LifeQ

Healthier by Design

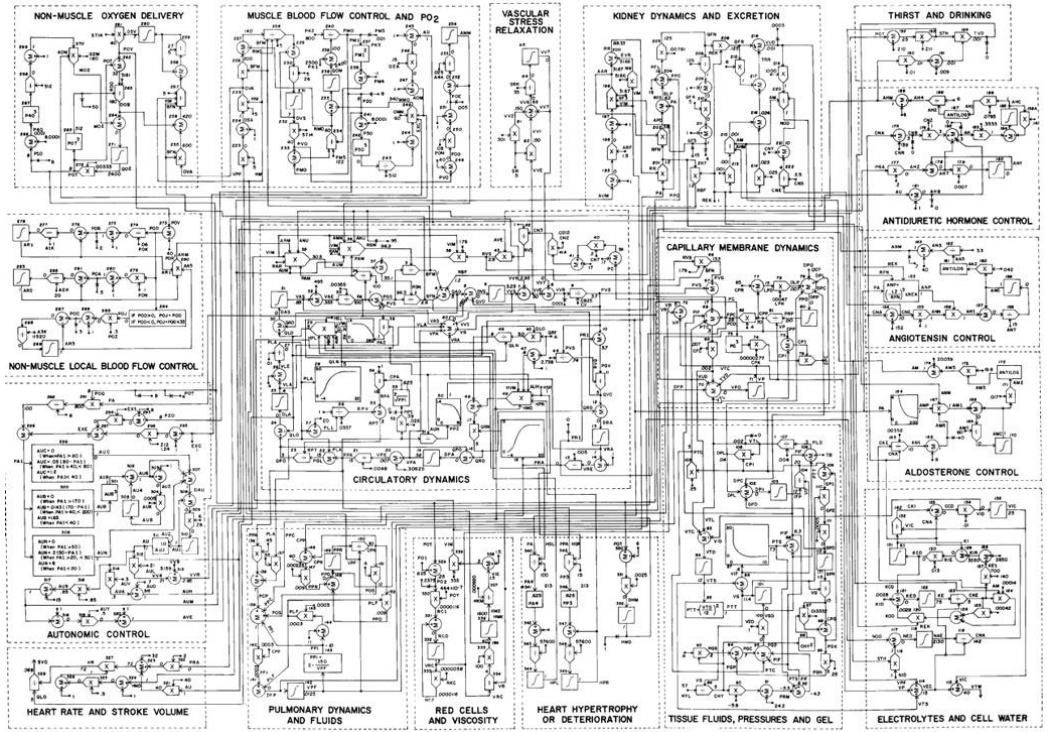
Building Mathematical Models to understand Human Health

LifeQ

We are a world leading science and technology company that wants people from all walks of life to enjoy optimal health

Human Physiology is Complex and Dynamic

- In the 1970's Dr. Arthur Guyton developed a model of cardiovascular physiology
- With the model he was able to **test various physiological hypotheses**
- Improvements in technology
  - More complex models
  - Better software and tools
  - Easier collaboration
  - More data



Hall, John E. (2004, November). The pioneering use of systems analysis to study cardiac output regulation. *American Journal of Physiology–Regulatory, Integrative and Comparative Physiology, 287(5).* Retrieved May 30, 2012, from http://ajpregu.physiology.org/content/287/5/R1009

LifeQ | Data Sources

- For the most part data came from **studies**
- Many factors that influence **sample size**, typically quite **small**
- Small samples VS complexity of human physiology
- For the same reasons, different studies often lead to **contradicting** results and conclusions
- Eg. Comparing Studies of **heart rate variability** as it relates to acute/chronic stress.
  - Different ways to measure HRV
  - Many factors influence HRV

Summary of HRV results: Changes in response to Stress

		Time domain				Frequency domain			Non-linear
		RR	SDRR	RMSSD	pNN50	LF	HF	LF/HF	D2
Castaldo 2015: Acute Stress						↑			
	N								
Lackner 2011	20	↓				↑			
Papousek 2010	65	↓↓					↓	↑	
Schubert 2009	50	↓↓	↑↑					↑	↓↓
Taelman 2011	43	↓↓	↓↓	↓↓	↓	↓↓	↓↓		
Tharion 2009	18	↓↓	↓↓	↓	↓↓	↓↓	↓↓	↓	
Visnovcova 2014	70	↓↓	↓↓			↑↑	↓↓		
Vuksanovic 2007	23	↓				↑↑	↑	↓	
Li 2009 (female)	84			↓↓			↓↓		
Li 2009 (male)	105			↓↓			↓↓		
Hjortskov 2004	12					↓↓	↓↓	↑	
Traina 2011	13					↑↑	↓	↑↑	
Kofman 2006	30							↑	
Melillo 2011	42								↓↓
Meta analysis pooled:		↓↓	↓↓	↓↓	↓↓	↑	↓↓	↑↑	↓↓
Mezzagappa 2001 (Exp 1)	27			↓↓					
Mezzagappa 2001 (Exp 2)	31			↓↓					
Weber 2010	44			↓↓					
Jarczok 2013: work stress (Chronic Stress)									
Chandola 2008	3290		↓↓			↓↓	↓↓		
Clays 2011	653		↑		↓	↑	↓	↑↑	
Collins and Karasek 2010	36						↓↓		
Collins 2005	36		↑				↓↓	↑	
Eller 2011a	231						↓↓	↑	
Hanson 2001	70						↓↓		
Hemingway 2005	1461		↓↓			↓↓	↓↓		
Hynynen 2011	99		↓↓	↓↓		↓↓	↓↓	↑	
Kang 2004	169		↓			↓	↓	↑	
Lucini 2007	91		↑			↓	↓	↑	
Uusitalo 2011	19		↓↓	↓↓		↓↓			
Van Amelsvoort 2000	135		↓↓	↓↓		↓↓			
Hjortskov 2004	12					↓↓	↓↓	↑↑	
Vrijkotte 2000	109			↓		↓	↓		

PNS indicators: RMSSD, pNN50, HF
Mixed SNS and PNS: RR, SDRR, LF, VLF, TP

Two arrows = statistically significant
One arrow = non significant trend

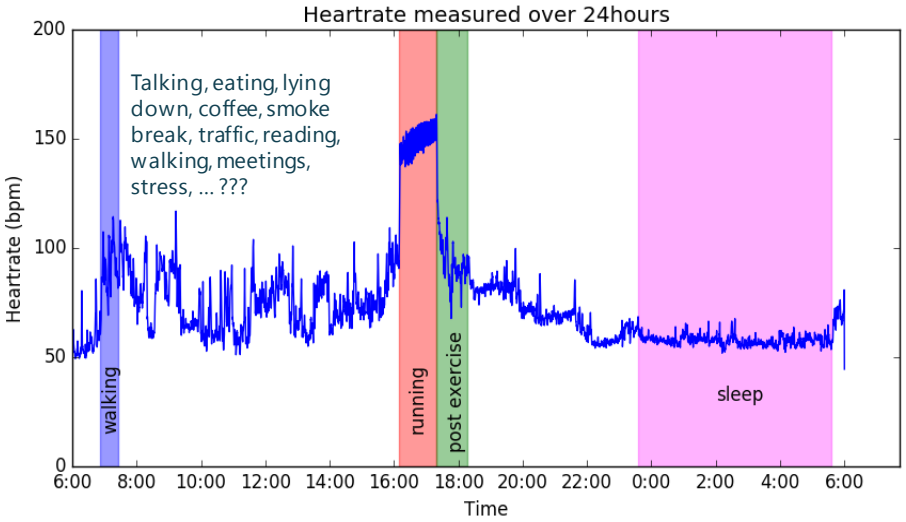
Blue = decrease during stress
Red = increase during stress

LifeQ | We are all different… to some extent

- Our bodies are very **dynamic**, with one system affecting another
- We all react somewhat **differently to the same stressors**
- We need:

More **relevant** and **contextualized** data (**quality**)

At **a higher resolution (frequency)**



- More relevant- because garbage in garbage out
- Higher resolution – helps to leverage time dynamics in physiology

LifeQ | Wearables and data

- Welcome **wearable technology** revolution!
- Technology is starting to give us the **information** we need
- Large number of new, real time and high resolution **information streams (non-invasively)**
- **Interpretation-** We are often interested in that which we cannot observe- internal physiological state
- Without **context** it is difficult to know which (hidden) factors driving the the data we observe

What if data is still not enough?

- What can we do instead of just collecting masses of data and trying to make sense of it?
- Build **mathematical models** to simulate certain aspects of of human physiology
- **Computational physiology** involves modeling and simulation of complex biological systems
- This not only a set of mathematical tools but a **mind set**
- Even better, why not **combine** mathematical modelling of physiology with data driven techniques?

Depiction of an integrated respiratory model

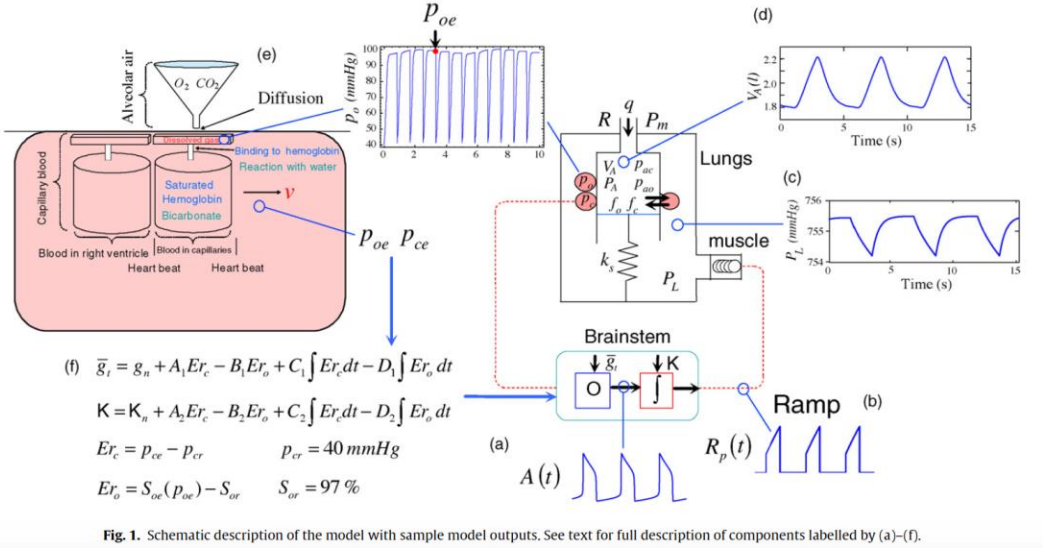
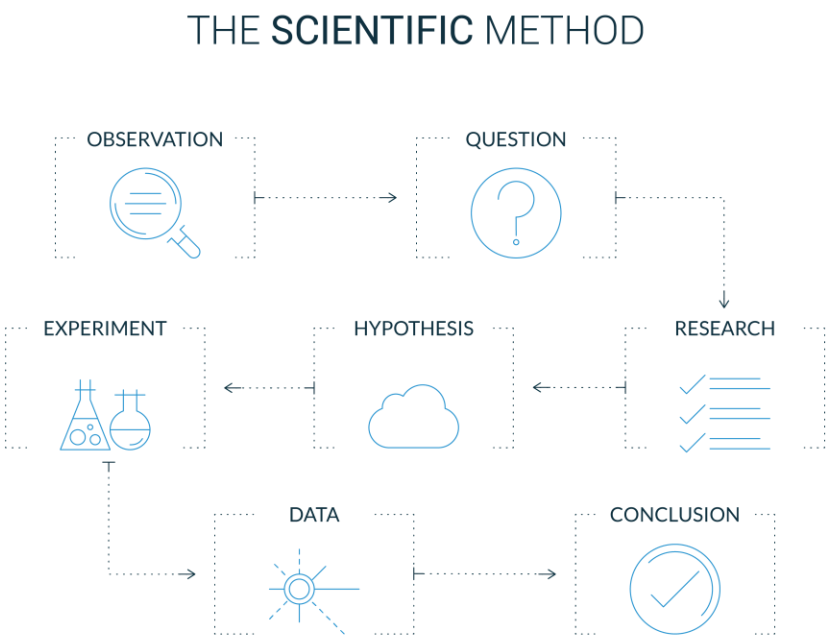


Fig. 1. Schematic description of the model with sample model outputs. See text for full description of components labelled by (a)–(f).

A Ben-Tal, JC Smith - Respiratory Physiology & Neurobiology, 2010 - Elsevier. Control of breathing: two types of delays studied in an integrated model of the respiratory system

LifeQ | Combining Data Driven Approaches with Mathematical Modeling

- Combing mathematical modelling with machine learning and data driven approaches has many **advantages**:
  - Data generation/simulation
  - Provide a guide in the absence of data or unreliable data
  - Help explain phenomena observed in the data
  - Informed feature engineering
  - Fine tune model parameters with observed data to personalize model outputs
- There is **no standard framework** of combining pure mathematical modelling and data driven approaches



LifeQ | Use Case: Acute Stress Detection

- **Research question**: Can simple wearable data be used to detect acute stress events?
- Need a **definition** for the problem: WHAT IS STRESS?
  - Needs to be unambiguous
  - Needs to have a measurable output
  - Physiologically relevant
- One possible definition: **Activation of the HPA-axis** (Hypothalamus–Pituitary–Adrenal axis)
  - Measurable output: Cortisol
    - Steroid hormone that regulates many processes in the body, from metabolism to immune responses.
    - Plays an important role in the body during stress

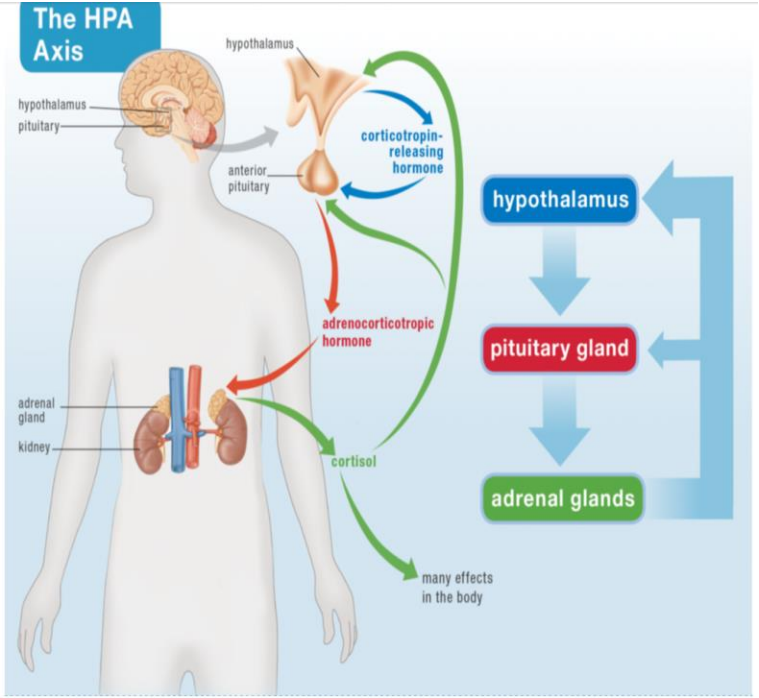


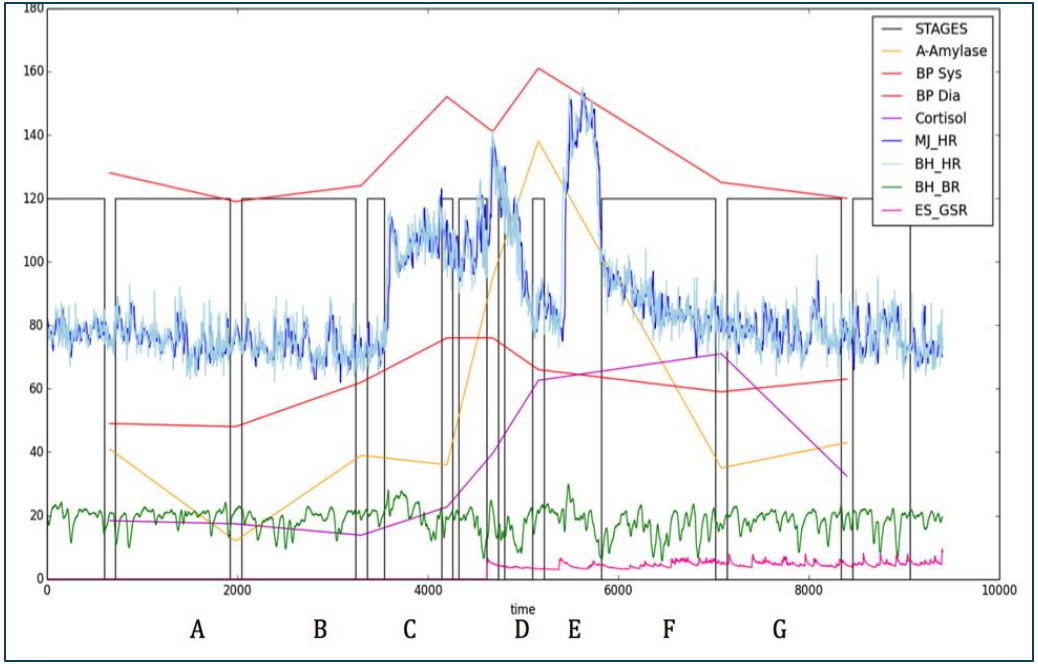
Image from The Paleo Approach – Copyright 2013 Sarah Ballantyne

LifeQ | Protocol Design and Data collection

- **Designed a protocol** based on a standardized test: Trier social stress test (TSST)
- Procedure to induce stress in research participants
- Carefully **control for confounding factors** (no stimulants, exercise, serious physical or mental health conditions, etc.)
- **Data collected**: Blood Pressure, enzymes (alpha amylase), salivary cortisol, a few others and wearable data

Data Driven Modeling: Feature Engineering

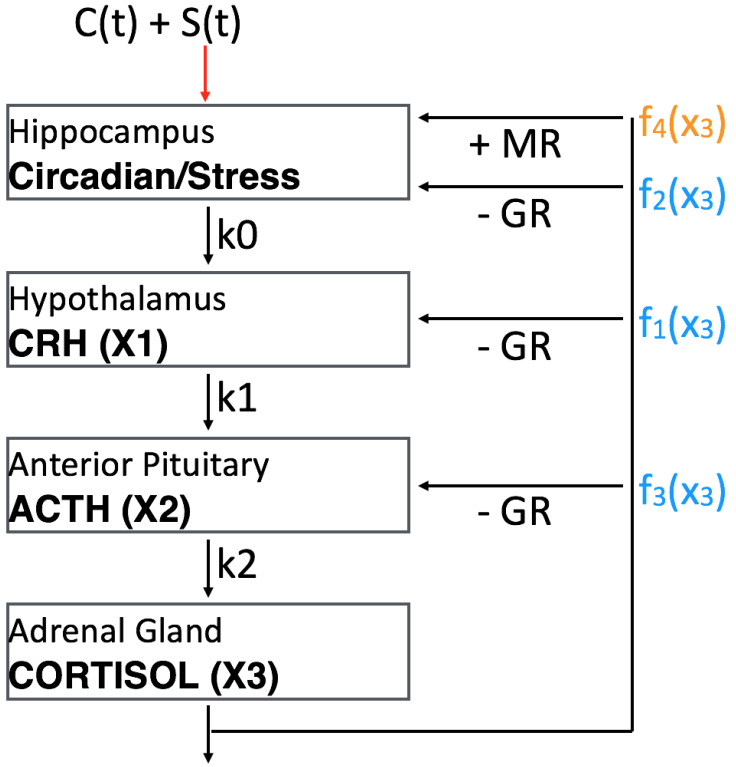
- Find **features**/factors of interest that will help detect the transition in the different states of the research participant
  - Guided by knowledge of physiology, and
  - (Unsupervised) Machine learning
- Note:
  - An increase in HR does not simply mean an increased stress level
  - You also get something like good stress, called Eustress
  - Difference between perceived and physiological stress



Various information streams collected during multiple acute stress events for a participant

LifeQ | Computational Physiology

- System of **differential equations** to model the HPA-axis
  - Model the changes in concentration of hormones with the appropriate time dynamics
- This enables the **prediction of cortisol** levels which can be compared against measured cortisol levels
- **Simple model**, the idealization removes the complicated details that are not essential for understanding the dynamics.
- Once we understand the basic principles, it is easy to **add complexity**

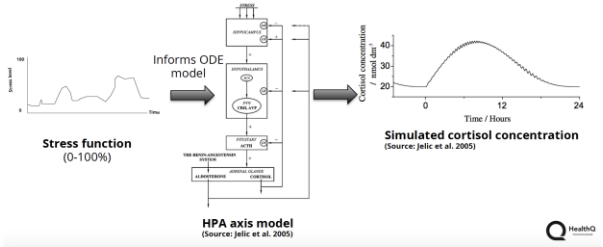


Simple model of the HPA-Axis

Combining Approaches

Estimate
stress score
from data

Simulate
cortisol levels



Compare
measured VS
Simulated

Make
adjustments
and
improvements

Current Challenges in Health and Wellness

- **Free living data** is more complex and does not play well with laboratory conditions
- Little guidance from **literature**
  - Not enough longitudinal studies
  - Ignoring complex interactions
  - Population based studies, not focused on individual and one-dimensional
- **Big data** not always so big
- **Data Quality**
- Also, **Gold standards** are hard to obtain or does not even exist!
- **Ethics** can be challenging
- **Data Security** and laws

Where is this heading?

Healthcare on the P4 Spectrum

Preventative

(changing lifestyle in order to track and improve health)

Predictive

(e.g. predicting cardiovascular disease)

Participatory

(individuals engage with their own data and develop an awareness of the impact of their choices)

Personalized

(getting feedback that is specific to your physiology)