Modulome Theory

2023, December 13, Oliver Midbrink

0. Introduction

Life Science, Pharmacology and Medicine need innovation. It needs Modulome Theory. Modulome Theory is how biology would be defined today if it was reinvented with our current technologies. Modulome Theory is the cure to disease and path to well being. Modulome Theory is AI compatible biology. AI and biology have just become friends this decade. Let us see what they can do together.

1. Applications

Modulome Theory can be used to derive Multi Target Molecule Combinations (MTMCs) **that cure untreatable disease** and **eliminate (almost) all side effects**.

Furthermore, It can be used to figure out why individuals respond differently to treatment (Personalized Medicine).

2. Purpose

The purpose is to **benefit humanity**. This is achieved through the unification of biology and artificial intelligence through a **framework** that **encapsulates the biology** while providing a clear, AI adapted framework as a **foundation for AI applications in biomedicine**.

3. Validity

Since this is in theory the mathematically perfect way to treat disease, it can never be replaced and will forever be the future of medicine. However, the practical implementation can be improved through restructuring of the framework, advances in artificial intelligence and advances in data gathering methods for biology which includes new biomarkers, analysis methods (for example cheaper and more available single cell transcriptomics, ATAC-sequencing etc).

4. Pronunciation

Modulome is pronounced like Module and Home. In Swedish it is pronounced as Modul + å + m.

5. Legal and Business use

Modulome Theory was created to benefit humanity. Hence you are free to use it for any commercial, philanthropic, research or other purpose. You have to cite the original author (Oliver Midbrink) and reference Modulome Theory so it is clear your application builds entirely or in part by “Modulome Theory” by “Oliver Midbrink”. These two sentences have to be clear.

6. Iterations

Because Modulome Theory is not perfect from the start (like everything else), we strive to continually redefine it in accordance with new discoveries, better suited terminology etc. However we utilise a top down perspective like McKinsey and Company, where we describe reality from and abstract to more concrete direction, taking into consideration the details when designing the higher abstraction levels. This way we create a timeless framework to build the future of medicine. A funny story is how BMW and Telsa differentiate. Tesla accepts non-perfection and uses automatic updates to improve efficiency, power output, security, convenience etc of their cars. BMW i3 do not. It is stuck. It is non improving. Unlike Tesla and Modulome Theory.

7. Collaborations

To help accelerate the worlds transition to modulome theory, fast development is needed. Hence you are free to fork (expand or modify) Modulome theory to create your own version and publish/send it to me as long as you reference modulome theory of course. This way we can benefit the world together.

8. Definitions

1. The **Modulome**

Def: The modulome is the effect a biovector has on a biological system. A biological system is a human (Homo Sapiens), dog (Canis), cat (Felis Catus) or an ecosystem (rainforest) or a colletion of the previous. The modulome is preferentially a time dependant or time independent high dimensional column vector with elements representing the change of each aspect chosen to be measured of the biosystem. A matrix multiplication of the biosystem with the modulome can be used to derived the new biosystem state after biovector introduction. Since Modulome combination is generally non linear, a deep learning method or better method is required for the modulome of several biovectors to be combined. The modulome M(BV) is not equal to the sum M(BV1) + M(BV2).

2. The **Single Modulome**

Def: the Modulome of a single biovector.

3. The **Modulome Combination**

Def: A combination of Modulomes from different biovectors. Often nonlinear and requires machine learning or other approach to derive.

4. The **BioVector**

Def: the biovector is the agent that causes a change in a biological system. It could be a small molecule or biomolecule (**medication**), a cognitive agent (cognitive behavioral theory), a behavioral agent (exercise, meditation) or an environment feature (a forest painting). The BioVector can be represented as having the modulome M(BV, T, S) where BV is the biovector, T is the time and S is the biostate or stome. The term biovector is derived from latin, bio means biology and vector in latin has its roots in transportation from A to B. A vector in mathematics does a linear translation from A to B and a vector in traditional biology carries information from A to B, for example a viral vector or a liposome that carries DNA/mRNA information respectively. The term BioVector or biovector hence represents an entity that carries (vector) a biosystem (bio) from state A to state B. It is a generalisation of medication, surgery or other medical intervention, exercise, habit, environment design or any other factor (latin meaning factor=doer, something that does something) that changes a biosystem. A biovector can in theory also be a bad habit, like poor diet, lack of exercise, smoking or another factor that causes a negative health delta (change) in a biosystem (stome).

5. The **BioEngine**

Def: The **BioEngine**, just like in a car, **creates the power for the** carrier (**BioVector**) to exert its transportation. Vector means carrier, like the car as a whole and Engine is the powersystem for the car. In biomedicine, the BioEngine would be the mechanism through which the biosystem achieves its effect (for example drug mechanism or pharmacodynamics) and would appropriately be a binary vector where elements represent unique mechanism. These could be (AGONISM, ANTAGONISM, NEGATIVE AGNONISM etc) combined with (PROTEIN 1, PROTEIN 2.. PROTEIN N), and the BioEngine of a BioVector is an indications of which mechanism are active, 1 hot encoded for single mechanism and multiples 1's if multiple mechanisms. The BioEngine is the collection of mechanisms that drives a biovector. If a biovector contains multiple molecules, it would most often have multiple mechanisms and hence the bioengine would be complex (multiple parts). A simple bioengine is a bioengine with one mechanism. The mechanism could be variable with time and dose. For example methotrexate (cell division inhibitor for cancer and immunosuppressant for rheumatoid arthritis) has different mechanisms at different dosage. Hence it would have multiple BioEngine whose composition changes with dosage. It would be positive (element x = 1) at low dose for AICAR Transformylase inhibition, and negative for Dihidrofolate Reductase inhibition since the dosage is low, but be positive for Dihidrofolate Reductase inhibition at higher dose. The BioEngine could be discretised as different bioengines depending on dose (eg X mg = BioEngine 1, Y mg = BioEngine 2) or be a continuous function (for example through deep learning) where the Bioengine is calculated based on the dosage and/or time as input. **BE(D, T) = Vector**

Summary: The BioVector is powered by a BioEngine and creates a Modulome that changes a biological system.

9. The Biosystem state (BioState) or **Stome**

Def: the BioState or Stome (State + ome=biosystem state) **represents the system state of a biological system**. This could be defined as the transcriptome (sc-RNA-seq), the genome, the epigenome (ATAC-seq) the functome (the proteome functions, i.e. what proteins are active and how active they are), the amount of each species in an ecological system, the echogeniticy of an ultrasound for different locations (each location is an element of the BioState). The same goes for CT scans attenuation and MRI scans signal intensity, that can be mapped as a description of whole body state. Biomarkers like blood values can also be a description of system state. The BioState is hence one of the mentioned, another value set, or a combination of multimodal measurements that describes the state of a system. The BioState can also be a latent space vector created using encoding technologies like AI (machine learning) that combines any given data points into a latent space embedding (encoding).

10. **BioVector Synergy and Selective Destructive Interference** (BioVec SSDI)

Def: The goal for a BioVector is always to achieve high synergy for therapeutic effect and side-effect cancellation. This is used today in hospitals, however is strongly underutilised (thousands of times). The synergy (or selective constructive interference) of BioVector components (for example a combination of different medications) represents how the mechanisms of different medications together amplify to create a stronger therapeutic effect. This is used in blood preassure medications all the time when one medication can not do all by itself. Selective destructive interference refers to when the side effects of one molecule is canceled out by another molecule, hence their combined effect cause a selective destructive interference of the side effects, since the side effects are reduced, while maintaining the therapeutic effect. This is also used today but strongly underutitilsed. For example when administrating thiazide or Loop diuretics, Potassium sparing diuretics (ENaCs or Aldost. Rec. antag.) are often combined to eliminate the hypokalemic effects of thiazide and Loop diuretics. The diuretic effect is maintained while the side effects are “cancelled out”.

11. Multi Target Theory

Def: Some disease are complex, meaning multiple pathways or factors contribute to the disease. In theory the best way to treat this is to treat all the causes proportional to their contribution. Hence Multi Target Theory is born.

12. Multi Target Molecules (MTMs)

Def: The **biovector** represented as a small molecule following Lipinskis Rule of 5 (for oral availability) that targets multiple proteins at the same time to **eliminate a complex disease** like **Alzheimers, Osteoarthritis, Cancer or CardioVascular** disease. This could be represented in standard cheminformatics format like a SMILES string or InChI Key. This is a practical application of Multi Target Theory.

13. Multi Target Molecule Combinations (MTMCs)

Def: The **biovector** represented as a combination of Multi Target Molecules (MTMs). This gives a **powerful disease curing** effect by combining Multi Target Molecules synergistically while utilizing selective destructive interference to **eliminate side effects**. This could be represented as a 2 vectors, the first containing identifiers for each MTM. The second containing the dosage of each molecule. Alternatively if you want to incorporate temporal data (time data), you can have the first vector of MTM identifiers in combination with a list of (MTM ID, dosage, timepoint), hence a 3xM or Mx3 matrix where M is the number of entries.

This could be the number of each medication administered at white time. Or the number of contaminants released from industries at different time points. This is a practical application of Multi Target Theory and BioVec SSDI (Synergy and Selective Destructive Interference).

14. The Vitality

Def: the **Vitality is the number of lifeyears a person has left**. the BioState of a person (for example blood values or epigenetic measurement, for example epigenetic clock) can be used to infer the Vitality of a person (the number of years remaining). The Vitality function of the biosystems can be used to infer the vitality of a person. This is represented as a deep learning transformation function V(S) = Vitality of person with Stome S. The average V(S_i) for a population of newborns represent the life expectancy and can be used for calibration and training of Vitality function.

15. The Health

Def: the **Health is a measure of overall health** of an individual. It is represented as the **Vitality times average quality of a persons lifeyears**. H(S) can be used to calculate health of a person. World Happiness report and other data can be used to train the Health function **H(S) = Health of person with stome S**.

16. **The Health Delta**

Def: The health delta is a **measure of the change of health** of a person or population given an intervention (Modulome). **HD(BV, S) = Health delta** or change of health.

17. The **Vitality Delta**

Def: The **vitality delta is a measure of the change in vitality caused by a lifestyle change or medication** for a person. The lifestyle change is a biovector and also the medication, so the vitality is a function of the a biovector in combination with a person S. **VD(BV, S) = Vitality Delta**.

3. Elaborations

The modulome is preferably a **high dimensional vector**, time dependant or static, that represents the change of each element of a biological system caused by a biovector. For example a small molecule medication like aspirin could have a modulome that represents the transcriptome change caused by addition of aspirin to a system. This is called a state modulome where the modulome given the initial state M(S) would represent the change in the transcriptome, or the transcriptome_delta. M(S_0) = transcriptome_delta. Another example is the **modulome of aspirin** in terms of protein functions. Here the modulome would be a vector with a **negative spike for COX1** since this protein is inhibited. This is a functional modulome. Both of these are time independent modulomes since they do not take into consideration the time. Morphine would preferably have a time dependant modulome, since tolerance builds up over time. All cases of modulomes could be represented as time dependant modulomes, but time independent modulomes would be time invariant, meaning the have the same values over time. You could represent the aspirin modulome as going from 0 to full effect back to 0 as the medication is absorbed, metabolised and exctreted. Or you could set the modulome to be the average effect of aspiring when taken once daily, so

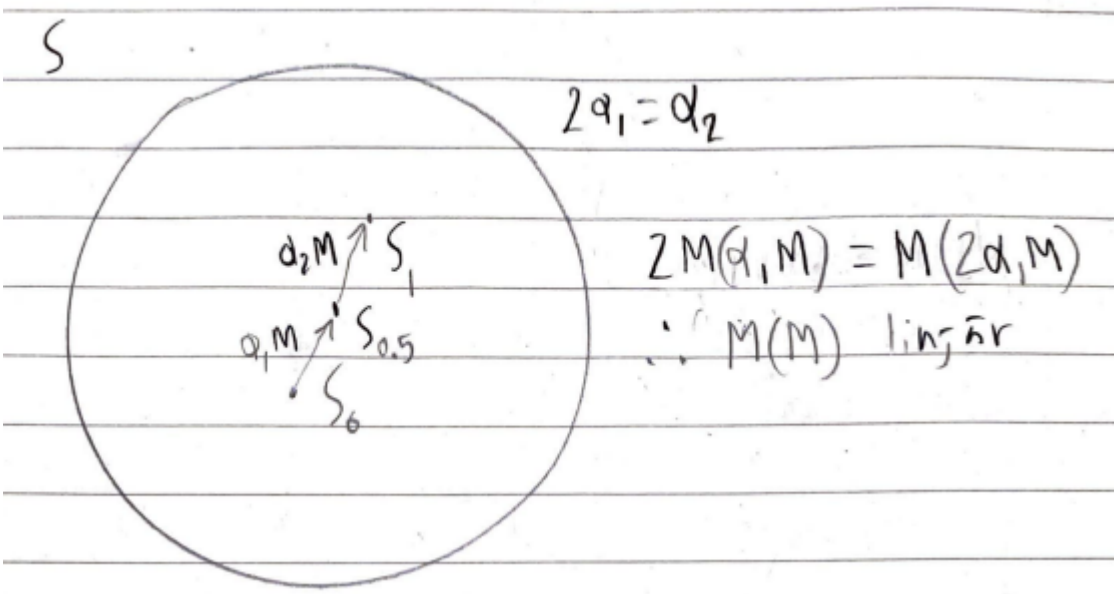
this would represent the modulome of aspirin for a steady state concentration in the blood. The modulome is a flexible tool.

The focus of modulome theory is the modulome, **how it can be used to treat disease** and increase well being, **how modulomes combine** and **how modulomes change over time**. One biovector generally has the same modulome. What modulomes a biovector has for different cell types, cell states, different individuals.

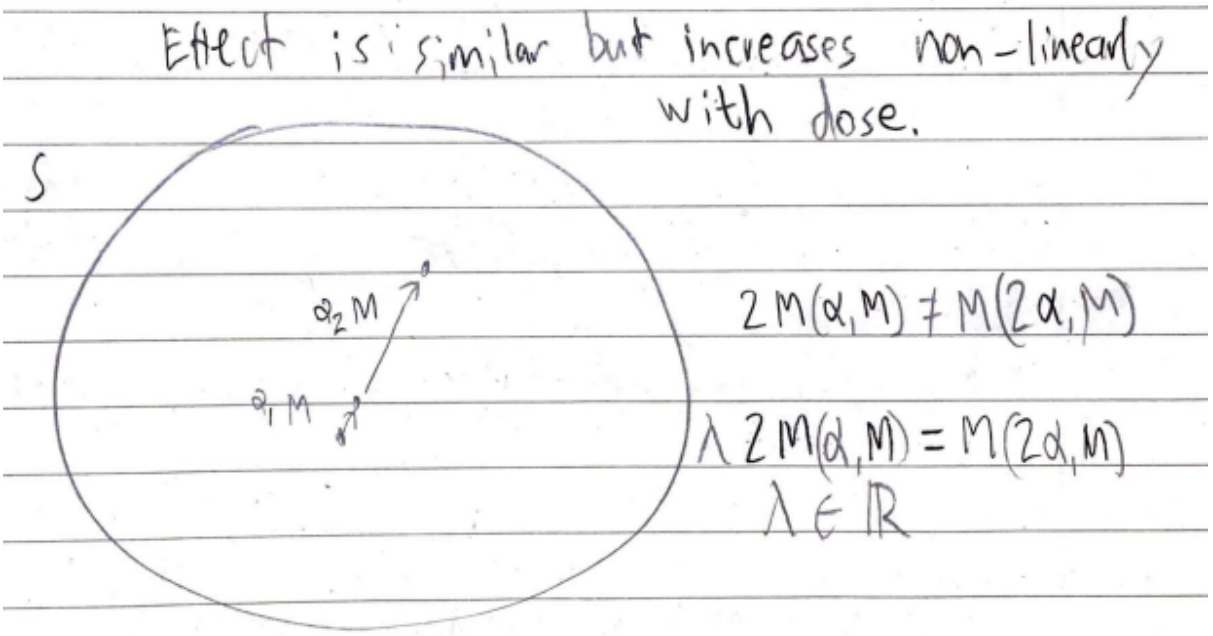
Modulome Theory also encapsulates Stome Theory (State + ome=biosystem state theory). Stome theory is used to calculate the modulomes required for curing a disease, modulome theory is then used to find what biovectors are required at what times to make the disease go away. However, since the modulome is very central in Stome Theory. It is included in Modulome theory and not considered to be its own theory.

4. Classification of Modulomes

1. The Simple Modulome
2. The Linear Modulome Combination (uncommon but good to have seen)



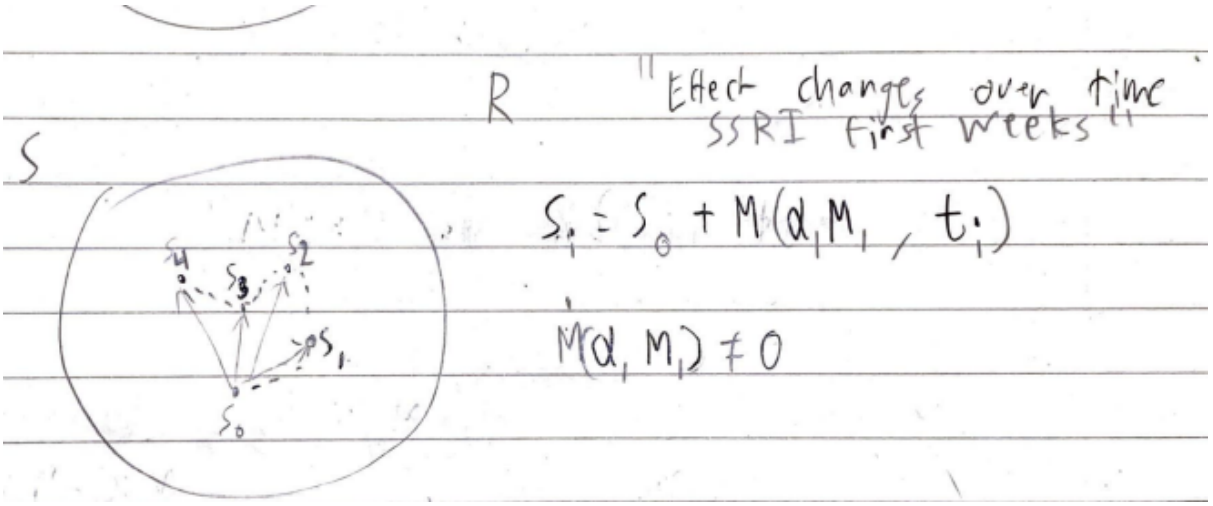
3. The Nonlinear but linearly dependant Modulome Combination (good to have seen)



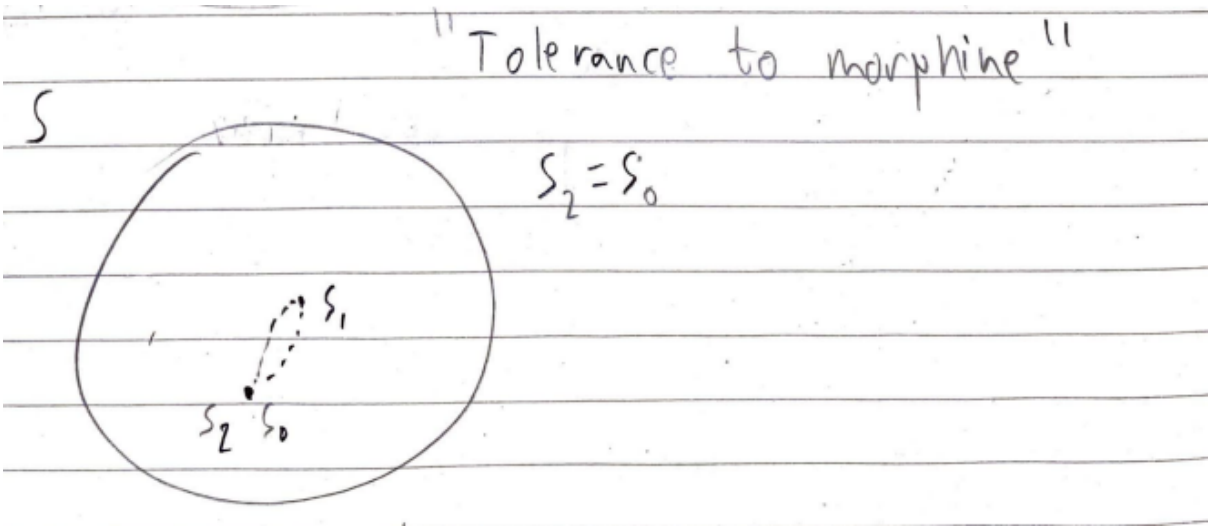
Here the Modulomes of two biovectors (for example two small molecules) align, but theyr combination is synergistic. Also it could be illustrate this, the same biovector in two doses, the effect is nonlinear where a double in dose yields more than double the effect. The same picture could hence illustrate these both concepts.

4. The Modulome Combination

5. The Time (or dose) dependant Single Modulome

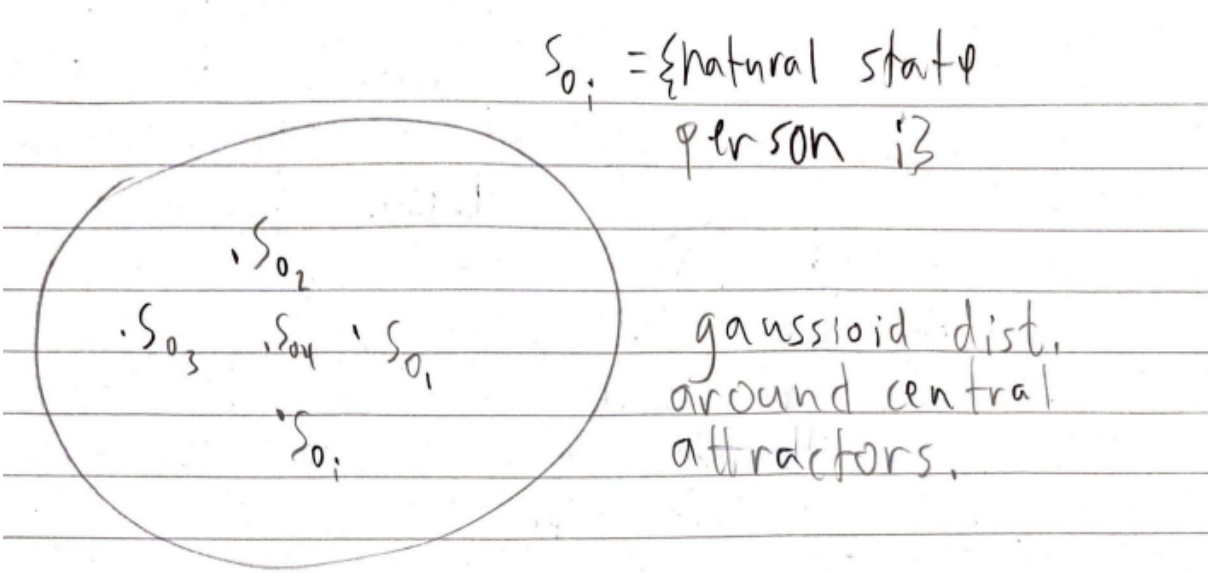


6. The Time dependant Single Modulome of Morphine



Here the morphine transfers the stome from a state of pain (S0) to a state of relief (S1). But as tolerance is built, the pain comes back and the patient is left near the starting point (S2). Modulome theory seeks to find a way to cure tolerance so pain medications like these do not lose their effects.

7. The linear combination of non-linearly dependant Modulomes
8. The non-linear combination of non-linearly dependant Modulomes (most common)
9. Synergistic Modulome Combination
10. Surprising Modulome Combination
11. Different individuals have different resting states



12. The optimal Stome of a person

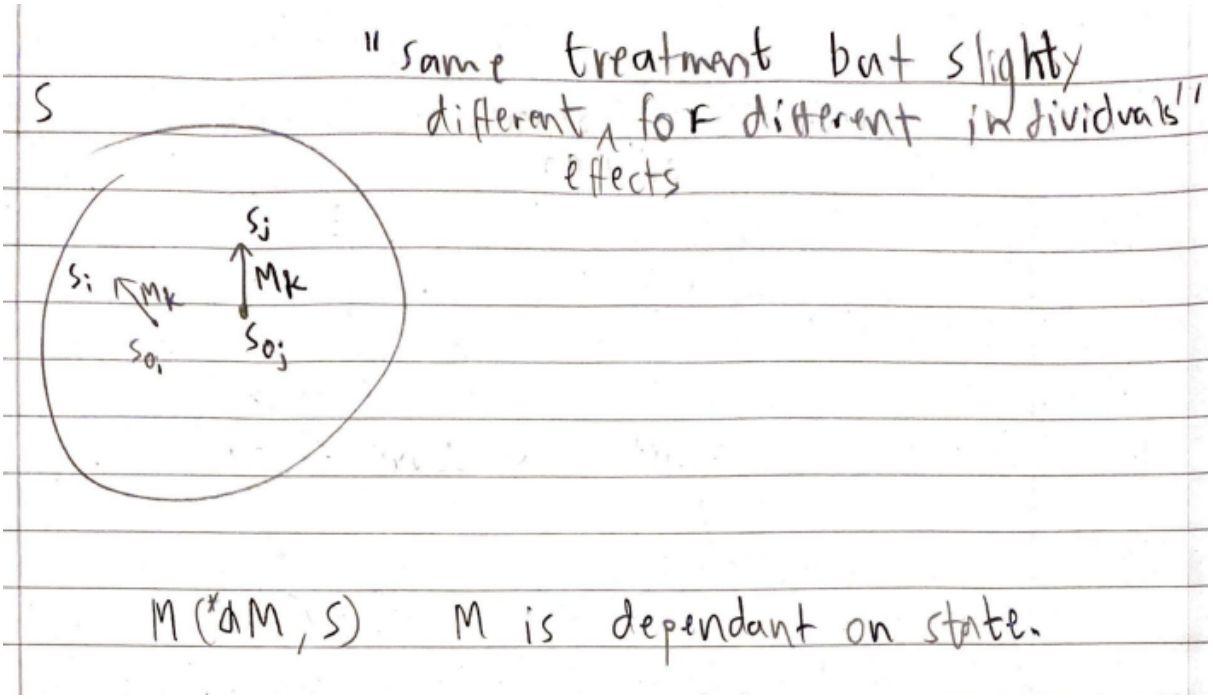
$S_{p_i} = \{$ perfect/optimal state person $i\}$

13. The stomes are not perfect today

Today: $\frac{1}{n}\sum_{i=1}^{n} S_{0_i} \neq \frac{1}{n}\sum_{i=1}^{n} S_{p_i}$ and $S_{p_i} \neq S_{0_i}$

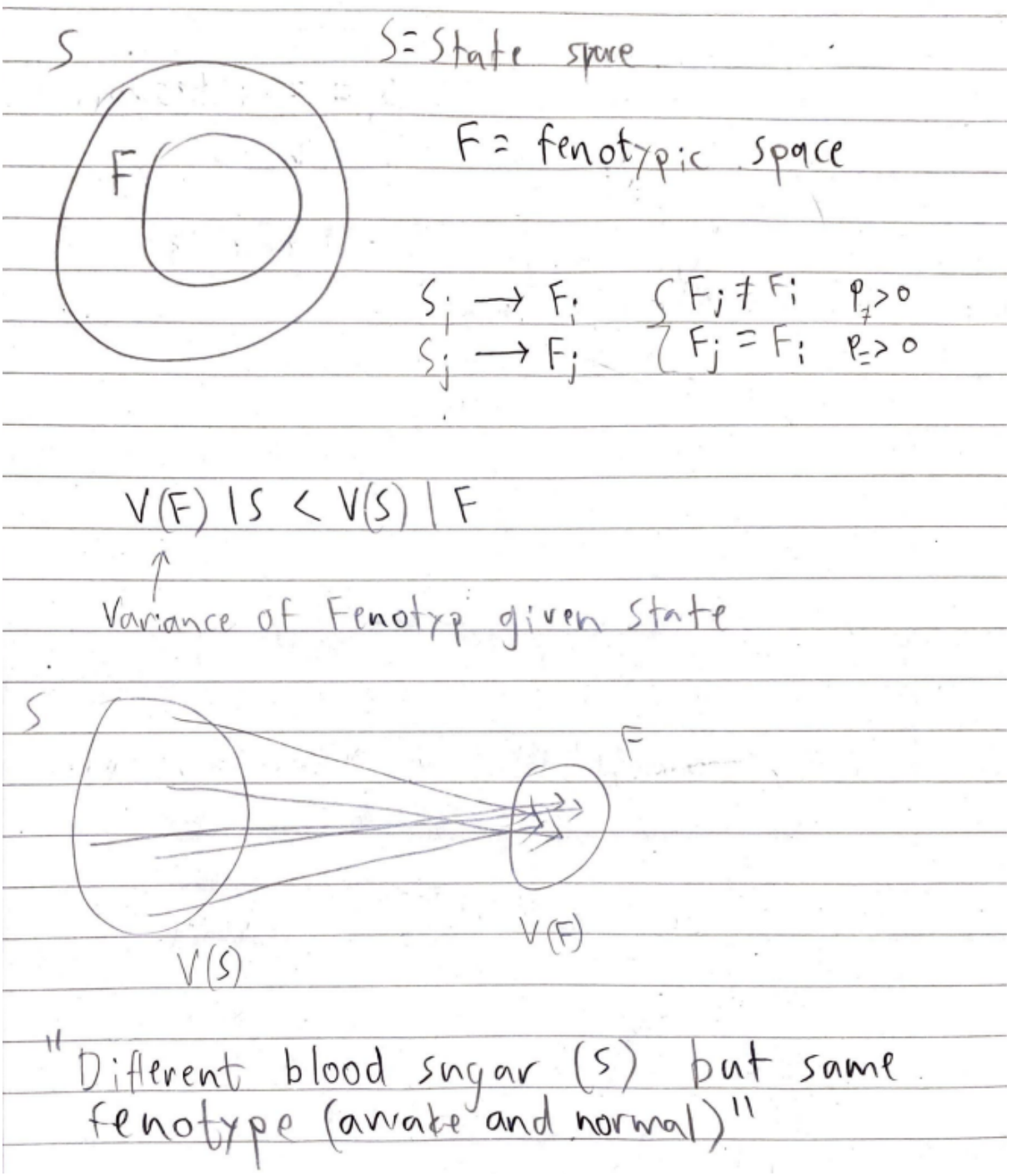
$\forall i \in [0,n] \cup \mathbb{N}$

14. The Modulome for different individuals (stomes)



5. Phenotype space (Phome)

The phenotype space is a subspace of the stome (biosystem state). It could be for examples the blood biomarkers of a person (stome). It can be used to infer the biostate (stome) of a person based on the biomarkers (phenotype space or phome).



6. The Goal

The goal of modulome theory is to maximise the Health of all individuals.

Maximise H(Si) given Si, S_p_i, All fujture states Si, all biovectors currently available BVi as well as all thinkable new Biovectors BV_t_i