



LONG THESIS TITLE

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der Technischen Universität Darmstadt

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Doctor rerum naturalium (Dr. rer. nat.)

vorgelegte Dissertation von

HANS WURST

Erstgutachter: Prof. Dr. Musterprof

Zweitgutachter: Prof. Dr. Musterprof2

DARMSTADT 2022

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Abstract

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Zusammenfassung

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CHAPTER 1

Prologue

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“... Ion channels are involved in every thought, every perception, every movement, every heartbeat.”
- Clay M. Armstrong (1999)

1.1 THESIS OUTLINE

Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language. Finally, some text with citations here.¹

¹ Abraham et al. (2015); Alam and Jiang (2009).

1.2 PUBLICATIONS

The following thesis draws on the ideas and writing of the following published works. They are the result of my own research performed during my doctoral studies together with several coworkers and collaborators:

Marini, C., Porro, A., Rastetter, A., Dalle, C., Rivolta, I., **Bauer, D.**, et al. (2018)

[HCN1 mutation spectrum: from neonatal epileptic encephalopathy to benign generalized epilepsy and beyond.](#) *Brain* 141.11, pp. 3160–3178. DOI: [10.1093/brain/awy263](#).

Porro, A., Saponaro, A., Gasparri, F., **Bauer, D.**, Gross, C., Pisoni, M., et al. (2019)

[The HCN domain couples voltage gating and cAMP response in Hyperpolarization-activated Cyclic Nucleotide-gated channels.](#) *eLife* 8, e49672. DOI: [10.7554/eLife.49672](#).

Jenewein, T., Kanner, S. A., **Bauer, D.**, Hertel, B., Colecraft, H. M., Moroni, A., et al. (2020)

The mutation L69P in the PAS domain of the hERG potassium channel results in LQTS by trafficking deficiency. *Channels* 13.1, pp. 163–174. DOI: [10.1080/19336950.2020.1751522](https://doi.org/10.1080/19336950.2020.1751522).

Hauf, K., Barsch, L., **Bauer, D.**, Buchert, R., Armbruster, A., Frauenfeld, L., et al. (2020)

GlyT1 encephalopathy: Characterization of presumably disease causing GlyT1 mutations. *Neurochemistry International* 139, p. 104813. DOI: [10.1016/j.neuint.2020.104813](https://doi.org/10.1016/j.neuint.2020.104813).

Schmidt, M., Schroeder, I., **Bauer, D.**, Thiel, G., and Hamacher, K. (2021)

Inferring functional units in ion channel pores via relative entropy. *European biophysics journal* 50.1, pp. 37–57. DOI: [10.1007/s00249-020-01480-7](https://doi.org/10.1007/s00249-020-01480-7).

Saponaro, A. *, **Bauer, D. ***, Giese, M. H. *, Swuec, P. *, Porro, A., Gasparri, F., et al. (2021)

Gating Movements and Ion Permeation in HCN4 Pacemaker Channels. *Molecular Cell* 81.14, 2929–2943.e6. DOI: [10.1016/j.molcel.2021.05.033](https://doi.org/10.1016/j.molcel.2021.05.033).

* indicates equal contribution.

CHAPTER 2

Introduction

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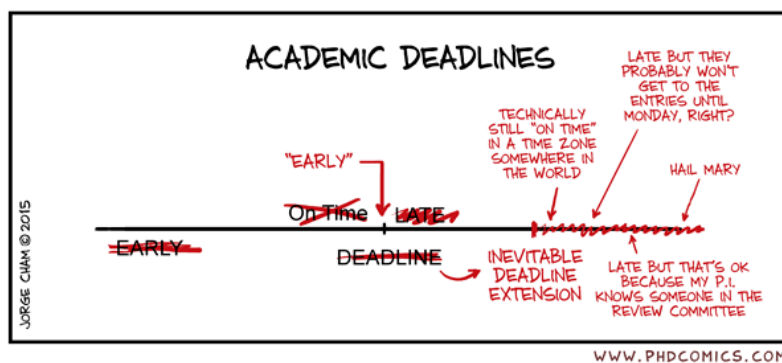


Figure 2.1: Taken from phdcomics.com. Here is an inline reference that has nothing to do with the graphic: Trudeau and Zheng (2015).

2.1 SECTION 1

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Figure 2.2: A cat.

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2.1.2 Subsection 2

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CHAPTER 3

Results

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CHAPTER 4

Discussion

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- Alam, A. and Jiang, Y. (2009)
[High-Resolution Structure of the Open NaK Channel](#). *Nature Structural & Molecular Biology* 16.1, pp. 30–34. DOI: [10.1038/nsmb.1531](#) (cited on p. 1).
- Trudeau, M. C. and Zheng, J. (2015)
Handbook of Ion Channels. 1st ed. CRC Press (cited on p. 3).

Part I

Appendix

Abbreviations

AA	amino acid
Ca ²⁺	calcium
cAMP	cyclic-adenosine monophosphate
CF	cystic fibrosis
CFTR	cystic fibrosis transmembrane conductance reg- ulator
cGMP	cyclic-guanosine monophosphate
Cl ⁻	chloride
CNBD	cyclic-nucleotide binding-domain
COM	center-of-mass
CV	collective variable
FES	free energy surface
HCN	hyperpolarization-activated cyclic nucleotide- gated
HCND	HCN domain
I _f	funny current
K _v	voltage-gated potassium channel
K ⁺	potassium
K ⁺ channel	potassium channel
KTN	nucleotide-binding domain
LBD	ligand-binding domain
LJ	Lennard-Jones
MD	molecular dynamics
MFEP	minimal free energy pathway
Na ⁺	sodium
NEB	nudged elastic band
PBC	periodic boundary conditions
PD	pore domain
PME	particle-mesh Ewald
PMF	potential of mean force
POPC	palmitoylcholinephosphatidylcholine
RDF	radial distribution function
SAN	sinoatrial node
SF	selectivity filter
TEA ⁺	tetraethylazanium
TMH	transmembrane helix
TPCs	two-pore channels
TRIP8b	tetratricopeptide repeat-containing Rab8b- interacting protein
TST	transition state theory
US	umbrella sampling
VdW	Van der Waals
VGIC	voltage-gated ion channel

VSD	voltage sensor domain
WHAM	Weighted Histogram Analysis Method
wt	wildtype

Experimental details

HOW TO BUILD A FLUX COMPENSATOR

Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

SOME OTHER TECHNICAL STUFF

Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

Additional data

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Acknowledgements

A page to put acknowledgements.

Thank you!

Ehrenwörtliche Erklärung

Ich erkläre hiermit, dass ich die vorliegende Arbeit entsprechend den Regeln guter wissenschaftlicher Praxis selbstständig und ohne unzulässige Hilfe Dritter angefertigt habe.

Sämtliche aus fremden Quellen direkt oder indirekt übernommenen Gedanken sowie sämtliche von Anderen direkt oder indirekt übernommenen Daten, Techniken und Materialien sind als solche kenntlich gemacht. Die Arbeit wurde bisher bei keiner anderen Hochschule zu Prüfungszwecken eingereicht.

Die eingereichte elektronische Version stimmt mit der schriftlichen Version überein.

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