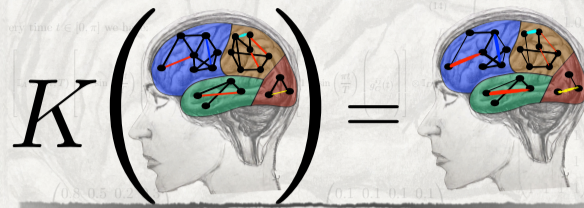


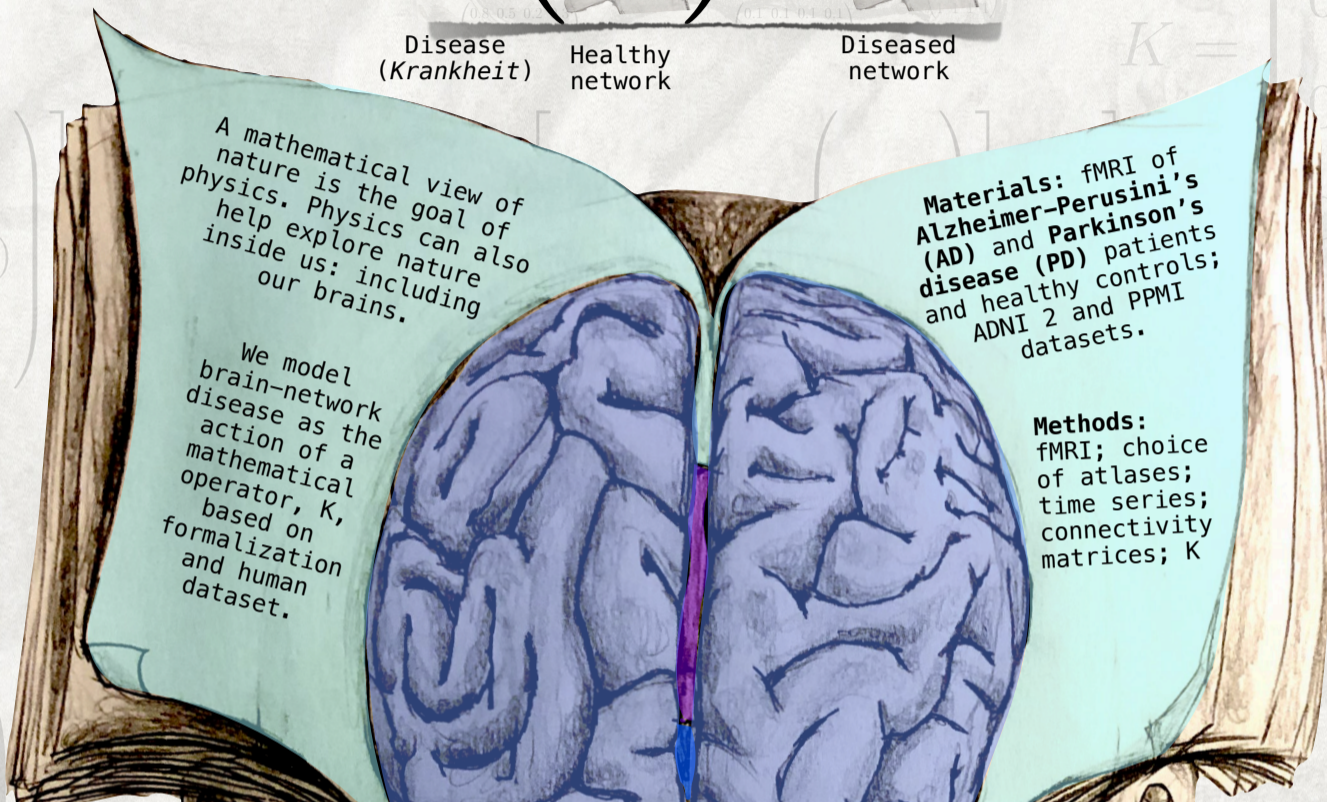
# A Dialogue between Formalization and Data: Neurological Disease as the Action of a Mathematical Operator

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Disease (Krankheit)    Healthy network    Diseased network



A mathematical view of nature is the goal of physics. Physics can also help explore nature inside us: including our brains.

We model brain-network disease as the action of a mathematical operator,  $K$ , based on formalization and human dataset.

**Materials:** fMRI of Alzheimer-Perusini's (AD) and Parkinson's disease (PD) patients and healthy controls; ADNI 2 and PPMI datasets.

**Methods:** fMRI; choice of atlases; time series; connectivity matrices;  $K$

### Discussion:

Inverse  $K$ -operator: information on the areas to be more targeted by therapy. Comparison between existing therapies and the not-yet-addressed areas, to find new drugs.

### Results:

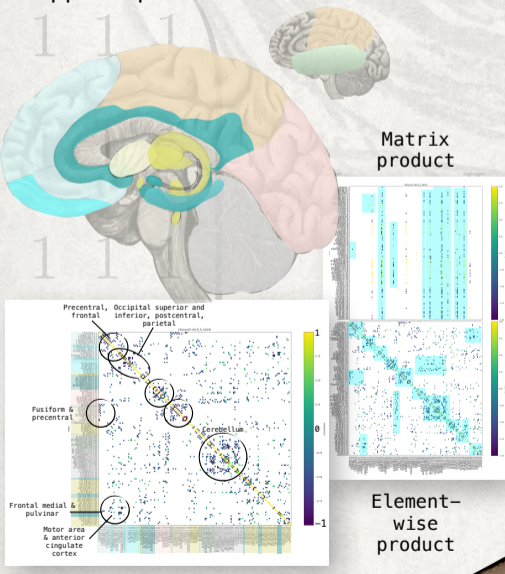
$K$  helps find the brain areas most impacted by the disease, confirming findings of the medical literature.

### AD:

Connectivity alterations mostly concerning occipital lobe, cerebellum crus I/II and vermis 9, nucleus accumbens, ventral tegmental area, frontal, hippocampus.

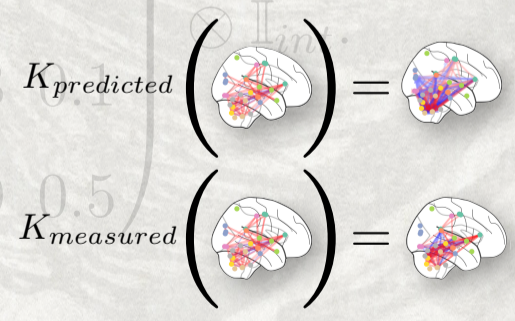
### PD:

Connectivity alterations mostly concerning dorsolateral prefrontal cortex, frontopolar cortex, intraparietal sulcus, Broca's area, temporo-parietal junction, anterior cingulate cortex, basal ganglia, ventral tegmental area, and insula.



Example:  $K$  between baseline and follow-up of a 63-year-old female AD patient

An example of prediction (AD)



### Conclusions and next research:

Future *in vitro* and *in silico* research, with brain-on-a-chip and organoids, testing current drugs and their possible enhancements suggested by  $K$ .

Drawings and concept by Maria Mannone