



Biological Measures

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Towards biological quantity theory for nominal property metrology in polyenzymatic devices with living cells

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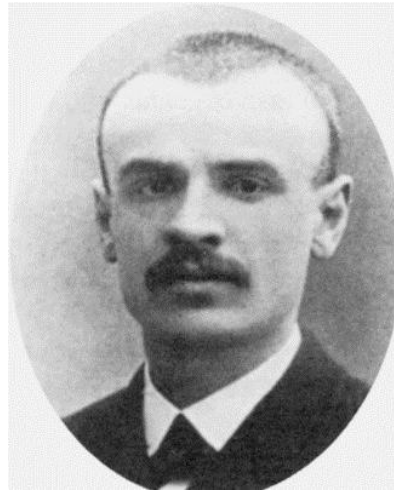
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Outlook

- Measure theory after the Metre Convention
- Axiom of Victor Hugo
 - The keys of mind: number, letter, note. Know, think, dream.
- Non-quantitative variables
 - letters, notes, keywords, images etc.
- A few examples of a lot of different measures
 - We plan to return to our buttons
- Birth of true biological metrology
 - Thanks & THE END



- *Bureau international des poids et mesures* (BIPM).
- The BIPM was created on 20 May **1875**, following the signing of the Metre Convention.

Émile Borel (7.1.**1871**-3.2.1956),

History

René-Louis Baire (21.1.**1874**-5.7.1932) &

Henri Lebesgue (28.6.**1875**-26.7.1941)

created measure theory. They "with mother's milk" absorbed «Liberté, Égalité, Fraternité» and ... measure.



Victor Hugo (26.2.1802 – 22.5.1885)

- «L'esprit de l'homme a trois clefs qui ouvrent tout : le chiffre, la lettre, la note. Savoir, penser, rêver. Tout est là.»
- “The mind of man has three keys which open everything: the **number**, the **letter**, the **note**. Know, think, dream. Everything is here.”
- «Разум человеческий владеет тремя ключами, открывающими все: цифрой, буквой, нотой. Знать, думать, мечтать. Все в этом».

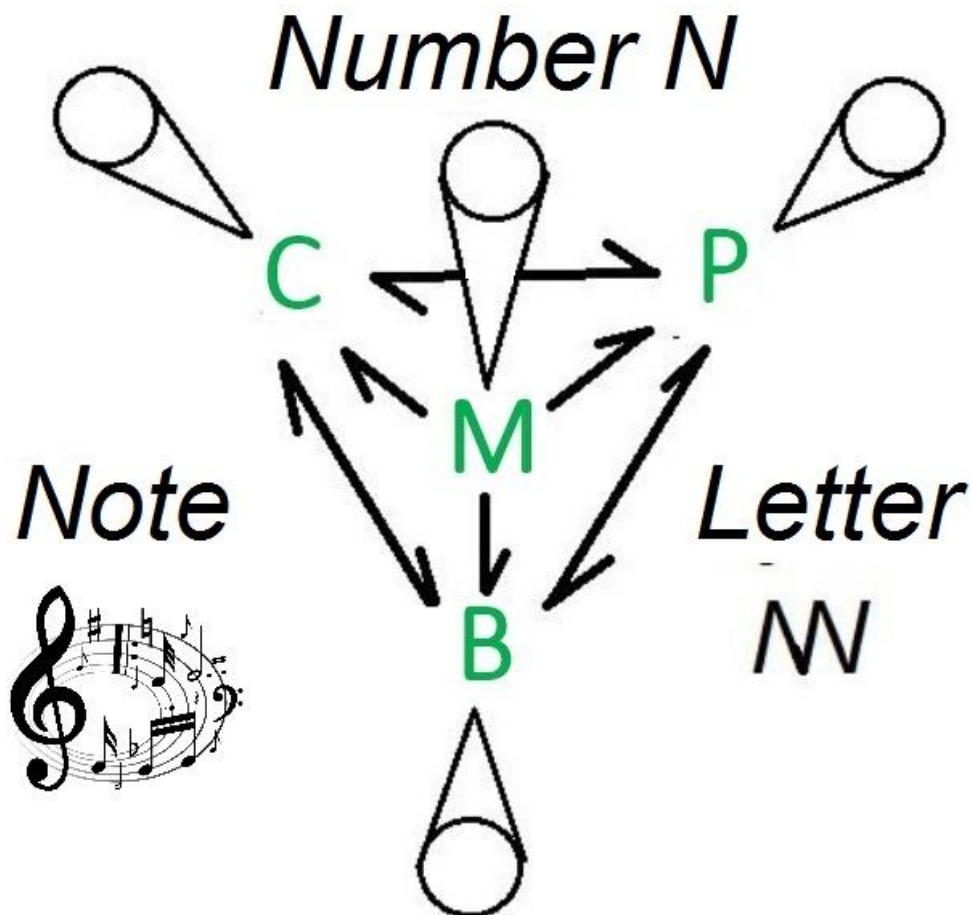


Variables, values etc.

- numbers and non-quantitative values:
 - letters,
 - notes,
 - keywords,
 - images ...
- Function values
 - numbers and non-quantitative values:
 - letter,
 - note,
 - keywords,
 - images ...
- But why only **quantity** with **nominal properties**?



The values = Hugo' axiom





The question arises

- Is it possible to make a general measure theory for any non-numeric variables?

- The answer is trivial: no, never, nobody. **NNN**

NNN – a non-numeric notation

- Why?

- The brain thinks in a very high dimension continuum field.

- That is why the word dimension has two meanings:
 - the actual number of dimensions of space and
 - the measurement process itself.

Garrett Birkhoff (19.1.1911-22.11.1996)

Mathematics and psychology // SIAM Review 11, 429 (1969).



- The first technique of **discrete** mathematics was that of counting (e.g., of a herd of sheep), while **continuum** mathematics dealt with the **measurement** of various quantities such as distance, area, time, weight and volume.
- Our mind can convert the letter into a mental image (imagination), but stupid supercomp can't.
- Robot-like "thinking machines" are not possible.
- We can look forward to ever increasing **man-computer symbiosis**, in which each partner performs the tasks for which it is most effective.

Allen measures



- μ_{AI2} – Allen Institute for Artificial Intelligence
- μ_{AB} – Allen Institute for Brain Science
 - NW Gouwens et al. // *Nature neuroscience* **22**, 1182 (2019)
 - H Choi, S Mihalas // *PLoS comp biology* **15**, e1006978 (2019)
- μ_{AC} – Allen Institute for Cell Science
 - Integrated Mitotic Stem Cell <https://imsc.allencell.org/>

Scholar Google measures

- μ_{SG} – the search of papers using a lot dimensions

Artificial Intelligence measures

- μ_{AI} – they never can think, the paste & copy only!
But they help us to think a lot!

BioNumbers measures μ_{BN}



- μ_{BN} – by Ron Milo (Bio Phys), Rob Phillips (Phys Bio) and Nigel Orme (Image measures)

- Ron Milo, Rob Phillips. Illustrated by Nigel Orme. Cell biology by the numbers. 2016. 395 p.
- <https://bionumbers.hms.harvard.edu/search.aspx>

B10NUMB3R5
THE DATABASE OF USEFUL BIOLOGICAL NUMBERS

Home Index Book About Us Misc. ▼

e.g. "ribosome coli"; "p53 human"; "transcription"



Popular BioNumbers

Recent BioNumbers

Key BioNumbers



Physiological measures

- Claude Bernard. Principe de médecine expérimentale. Paris: Baillière (1847).
 - Клод Бернар. Классики биологии и медицины. Лекции по экспериментальной патологии. Биомедгиз. 1937. 588 с.
- Claude Bernard (12.7.1813 – 10.2.1878) μ_{CB}
- Ivan M Sechenov (13.8.1829 – 15.11.1905) μ_{IS}
- Ivan P Pavlov (26.9.1849 – 27.2.1936) μ_{IP}
- Ilya I Mechnikov (15.5.1845 – 15.7.1916) μ_{IM}
- Vladimir M Bekhterev (20.1.1857 – 24.12.1927) μ_{VB}
 - Denis Noble. Claude Bernard, the first systems biologist, and the future of physiology // *Experimental Physiology* **93** (1), 16-26 (2008). → a few measures of D Noble below

1st measure of Denis Noble



- Denis Noble. **The music of life**: biology beyond genome. Oxford University Press, 2006. 168 p.

2nd measure

- Denis Noble. **Dance to the Tune of Life**: Biological Relativity. Cambridge University Press. 2016. 302 p.

3rd measure

- **Exosomes: A Clinical Compendium**. Eds: Lawrence Edelstein, John Smythies, Peter Quesenberry, Denis Noble. 1st Ed. Academic Press. 2020. 450 p.
- 2014 Theme Issue 'Epigenetic information-processing mechanisms in the brain' compiled and edited by Lawrence Edelstein, John Smythies and Denis Noble // *Philosophical Transactions of the Royal Society B: Biological Sciences* **369** (1652), all issue (2014).

4th μ_{DN} – principles of biology



1. Biological functionality is multilevel.
2. Information transmission is not one-way process.
3. DNA is not the sole transmitter of inheritance.
4. The theory of biological relativity; there is no privileged level of causality.
5. Gene ontology will fail without higher-level insight.
6. There is no genetic program.
7. There are no programs at any other level.
8. There are no programs in the brain.
9. The self is not an object.
10. There are many more to be discovered; a genuine 'theory of biology' does not yet exist.



Principles of biology – μ_{PB}

1. Life act is action (restless state for bio action)
2. Biological bonds have multidimensional nature
3. Cell has continuum state (continuum & discrete h.)
4. Diversity is a biological law (finite man – infinite life)
5. Life creates emergence (emergence is life fact)
6. Functions & function signals
7. Gene: genial complexity, organization and hierarchy
8. Heredity is the mixing of cell lineages & pedigrees
9. Integrity and individuality (bio etalon is impossible)
10. Joint conditional biological measures



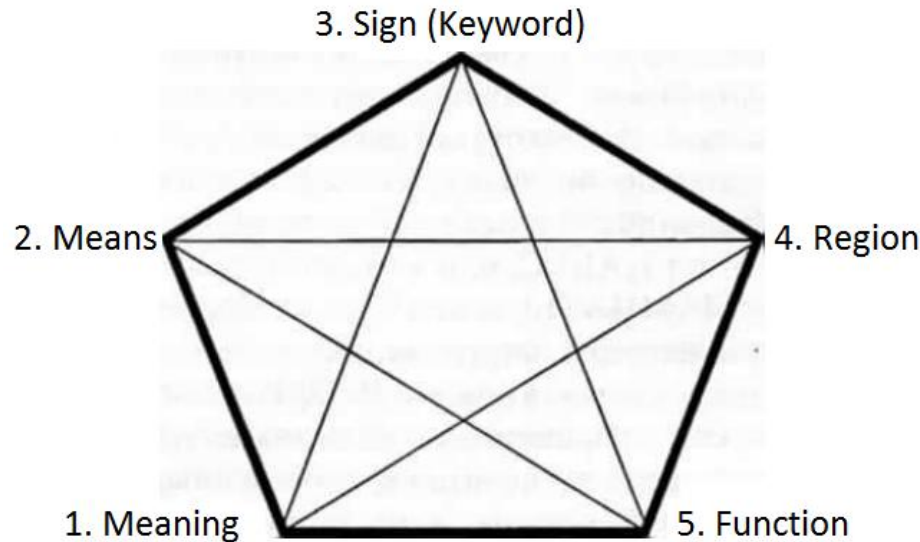
The bio lemma

- Bio action is never equal to bio counteraction, their difference is the driving force of development.
 - Rest only in our dreams.
 - A Blok: «The excitement never ends».

Physical side of Nature

- Newton's 3rd law: Action is equal to counteraction.
- Planck's constant is quantum of action h .
- $h = 6.62607015 \times 10^{-34}$ J·s (exactly now!)
 - Physical action $I = \int p \cdot dq = \int q \cdot dp$,
- where q – coordinate, p – momentum

Yu N Karaulov's cognome (2004)



Elementary unit of knowledge is the cognome, structured in the form of a “figure of knowledge”, connecting 5 parameters into a sign-cognitive unity-meaning, the specific way of forming this meaning, the corresponding keyword, an indication of the subject area of the world.

Linguistic measures of mind are the most difficult.

Electrical measures of neurons are much simpler.

C Koch. Consciousness: Confessions of a Romantic Reductionist. 2012.



A few notes on the start of novel measurement measures

- 2004 «Constructing measures»,
 - Mark Wilson wrote his book
- 2006 «Cognitive Dimensions of Language Mind»,
 - YN Karaulov in the book "Slavistics: Synchrony and Diachrony", pp.14-29 (in Russian)
- 2013 "Quantification is Neither Necessary Nor Sufficient for Measurement",
 - Luca Mari et al. // *J Phys: Conf Ser* **459**, 012007.
- 2018 "The quality of measurement results in terms of the structural features of the measurement process",
 - Andrew Maul et al. // *Measurement* 116, 611-620.



May 20, 2019

Quantum SI of Nature was born!

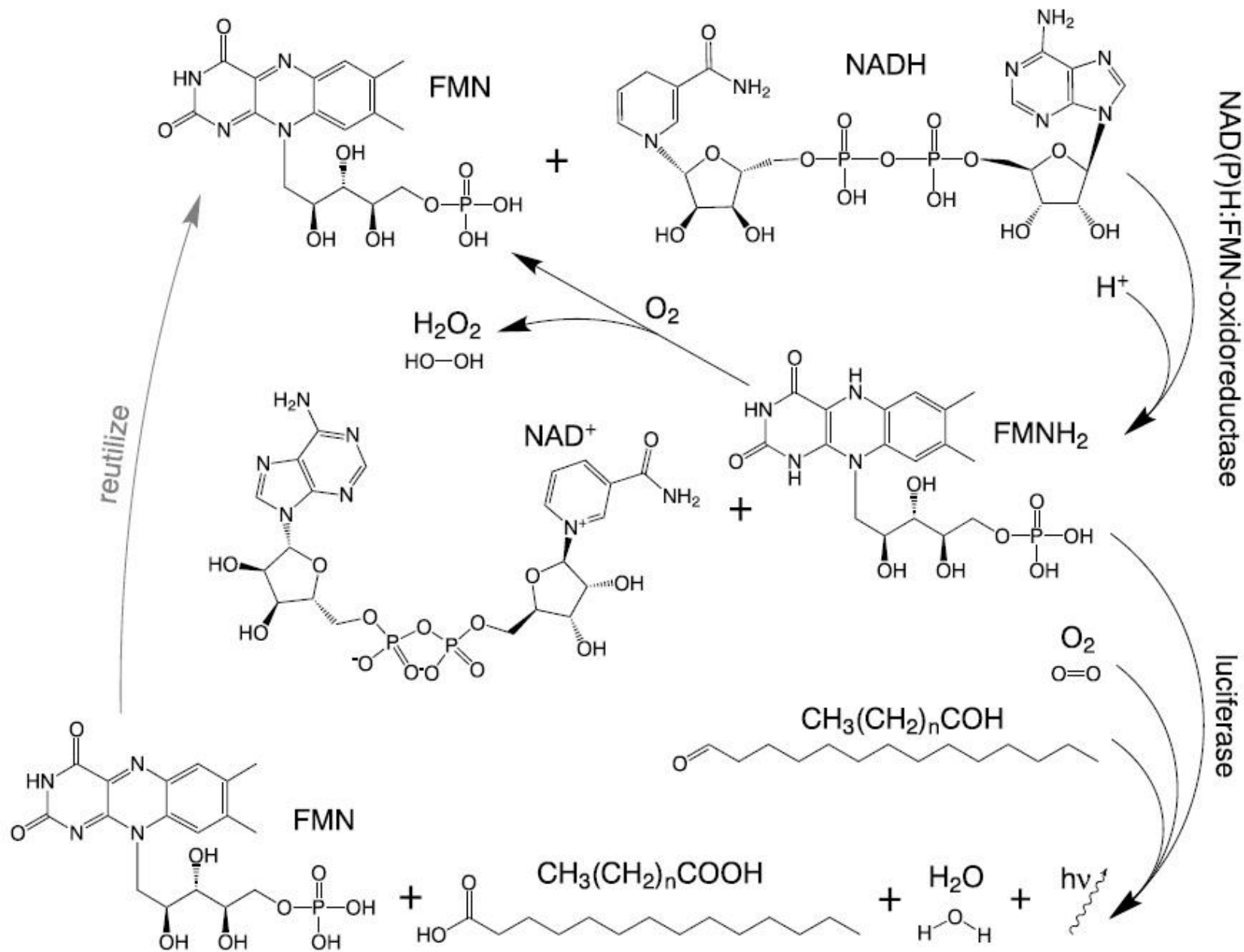
- Sorry, it is **numbers** only, i.e. quantitative, physical side of Nature!
 - What about the music of life (**notes**) and the meaning of my doctor words (**letters**)?
- How to measure the meaning and value of so many non-numeric variables that determine the quality of our life?
- The end of Great Metrological Revolution (Nov 16, 2018) is essentially the greatest beginning ... of what?

THE DEFINING CONSTANTS OF THE INTERNATIONAL SYSTEM OF UNITS

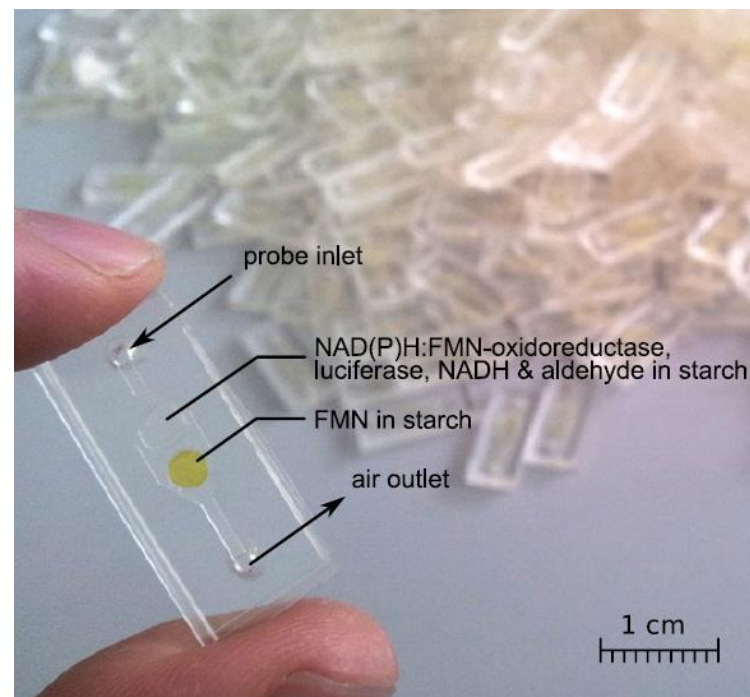
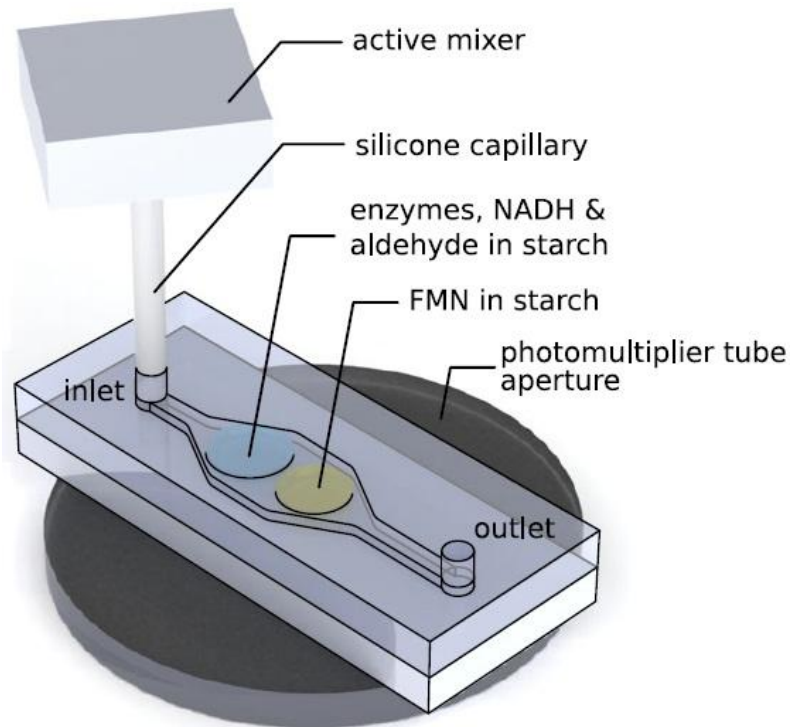
Defining constant	Symbol	Numerical value	Unit
hyperfine transition frequency of Cs	$\Delta\nu_{\text{Cs}}$	9 192 631 770	Hz
speed of light in vacuum	c	299 792 458	m s^{-1}
Planck constant*	h	$6.626\,070\,15 \times 10^{-34}$	J Hz^{-1}
elementary charge*	e	$1.602\,176\,634 \times 10^{-19}$	C
Boltzmann constant*	k	$1.380\,649 \times 10^{-23}$	J K^{-1}
Avogadro constant*	N_{A}	$6.022\,140\,76 \times 10^{23}$	mol^{-1}
luminous efficacy	K_{cd}	683	lm W^{-1}

*These numbers are from the CODATA 2017 special adjustment. They were calculated from data available before the 1st of July 2017.

SI WC – *Wallet Card*

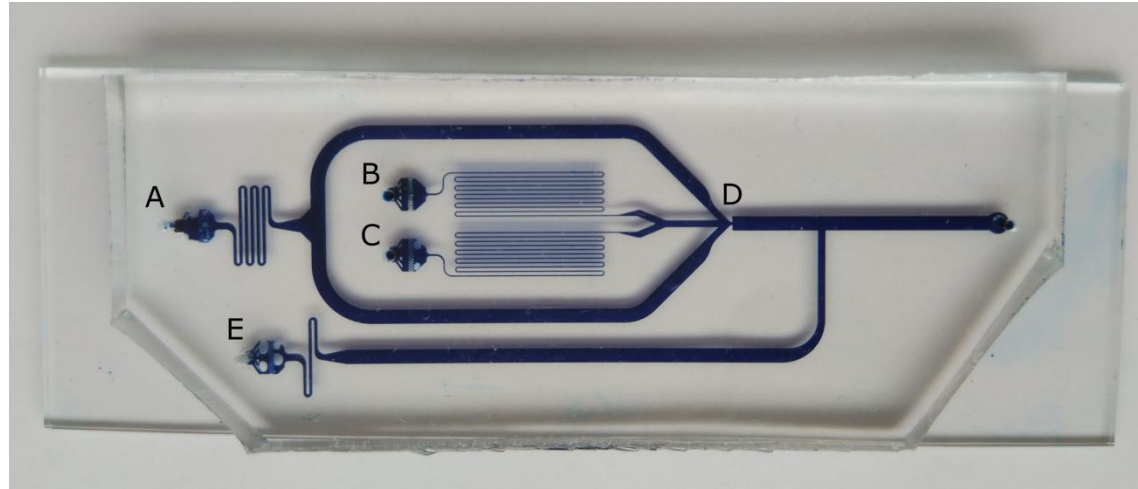


Transform bio to *hv* signal



- Our chips for the transformation of *bio* to *phys* signal
 - Ivan Denisov et al. // *Luminescence* **33**, 1054 (2018).

Overview of PDMS chip for Red + Luc sys based on droplet microfluidic platform.



Red + Luc system was fed into the chip in the form of two solutions. One solution (B) contained enzymes and NADH. The other solution (C) contained aldehyde, FMN, and the analyzed sample. After merging of B and C, the flow is compressed by the oil phase (A) at the point of hydrodynamic focusing (D) forming water-in-oil emulsion.

- More will be in the paper of IMEKO 2019

NNV – Non-Numeric Values



- Variables (N & NNV):

- letters,
- notes,
- keywords,
- images ...

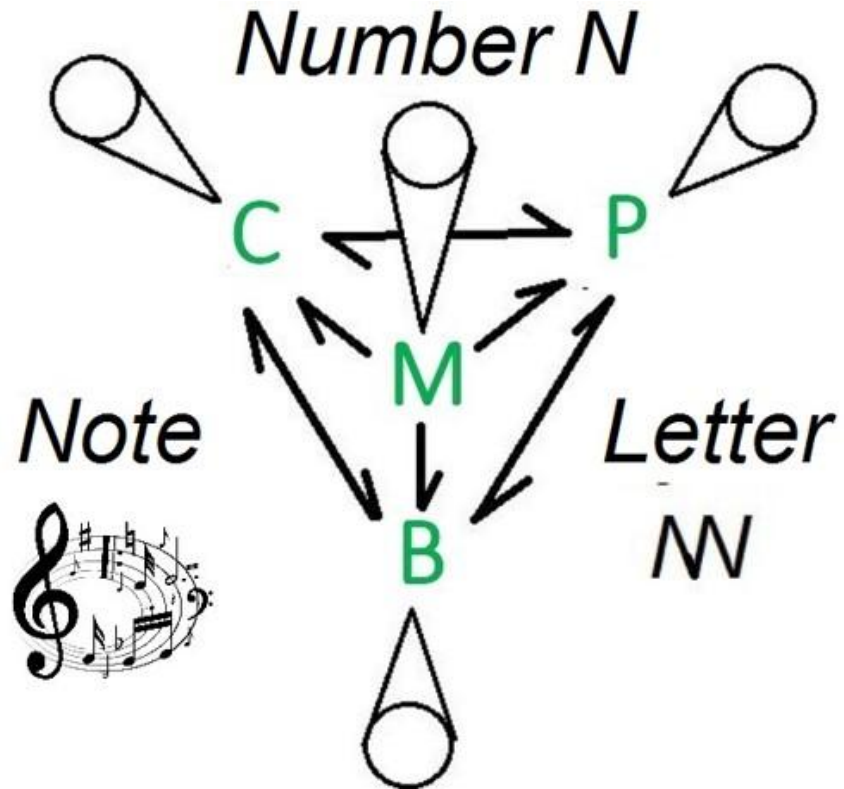
- Function values:

- letter,
- note,
- keywords,
- images ...

- From **quantity** with **nominal properties**

toward Non-Numeric Values & Measures

<https://sites.google.com/site/nnvmeasures/>





Intro to Non-Numeric Value & Math Measures Edu

- Paul R. Halmos. Measure Theory. 1950.
Google Book [URL](#) [Cited by 7567](#) (1 July 2019)
- Халмош П. Теория меры / Пер. с англ. под ред. проф. С.В. Фомина. 1953.
- Felix Hausdorff. Grundzüge der Mengenlehre. 1914. Mengenlehre. 1927.
- Google Book [URL](#) [Cited by 1661](#) (1 July 2019)
- Хаусдорф Ф. Теория множеств. / Пер. с нем. под ред. и с доп. П.С. Александрова и А.Н. Колмогорова. 1937.

<https://sites.google.com/site/nnvmeasures/>



Conclusions

- **Is it bio metrology? Why?**

- We can make living etalon never in principle.
- We transform bio signal into physical signal, using poly enzymatic chains into chip with luciferase.
- So luciferase microfluidic platform helps us to realize biological metrology.

All above is very simple

- Main problems are meaning of non-numeric biological variables and understanding «what we are measuring?»
- Here we hope on new biological measures.



Acknowledgments

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- I also thank Anton Yakimov, Ivan Denisov, Kirill Lukyanenko for many helpful comments, suggestions and discussions.
- I wish to thank the [Allen Institute](#) and [Paul G. Allen Frontiers Group](#) for vision, establish and support of open science.
- I'm sending the best wishes to all my friend who are feeling my thanks.

Know, think, dream ...



- Note
- Hunt
- Letter
- Photo
- Passion
- Number
- ..., ∞ etc.

Victor Hugo & my Boss

Boss helped
me to grasp:

**The Silence
is Freedom**

28



Босс