | 4 | 1 |
| Porsche 914-2 | 26.0 | 4 | 120.3 | 91 | 4.43 | 2.140 | 16.70 | 0 | 1 | 5 | 2 |
| Lotus Europa | 30.4 | 4 | 95.1 | 113 | 3.77 | 1.513 | 16.90 | 1 | 1 | 5 | 2 |
| Ford Pantera L | 15.8 | 8 | 351.0 | 264 | 4.22 | 3.170 | 14.50 | 0 | 1 | 5 | 4 |
| Ferrari Dino | 19.7 | 6 | 145.0 | 175 | 3.62 | 2.770 | 15.50 | 0 | 1 | 5 | 6 |
| Maserati Bora | 15.0 | 8 | 301.0 | 335 | 3.54 | 3.570 | 14.60 | 0 | 1 | 5 | 8 |
| Volvo 142E | 21.4 | 4 | 121.0 | 109 | 4.11 | 2.780 | 18.60 | 1 | 1 | 4 | 2 |

CHAPTER 3

Test part

This is a test

3.1 Abc

Bla bla ref Miskovic et al. [2019] and [Miskovic et al., 2019].

But in Béal et al. [2019] we have the Figure 3.1 as referenced in Chapter 3

```
par(mar = c(4, 4, .1, .1))  
plot(pressure, type = 'b', pch = 19)
```

And an external figure 3.2

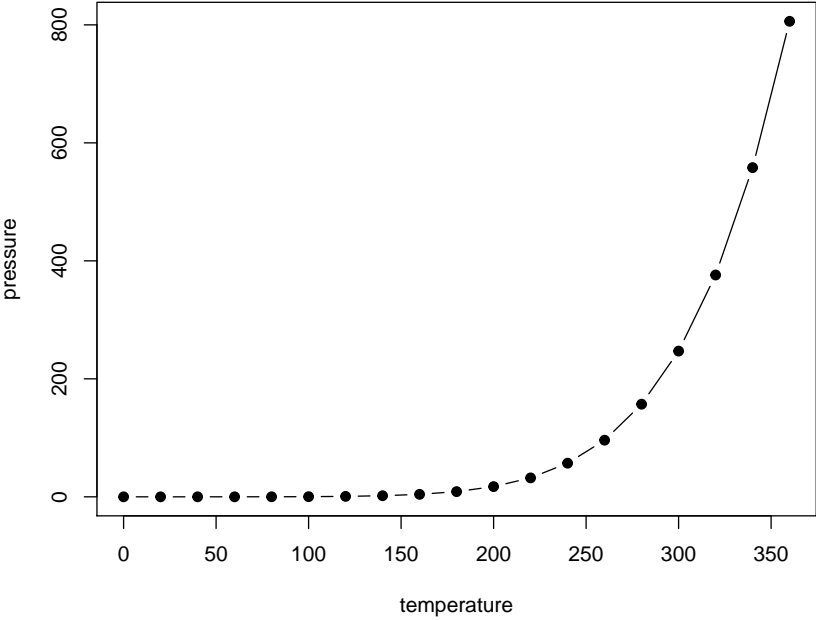


Figure 3.1: Here is a nice figure!



Figure 3.2: Example pic

Bibliography

- Jonas Béal, Arnau Montagud, Pauline Traynard, Emmanuel Barillot, and Laurence Calzone. Personalization of Logical Models With Multi-Omics Data Allows Clinical Stratification of Patients. *Frontiers in Physiology*, 2019. ISSN 1664-042X. doi: 10.3389/fphys.2018.01965. URL <https://www.frontiersin.org/article/10.3389/fphys.2018.01965/full>.
- Ljubisa Miskovic, Jonas Béal, Michael Moret, and Vassily Hatzimanikatis. Uncertainty reduction in biochemical kinetic models: Enforcing desired model properties. *PLoS Computational Biology*, 2019. ISSN 15537358. doi: 10.1371/journal.pcbi.1007242. URL <https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1007242>.

RÉSUMÉ

Cuius acerbitati uxor grave accesserat incentivum, germanitate Augusti turgida supra modum, quam Hannibaliano regi fratris filio antehac Constantinus iunxerat pater, Megaera quaedam mortalis, inflammatrix saevientis adsidua, humani cruoris avida nihil mitius quam maritus; qui paulatim eruditiores facti processu temporis ad nocendum per clandestinos versutosque rumigerulos conpertis leviter addere quaedam male suetos falsa et placentia sibi discentes, adfectati regni vel artium nefandarum calumnias insontibus adfligebant.

MOTS CLÉS

Caesar licentia post honoratis haec adhibens urbium honoratis nullum Caesar.

ABSTRACT

Verum ad istam omnem orationem brevis est defensio. Nam quoad aetas M. Caeli dare potuit isti suspitioni locum, fuit primum ipsius pudore, deinde etiam patris diligentia disciplinaque munita. Qui ut huic virilem togam dedit nihil dicam hoc loco de me; tantum sit, quantum vos existimatis; hoc dicam, hunc a patre continuo ad me esse deductum; nemo hunc M. Caelium in illo aetatis flore vidit nisi aut cum patre aut mecum aut in M. Crassi castissima domo, cum artibus honestissimis erudiretur.

KEYWORDS

Delatus delatus nominatus onere aut trahebatur quod tenus et bonorum.