TRIZ SUMMIT 2021

TRIZ IN MEDICINE

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- TRIZ Biopharma International, LLC,
- Noigel, LLC
- Farber's Center for Academic Success, Inc

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15 октября 2021 года

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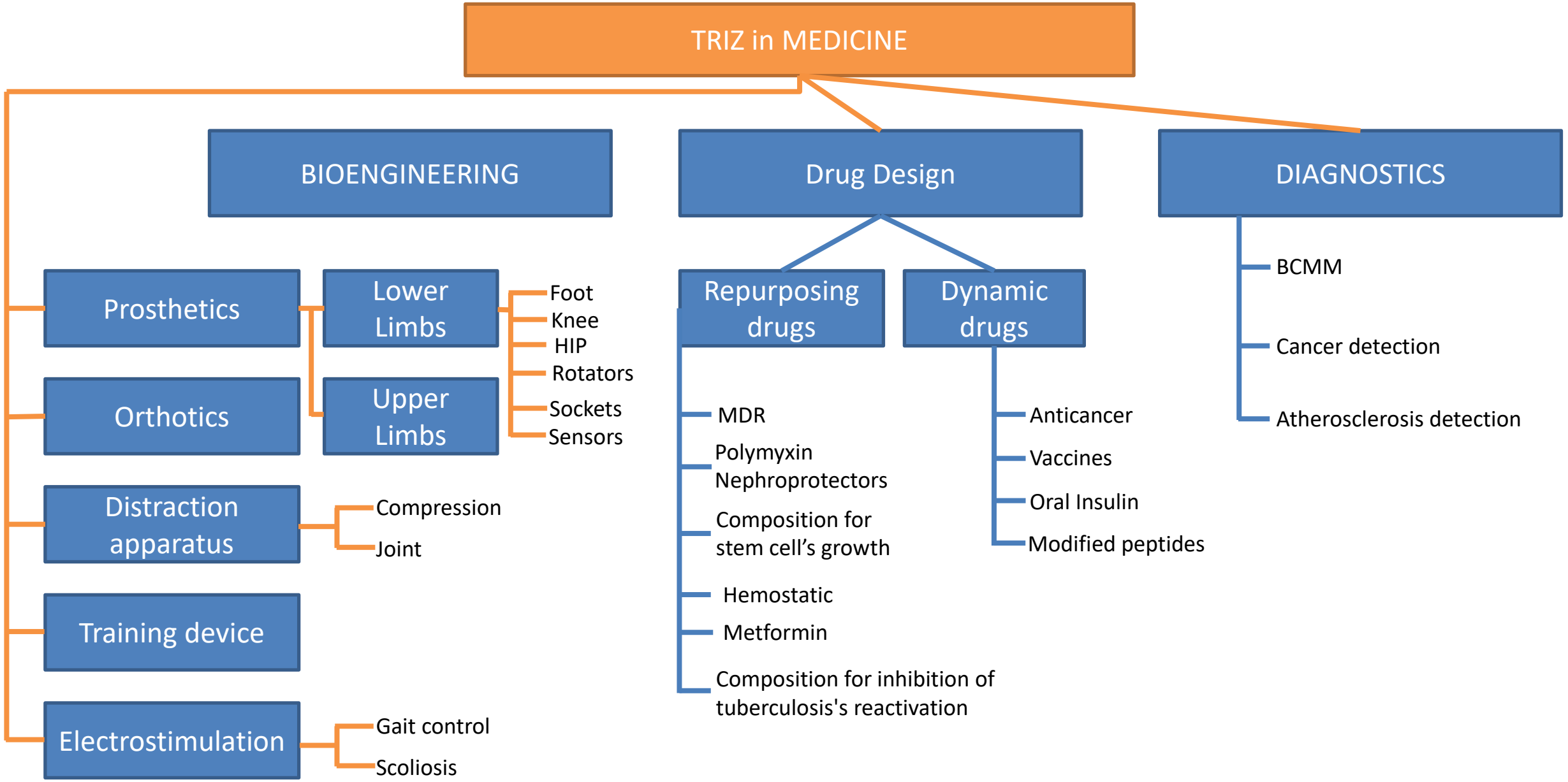
NOIGEL, LLC

http://triz-summit.ru


TRIZ in MEDICINE
BIOENGINEERING
Drug Design
DIAGNOSTICS
Prosthetics
Lower Limbs
Foot
Knee
HIP
Rotators
Upper Limbs
Sockets
Sensors
Orthotics
Distraction apparatus
Compression
Joint
Training device
Electrostimulation
Gait control
Scoliosis
Repurposing drugs
Dynamic drugs
MDR
Polymyxin Nephroprotectors
Composition for stem cell's growth
Hemostatic
Metformin
Composition for inhibition of tuberculosis's reactivation
Anticancer
Vaccines
Oral Insulin
Modified peptides
BCMM
Cancer detection
Atherosclerosis detection

WHY A FOOT ?-“The human foot is a masterpiece of engineering and a work of art.” Leonardo da Vinci

6.Genrich Altshuller’ publication,1956

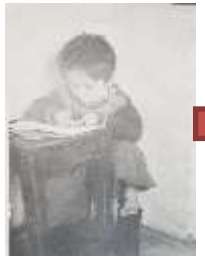
5.Mikhail Kalashnikov on a cover of “Sovetskij voin” 1949

4. Goryunov machine gun SG-43

3. 14th Separate Marine Corps Brigade Pacific Ocean Fleet Kamchatka 1949

2. Leonardo da Vinci Books (Academia 1932)

1.Slavin Farber- Marine Lieutenant,1949



7.Me

8. Da Vinci Legacy (“The human foot is a masterpiece of engineering and a work of art.”)

9. Studying TRIZ+da Vinci Legacy+ Foundation of Sciences

10. Post graduate School at Central Research Institute of Prosthetics (CNIIPP)- Head Institute in USSR domain

Acknowledgements1 The fundamental ideas of our research are results of many years Discussing of TRIZ applications with Genrich Saulovich Altshuller.
In ALL OUR PROJECTS we implement classical TRIZ in combination with Mathematical Modelling and Science

Marat S. Gafitulin

The research is a result of creative, dedicating and enthusiastic efforts of TRIZ Biopharma International LLC & Noigel LLC , Scientists Team, colleagues and partners. We thank our colleagues.

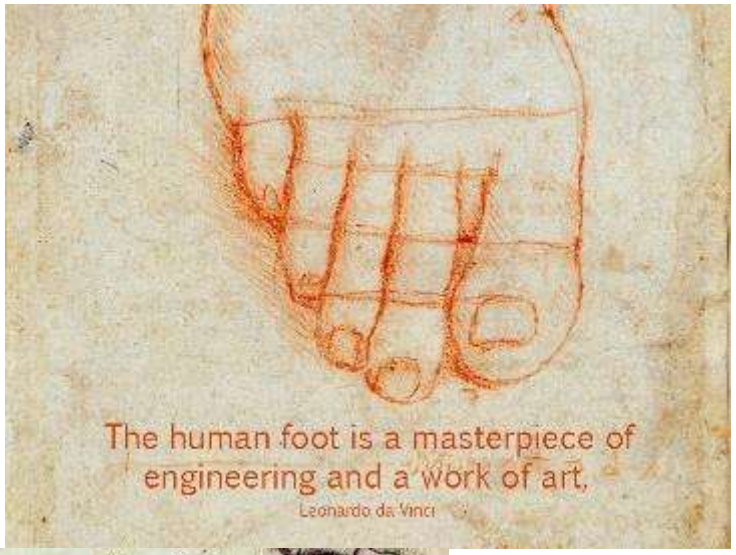
PART1 BIOENGENEERING

Part1.1 Artificial Foot (IDEALITY , includes Symmetry)

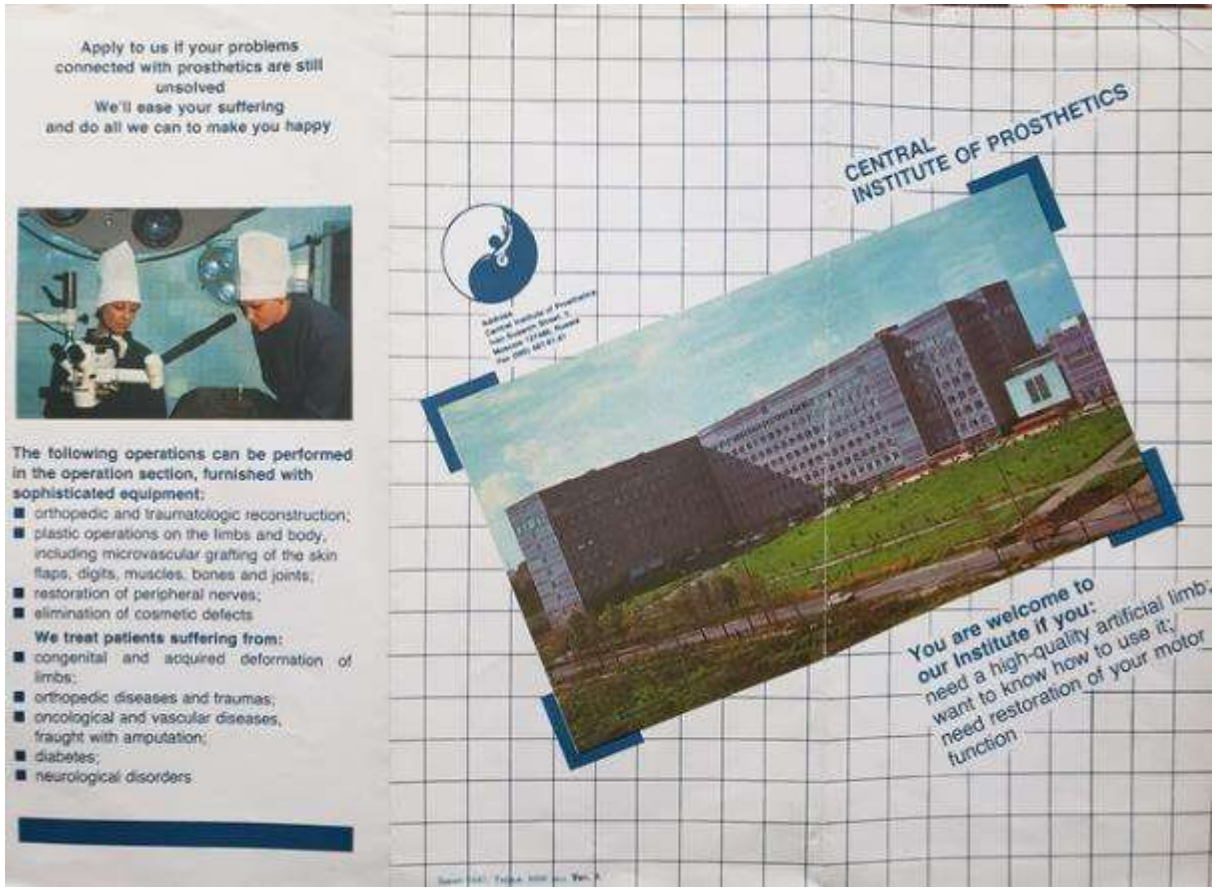
"The human foot is a masterpiece of engineering and a work of art." Leonardo da Vinci

«Человеческая стопа шедевр инженерии и настоящее произведение искусства»

Leonardo da Vinci



CENTRAL INSTITUTE OF PROSTETICS (CNIIPP)



Apply to us if your problems connected with prosthetics are still unsolved
We'll ease your suffering and do all we can to make you happy

The following operations can be performed in the operation section, furnished with sophisticated equipment:

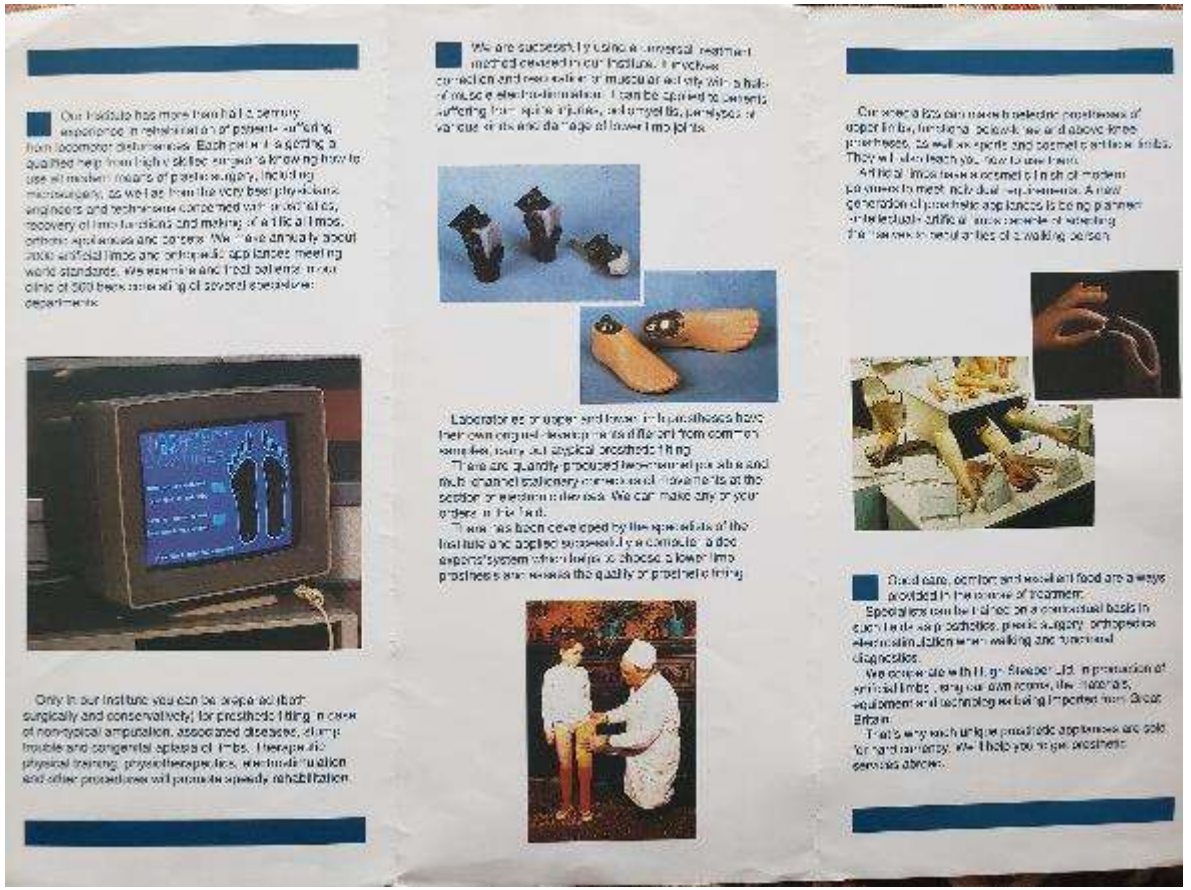
- orthopedic and traumatologic reconstruction;
- plastic operations on the limbs and body, including microvascular grafting of the skin flaps, digits, muscles, bones and joints;
- restoration of peripheral nerves;
- elimination of cosmetic defects

We treat patients suffering from:

- congenital and acquired deformation of limbs;
- orthopedic diseases and traumas;
- oncological and vascular diseases, fraught with amputation;
- diabetes;
- neurological disorders

CENTRAL INSTITUTE OF PROSTHETICS

You are welcome to our Institute if you:
need a high-quality artificial limb;
want to know how to use it;
need restoration of your motor function



Our Institute has more than half a century experience in rehabilitation of patients suffering from locomotor disturbances. Each patient is getting a qualified help from highly skilled surgeons knowing how to use all modern means of plastic surgery, including microsurgery, as well as from the very best physicians and engineers and technicians concerned with orthotics, recovery of limb functions and making of artificial limbs, orthotic appliances and corsets. We make annually about 3000 artificial limbs and orthopedic appliances meeting world standards. We examine and treat patients in our clinic of 300 beds consisting of several specialized departments.

Only in our Institute you can be prepared both surgically and conservatively for prosthetic fitting in case of non-typical amputation, associated diseases, stump trouble and congenital aplasia of limbs. Therapeutic physical training, physiotherapeutics, electrostimulation and other procedures will promote speedy rehabilitation.

We are successfully using a universal treatment method created in our Institute. It involves correction and reconstruction of muscular activity with a help of muscle electrostimulation. It can be carried to patients suffering from spinal injuries, and myelitis, paralysis of various kinds and damage of lower limb joints.

Laboratories for upper and lower limb prostheses have their own original developments different from common serially produced artificial limbs.

There are quantity produced two-channel portable and multi-channel stationary myoelectrical devices at the section or section otherwise. We can make any of your orders in the field.

There has been developed by the specialists of the Institute and applied successfully a computer aided expert system which helps to choose a lower limb prosthesis and evaluate the quality of prosthetic fitting.

Our specialists can make both electric prostheses of upper limbs, including bioelectrical ones of above knee prostheses, as well as sports and cosmetic artificial limbs. They will also teach you how to use them.

Artificial limbs have a cosmetic finish of modern garments to meet individual requirements. A new generation of prosthetic appliances is being planned – intellectual artificial limbs capable of keeping the balance in peculiarities of a walking person.

Good care, comfort and excellent food are always provided in the course of treatment.

Specialists can be trained on a commercial basis in such fields as prosthetics, plastic surgery, orthopedics, electrostimulation, gait walking and functional diagnostics.

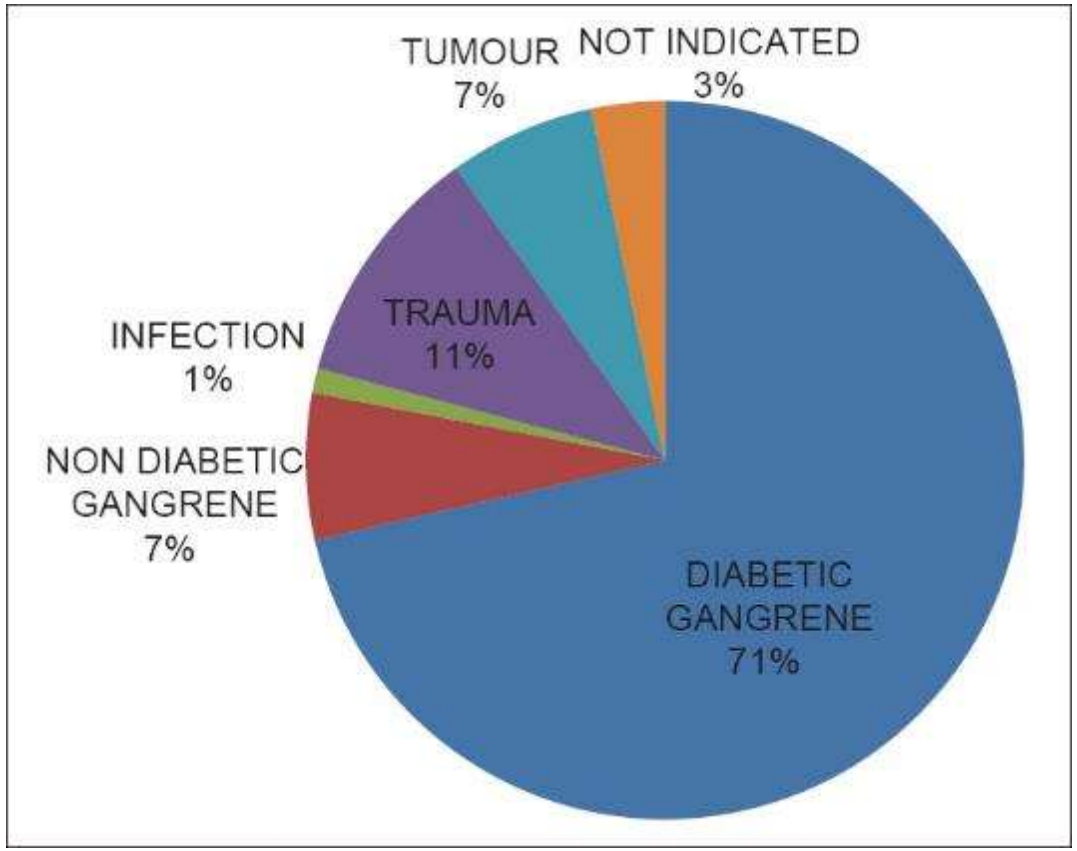
We cooperate with Otto Bock Ltd. in production of artificial limbs. Many our components, materials, equipment and technology are being imported from Great Britain.

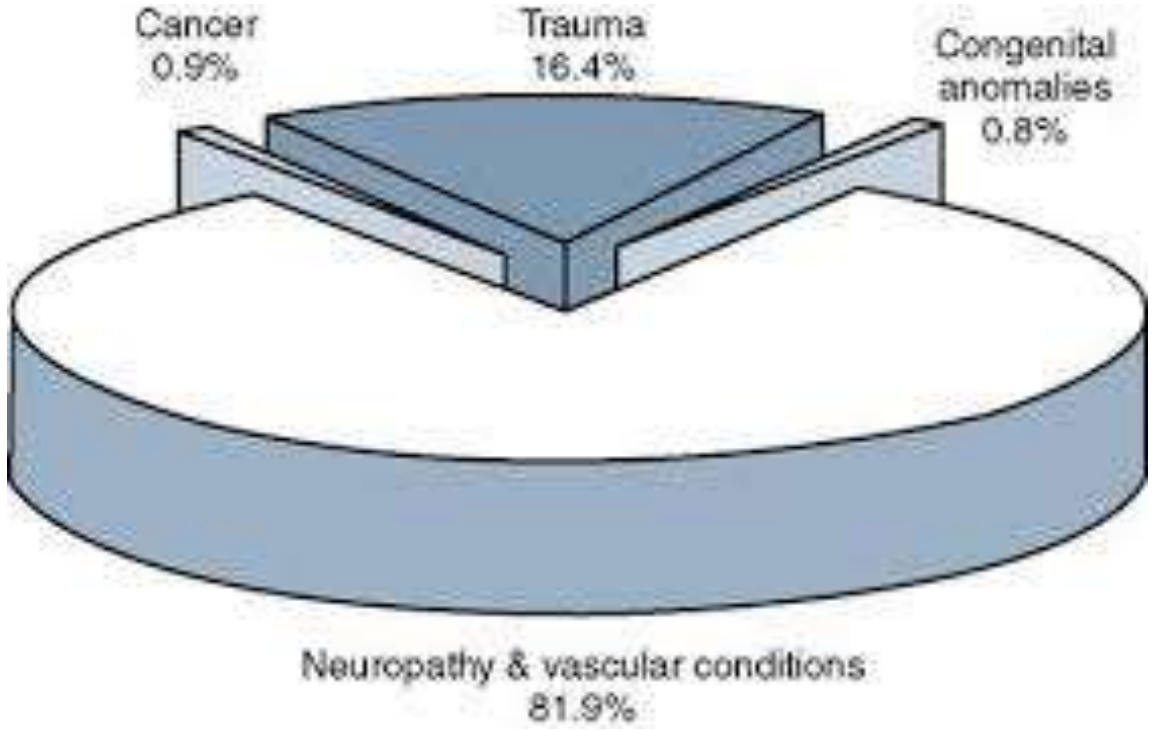
There are many such unique prosthetic appliances are sold for hard currency. We'll help you to get prosthetic services abroad.

Why “TRIZ in Medicine”?

- **Today we are: students, teachers, programmers, engineers, managers, sportsmen, supermen)**
- **Tomorrow we are patients (**

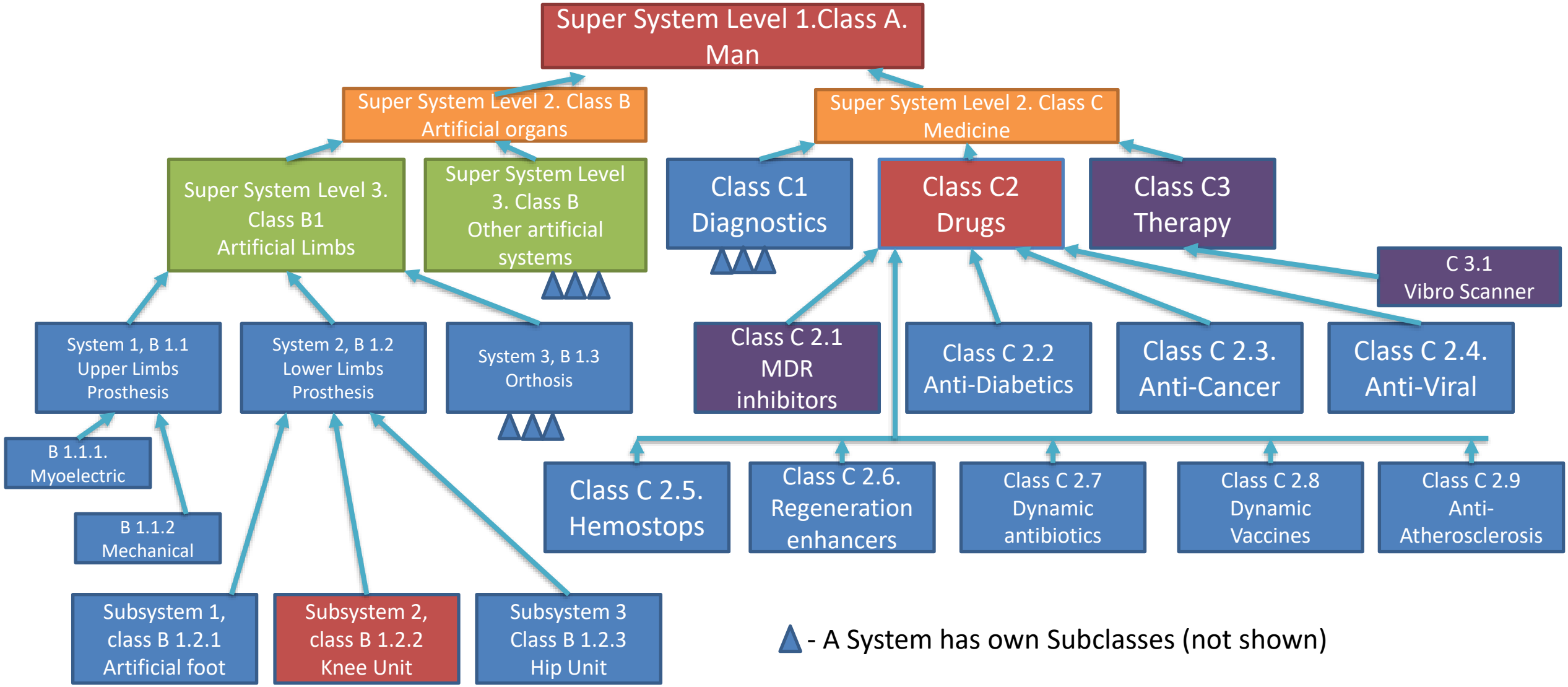
Cause of Amputations





Inheritance of System

"man-artificial organs-medicine-environment"

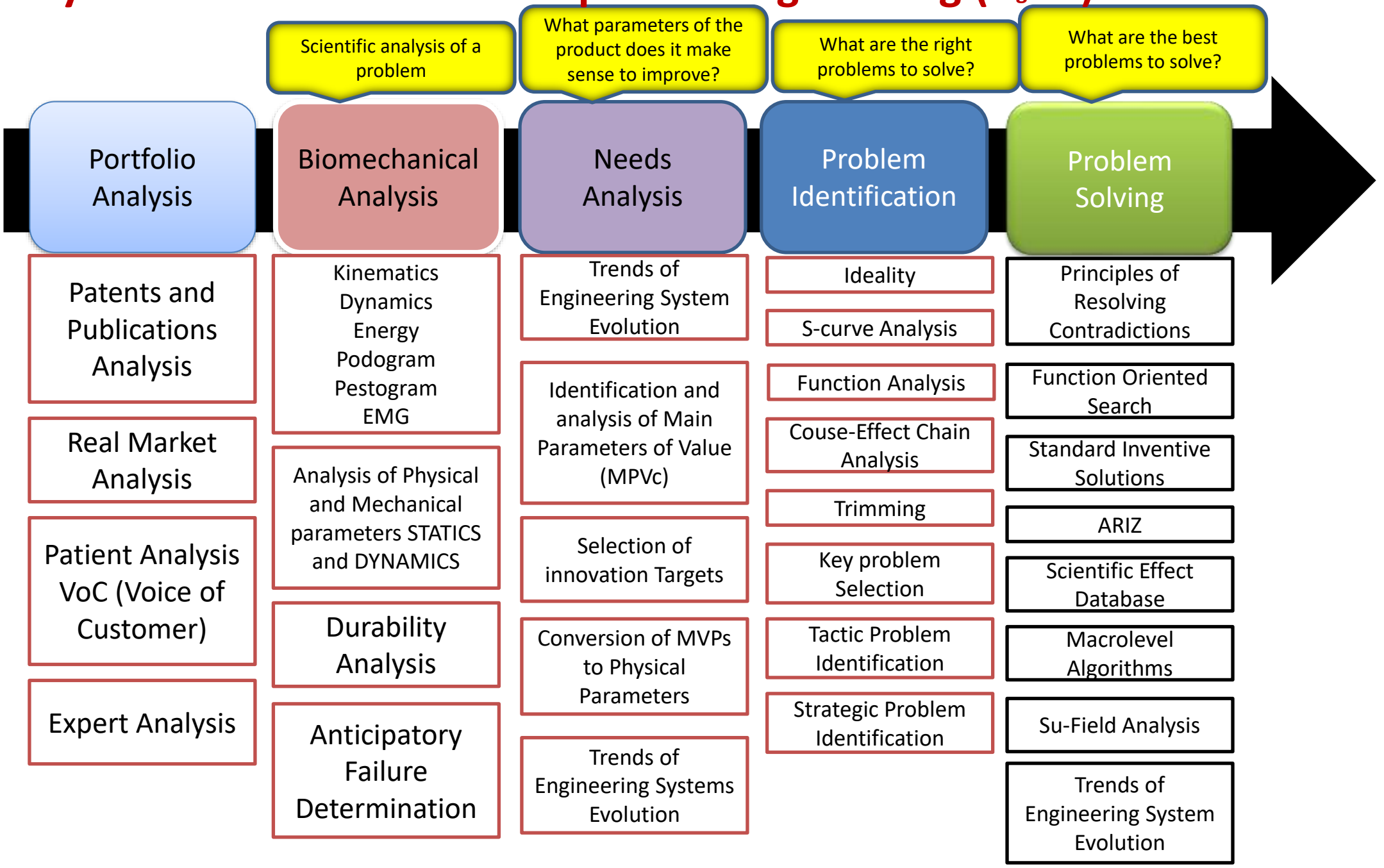


Our Methods of developing New Paradigms in all projects in medical field are based on:

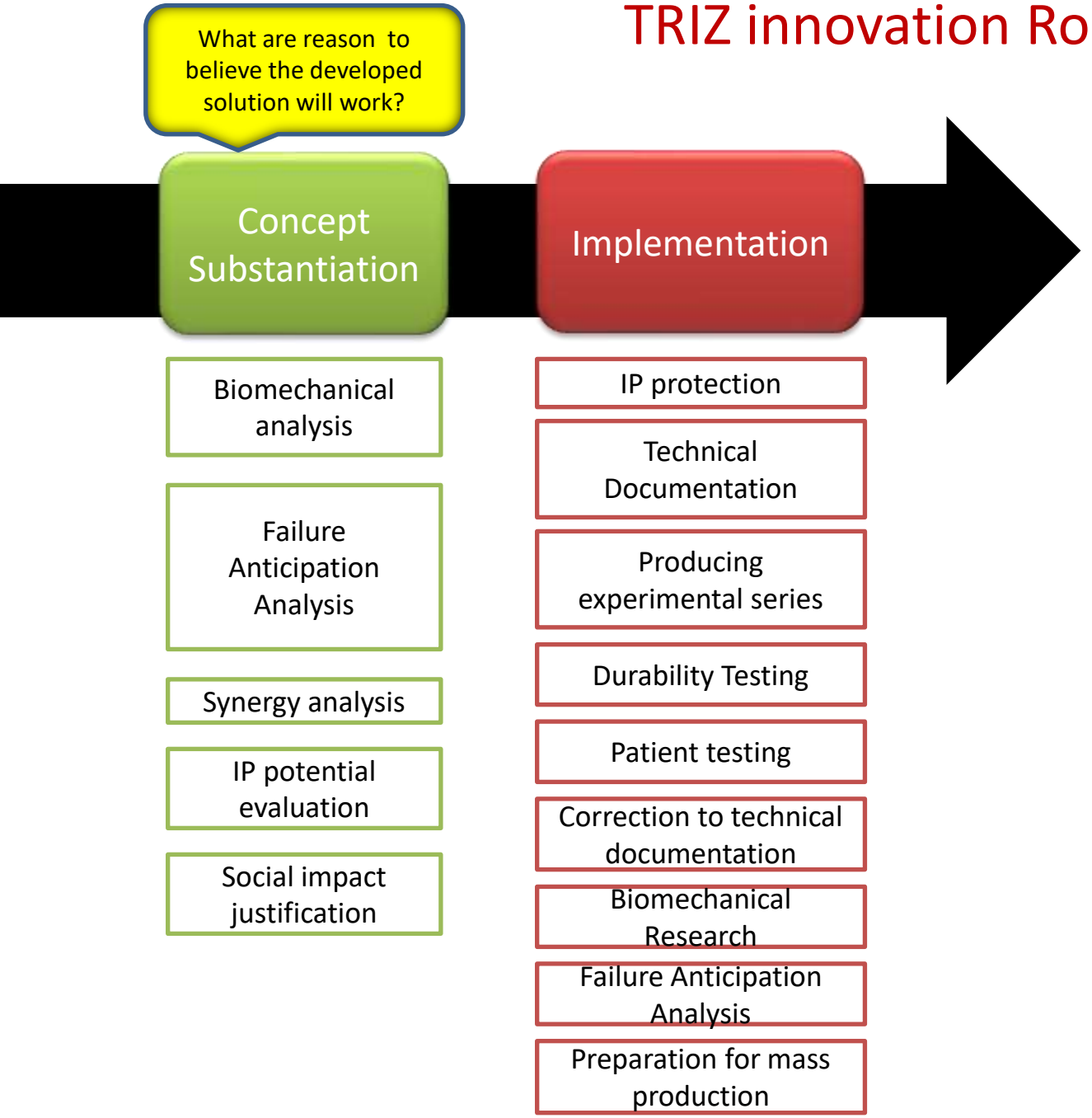
- *1Classical TRIZ (theory of inventive problem solving),*
- *2. Mathematical Modeling*
- *3.Multiple synergisms*
- *4. Modern Science, design and technologies in numerous different fields.*
- *5. Bionics*
- *6.Limited time and space limits with deep explanation of TRIZ application in each our project.*
- **TRIZ Biopharma International LLC & Noigel LLC are the only pharma companies in the World, which philosophy is TRIZ in Bioengineering and Pharma**

NOIGEL, LLC

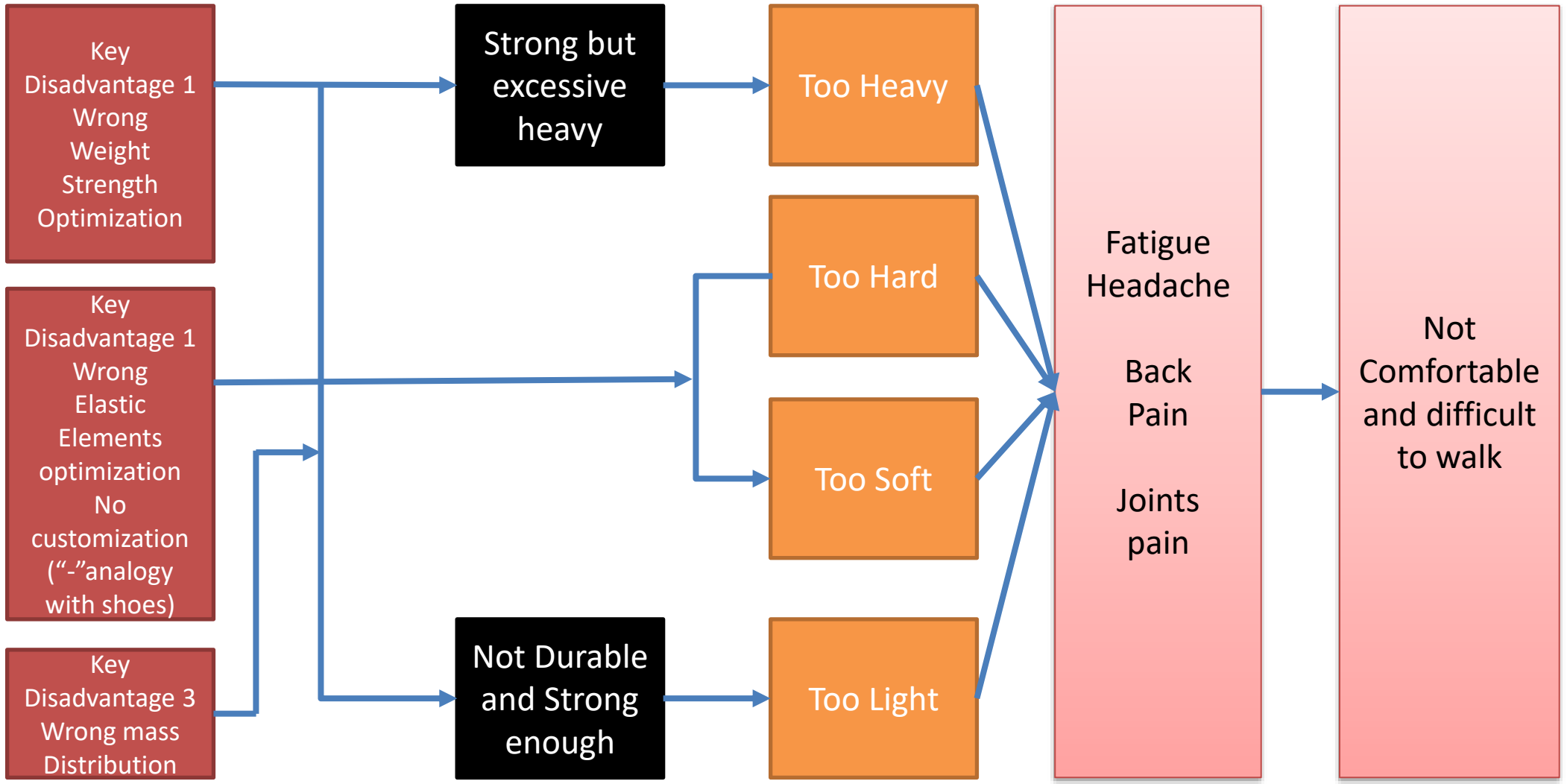
My TRIZ innovation Roadmap in Bioengineering (fragment)

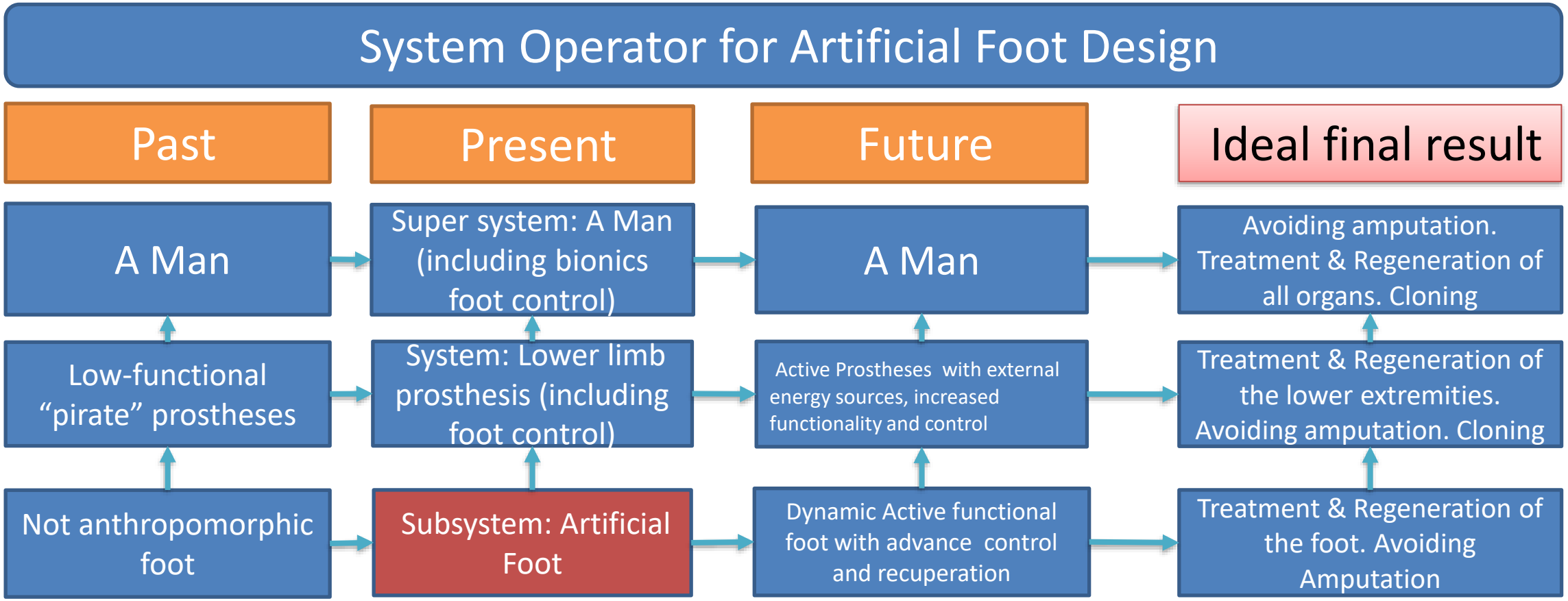


TRIZ innovation Roadmap in Bioengineering (continue)



Cause-Effect Chains Analysis for Artificial Foot Design (fragment)




System Operator for Artificial Foot Design
Past
Present
Future
Ideal final result
A Man
Super system: A Man (including bionics foot control)
A Man
Avoiding amputation. Treatment & Regeneration of all organs. Cloning
Low-functional "pirate" prostheses
System: Lower limb prosthesis (including foot control)
Active Prostheses with external energy sources, increased functionality and control
Treatment & Regeneration of the lower extremities. Avoiding amputation. Cloning
Not anthropomorphic foot
Subsystem: Artificial Foot
Dynamic Active functional foot with advance control and recuperation
Treatment & Regeneration of the foot. Avoiding Amputation

Tactics & Strategy for Foot design Problem Identification

Problem Identification

Tactics
In order to implement fast new foot for patients, based on MPVs, to avoid creating diverse forms of rigging and press forms for different shoe sizes, men, women, kids, different heal height from scratch (keeping in mind S-curve).
Solve problems:

1. Rationalize mass-inertia parameters distribution
2. Strength optimization
3. Parameters of elastic elements customize for a patient
4. Analyze system operator for solving supplementary problems

Strategy
Based on S-curve go to a new system:

1. Elastic elements for energy recuperation
2. External sources of energy
3. Feedback system
4. Foresee new ways to supersystem - subsystem

Farber B. et al., Biomechanical basis of choosing the rational mass and its distribution throughout the lower limb prosthesis segments

- Journal of Rehabilitation Research and Development Vol . 32 No. 4, November 1995 Pages 325-336

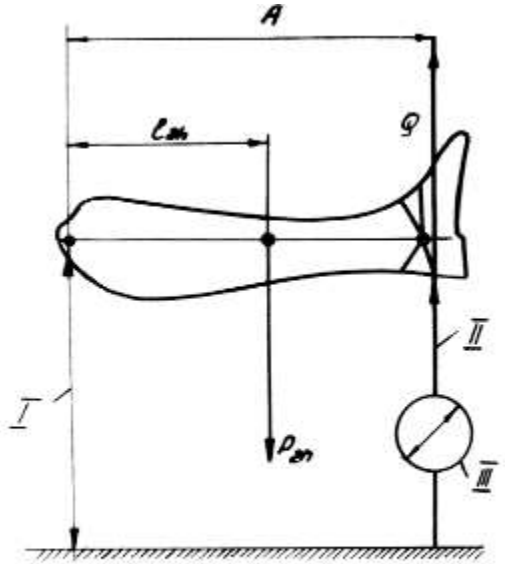


Figure 2.
Scheme of a device for determining the position of a center of mass of a chain.

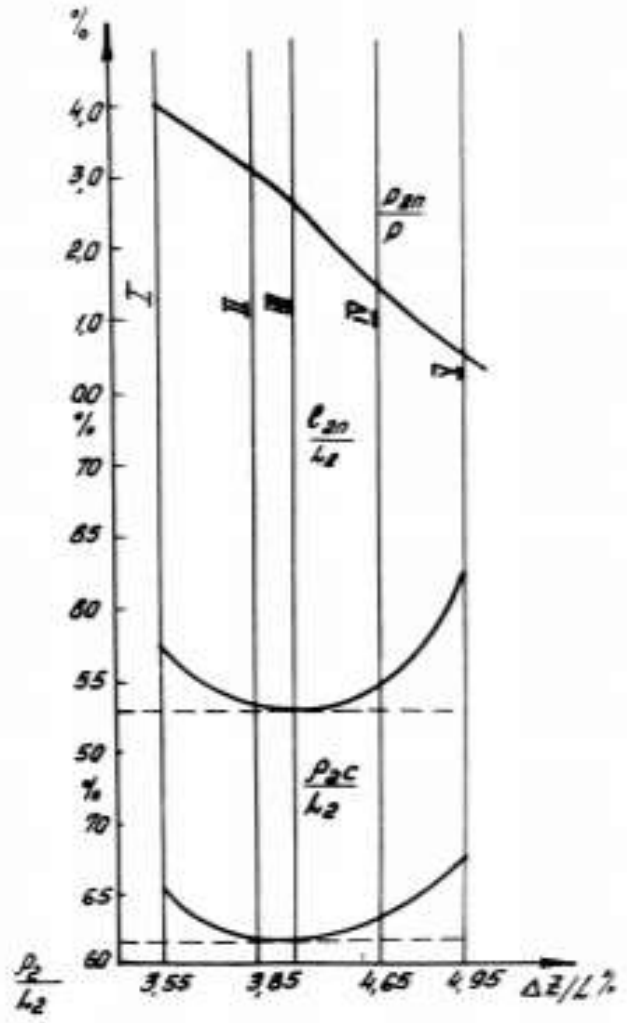


Figure 7.
Mass-inertial characteristics of a complex chain shank "+ foot + footwear" for AK prosthesis.
P_2 is the mass as a percentage of the human body mass; static radius l2 and inertial radius are expressed as a percentage of the distance "knee-floor" L2. On the X-coordinate is the frontal displacement of the total center of masses (TCM) related to the man's height.
I=Gritti stump; II=long stump; III=border of lower and middle third of a hip; IV=half of a hip; V=border of middle and upper third of a hip.

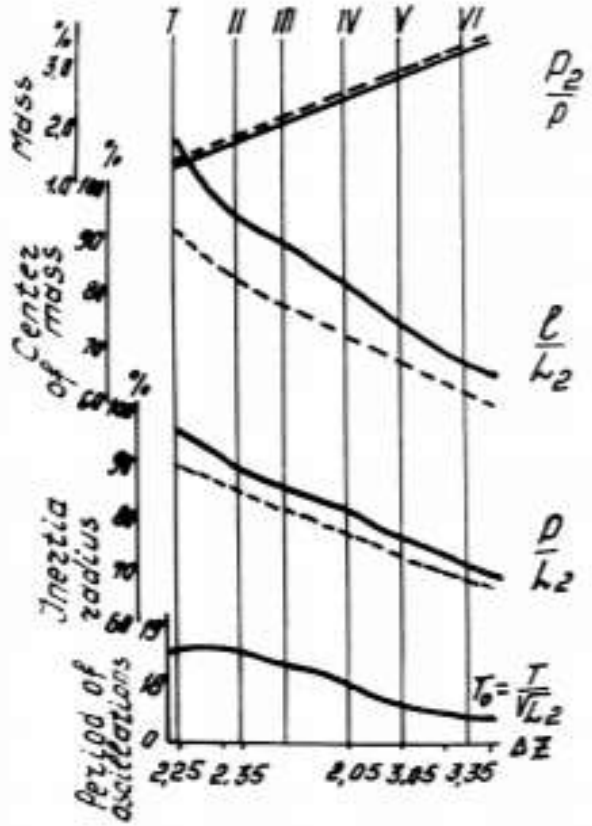
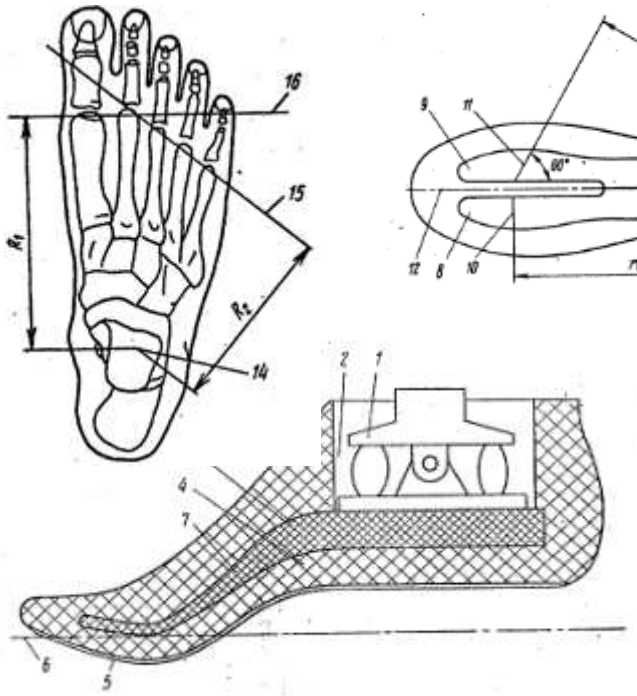
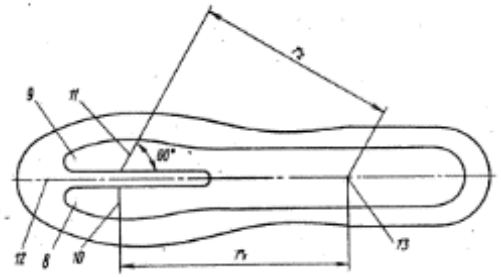


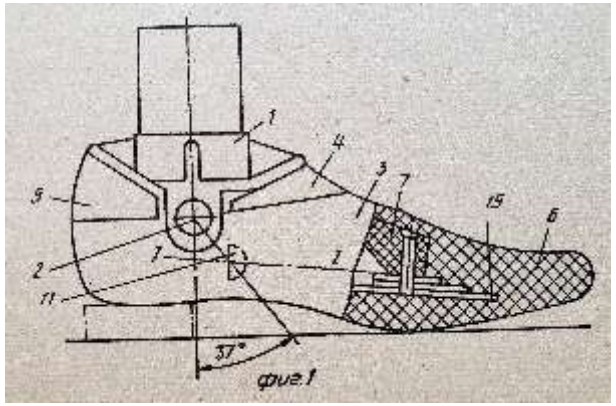
Figure 8.
Mass-inertial characteristics of a complex chain shank "+ foot + footwear" for BK prosthesis.
I=Pirogov stump; II=long stump; III=border of middle and lower third of a shank; IV=half of a shank; V=border of middle and upper third of a shank; VI=short BK residual limb.

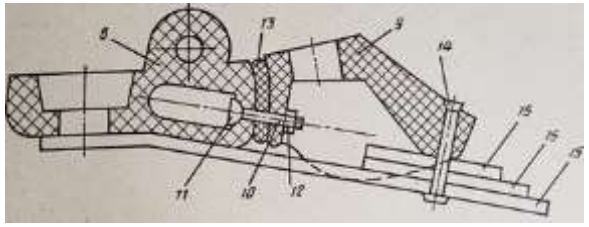
Evolution Toward Increased Dynamism and Controllability

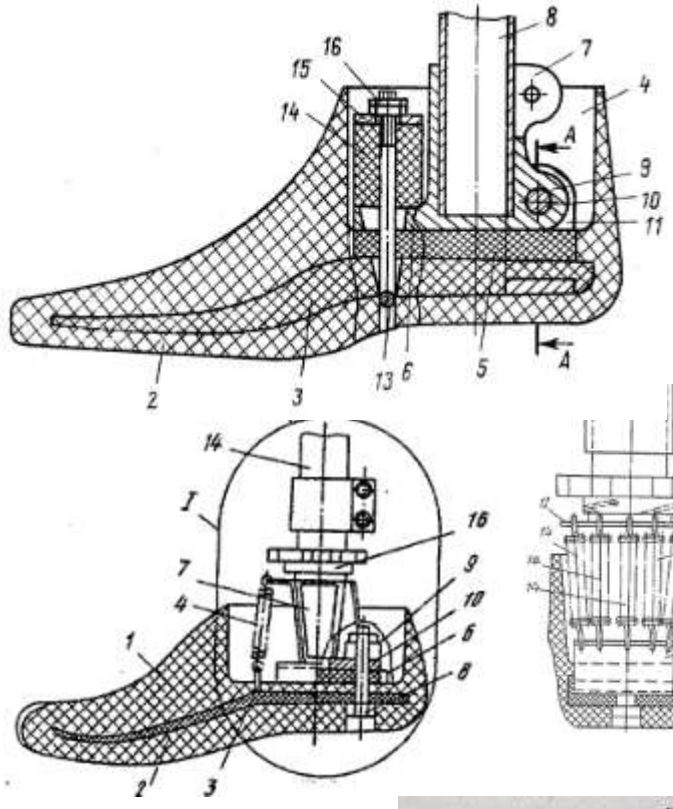
TRIZ Principle #40. Composite materials Farber B. et al., Artificial Foot, Eight Patents: #1498490, # 1454450 , # 1338856, # 1761136, # 1410970, # 1600759, # 1409258,TRIZ Principles #14. Spheroidal # 2012285

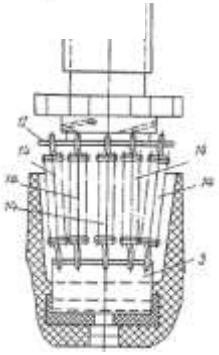


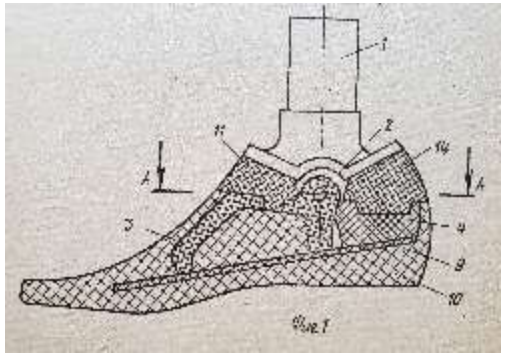


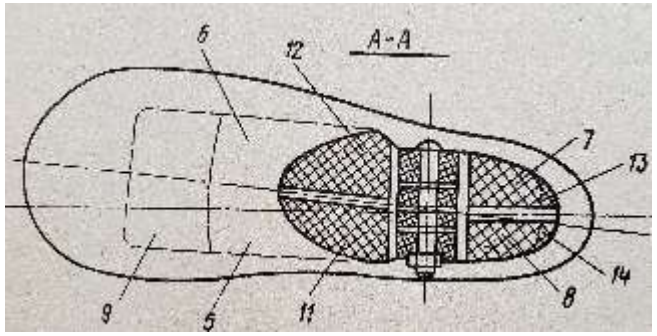


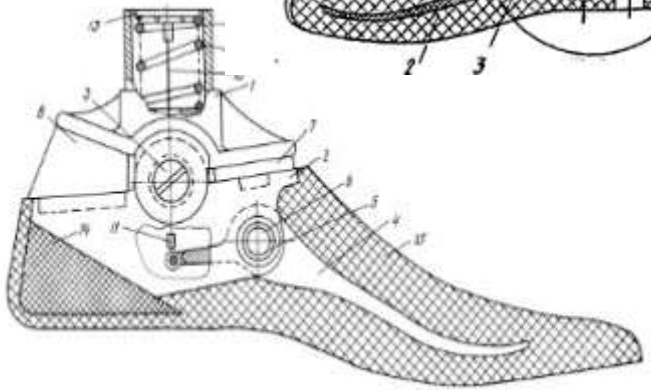


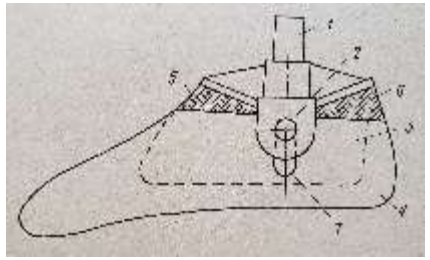






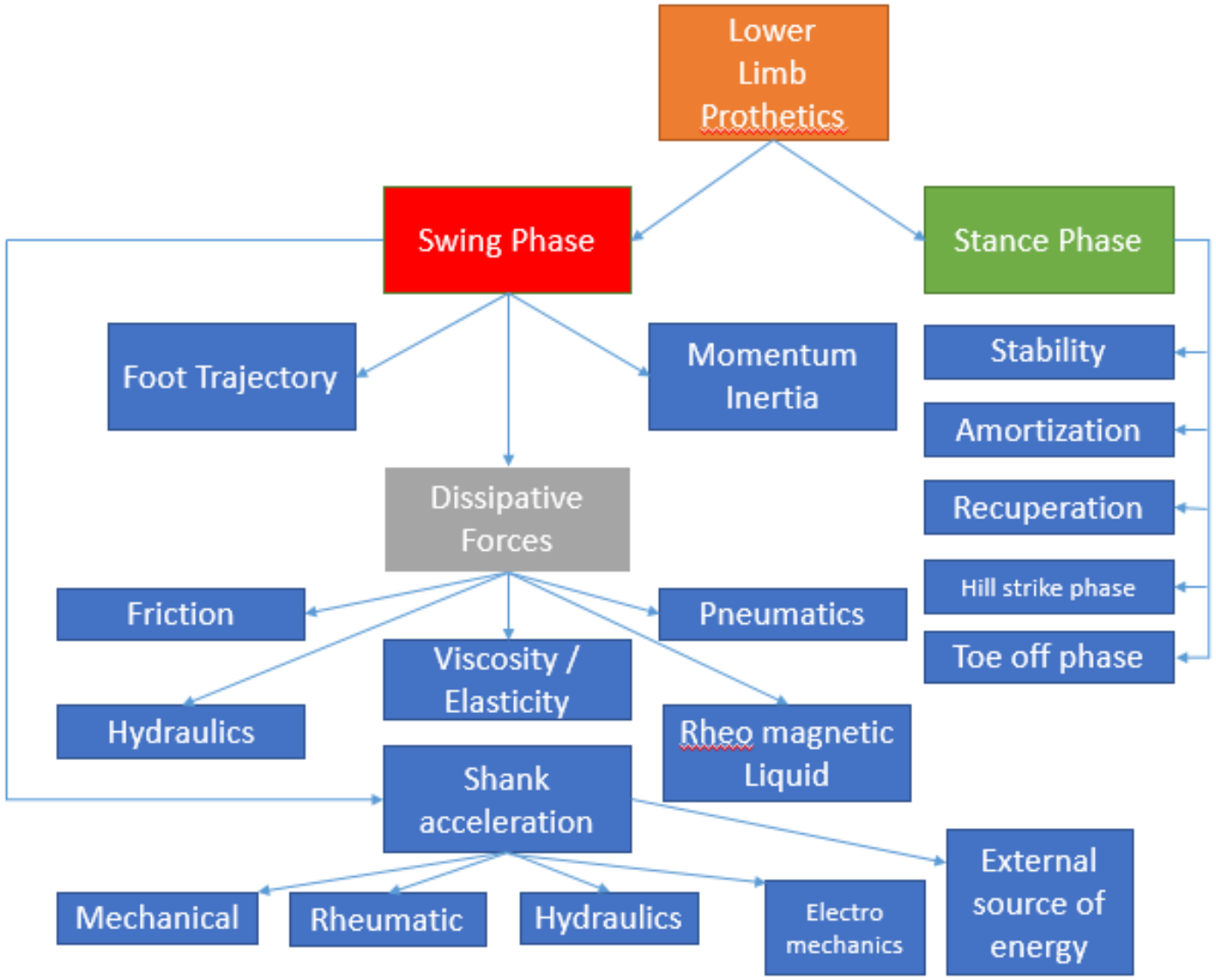




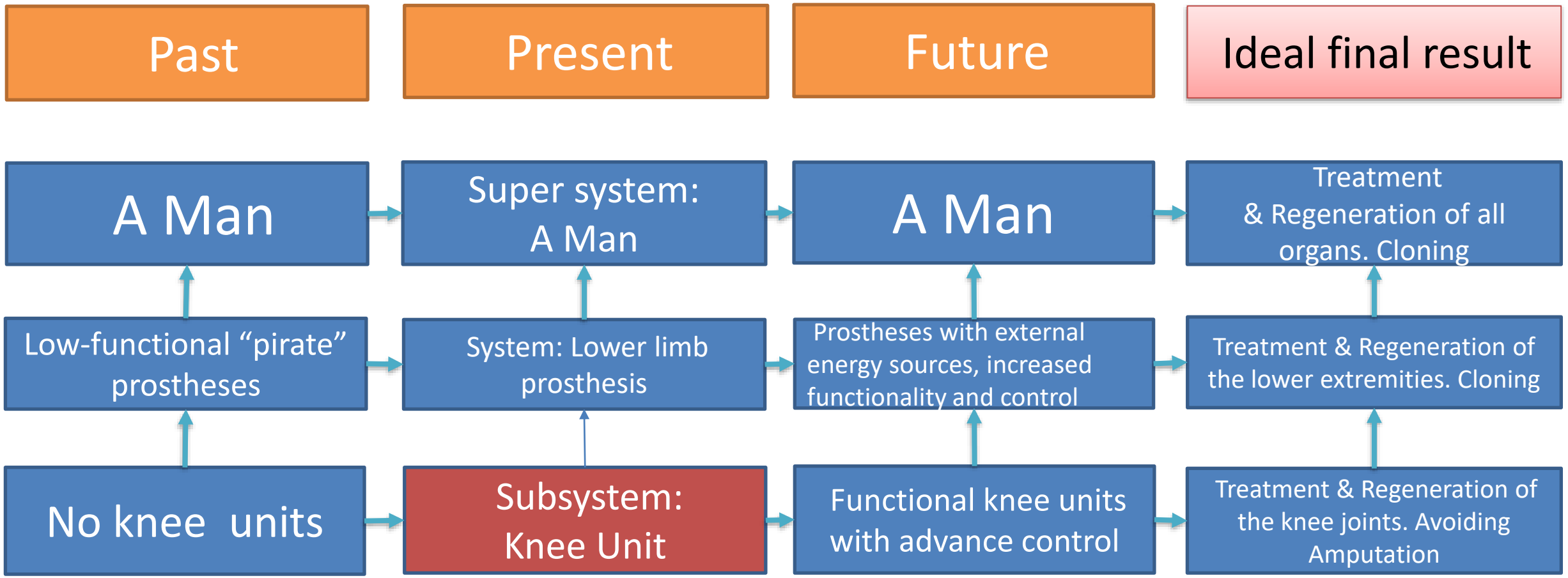


PART 1.2 KNEE UNITS

KNEE UNITS CLASSIFICATION

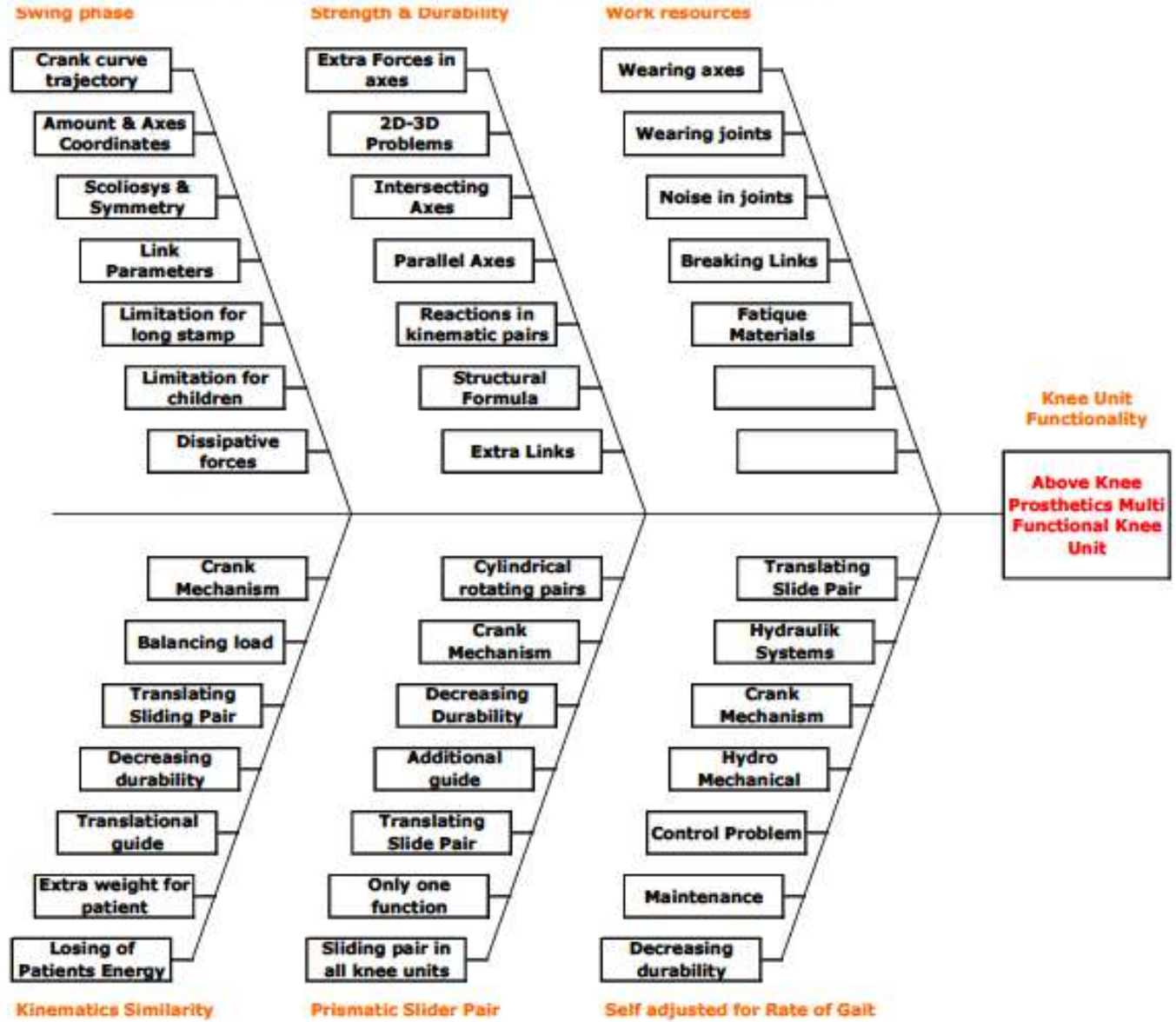


System Operator for Above Knee Prosthetics Unit Design Swing phase



Knee units

Ishikawa (Cause and Effect) Diagram for Above Knee Prothetcs Knee Unit Design



Functional analysis of the most typical knee units Swing Phase (fragment)

A: Cause:
Biomechanical functions
1. Swing Phase
2. Trajectory
3. Kinematic & dynamic

A:

Uniaxial knee units

- Uniaxial knee units
- Uniaxial with spring
- Friction
- Pneumatic
- Hydraulic
- Magneto Rheological

A: Negative effects:
1. Scoliosis
2. Patients extra energy lost
3. Vascular overloading
4. Lost of symmetry

B: Cause improved acceleration in swing phase

B

Uniaxial knee unit with balancing weight and crank mechanism

B: Negative effects:
1-4.All the same as in A
5.Extra weight
6.Lower durability

C: Cause:
1. Trajectory
2. Kinematic & dynamic
3. More symmetry
4. Less energy cost
5. Less scoliosis

4 bar knee
Units with rotating pairs

C1 Four bar knee units

C2 With crank mechanism

With spring

C3 Friction

C4 Pneumatic

C5 Hydraulic

C6 Magneto reological

C: Negative effects:
1. Increasing weight
2. Increasing a numbered elements
3. Decreasing durability
4. Decreasing resources

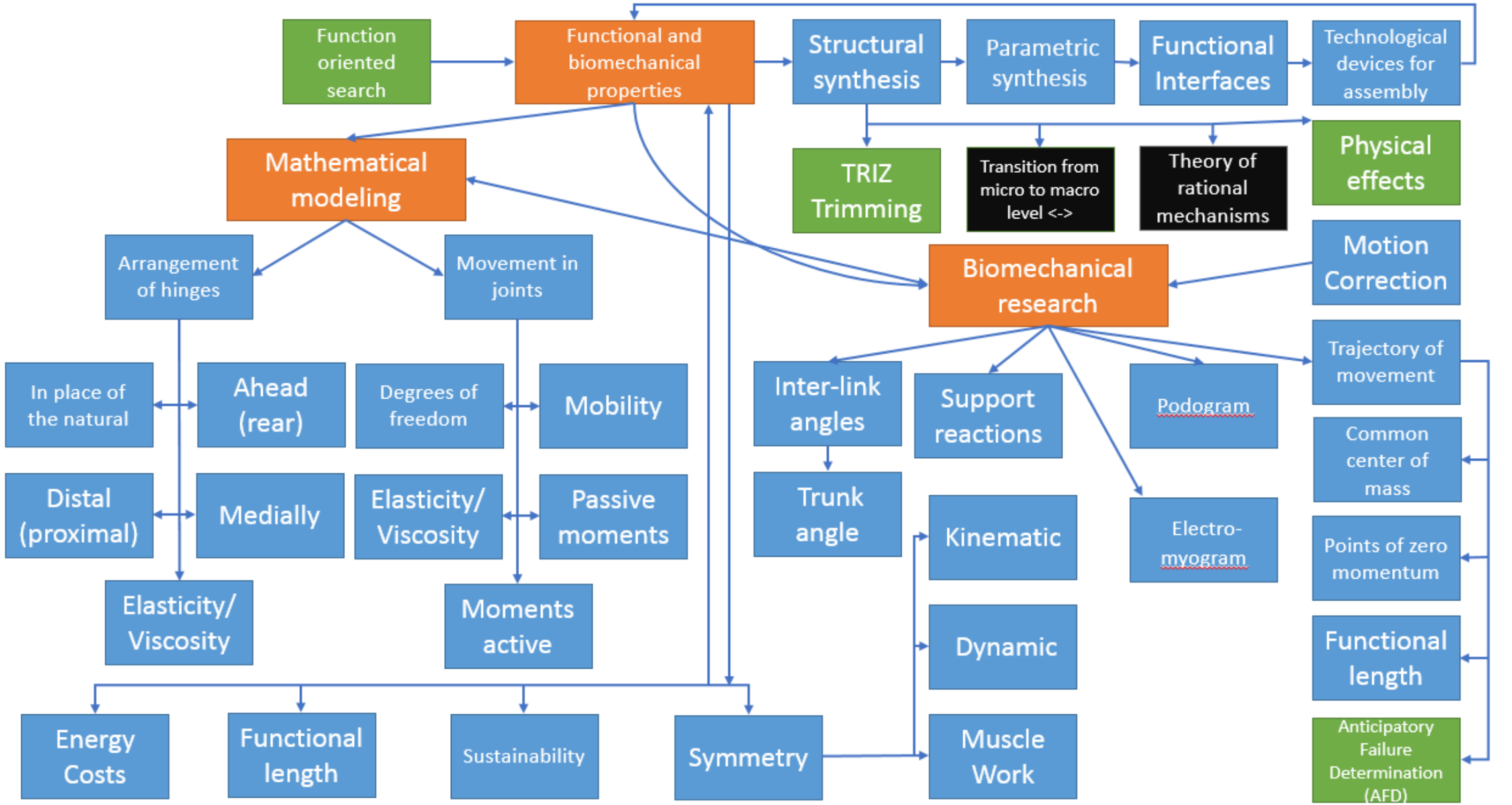
Our solution:
D: Cause
1. Improve durability
2 Improve trajectory
3 Improved centroid
4 Improved acceleration
5 Decrease weight
6 Improve kinematic & dynamic
7 Improve resource
8 Eliminate extra weight
9 Improve application of dissipative element

D: The 1-st in the World self adjusted guide knee mechanism without additional links

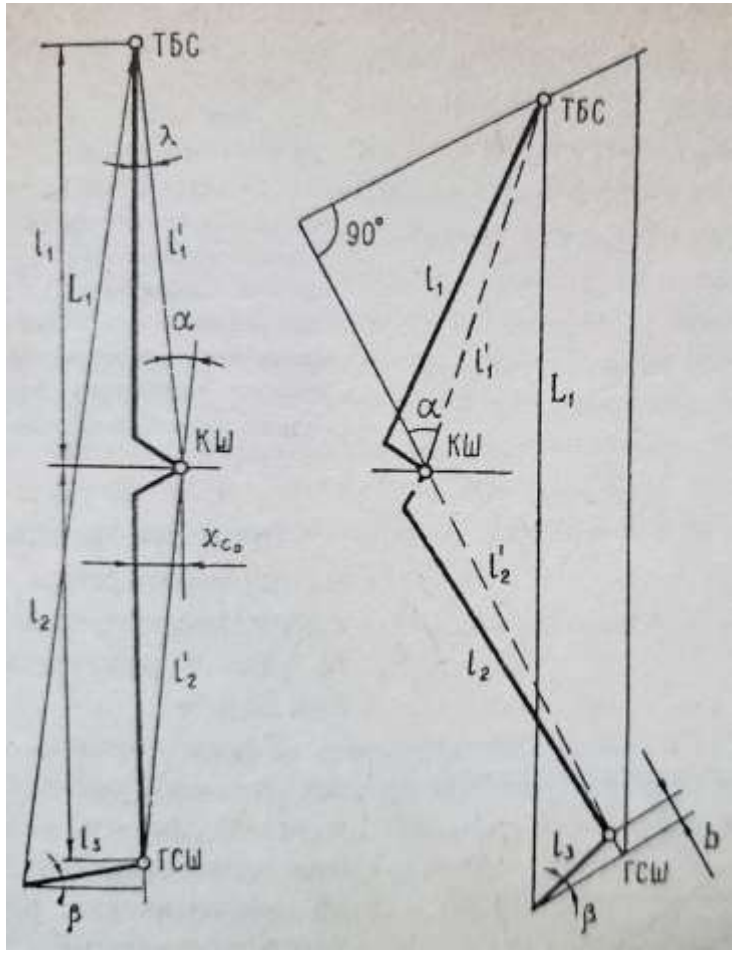
1 We combined all positive features of A,B,C
2 We made 3 trimmings
- 2.1 We trimmed extra links
- 2.2 We trimmed extra weight in structural synthesis
- 2.3 We trimmed crank mechanism

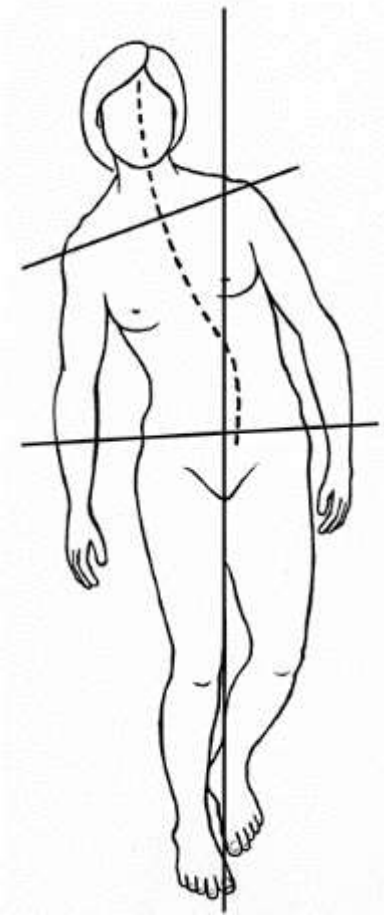
3 We increased ideality
4 We decreased negative effects

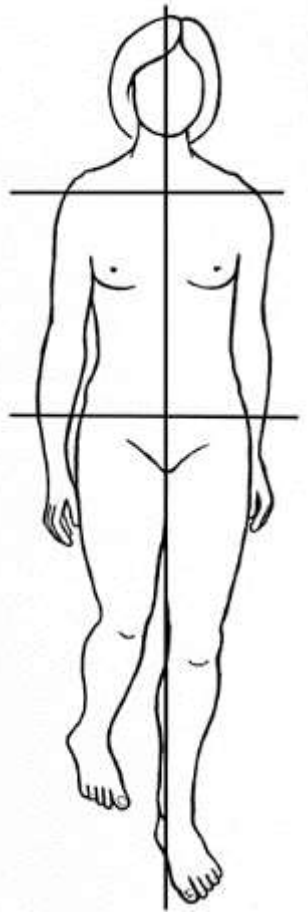
TRIZ structure of the functional-biomechanical method of improving the system “man - prosthesis (orthosis) - environment”



Swing phase prosthetic leg trajectory and scoliosis







Problem Identification for Knee Units and Super System Lower Limb Prosthetics

Problem Identification

Tactics
Program minimum
Design a knee unit which combines property of all 4 units on the market, including:

1. Multi axes knee unit
2. Knee unit with balancing ….
3. Light
4. Durable
5. Easy to produce
6. Easy to connect with control devices without extra element
7. Aluminum Version on this stage

Strategy
Based on S-curve
Create a new module TITANIUM system of prosthetics for any level of amputation

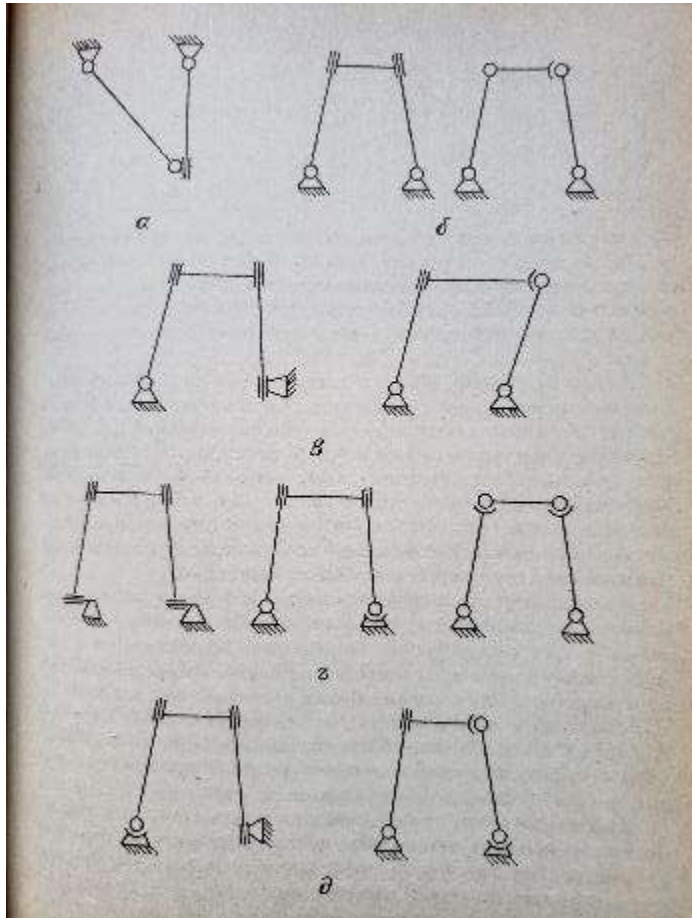
Modular system

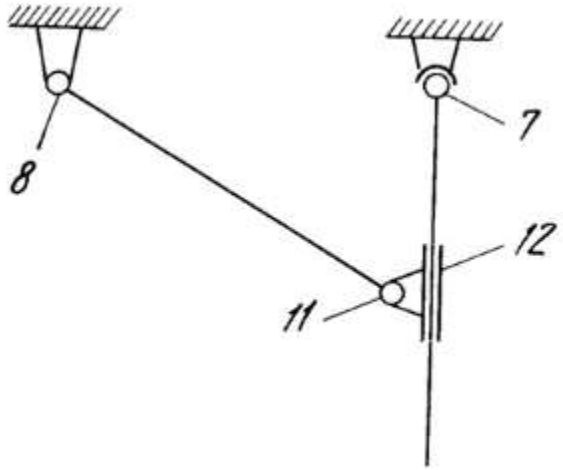
3-D movement knee units

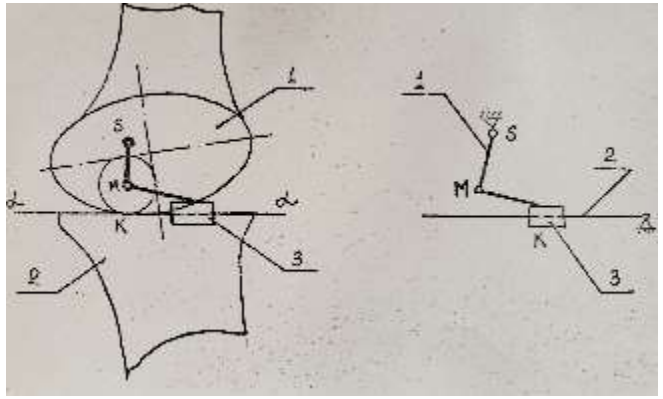
Magneto rheological and computer control

External source of energy for main biomechanic parameters

Farber B. et al., Kinematics of knee joint and Structural Synthesis of guide knee Mechanism







$$W = 6n - \sum_{k=1}^{5} k \cdot P_k =$$

$$= 6n - 5p_5 - 4p_4 - 3p_3 - 2p_2 - 1p_1$$

$$W_1 = 6 \cdot 3 - 5 \cdot 4 = -2$$

$$W_2 = 6 \cdot 3 - 5 \cdot 3 - 4 \cdot 1 = -1$$

$$W_3 = 6 \cdot 3 - 5 \cdot 2 -$$

$$-4 \cdot 1 - 3 \cdot 1 = 1$$

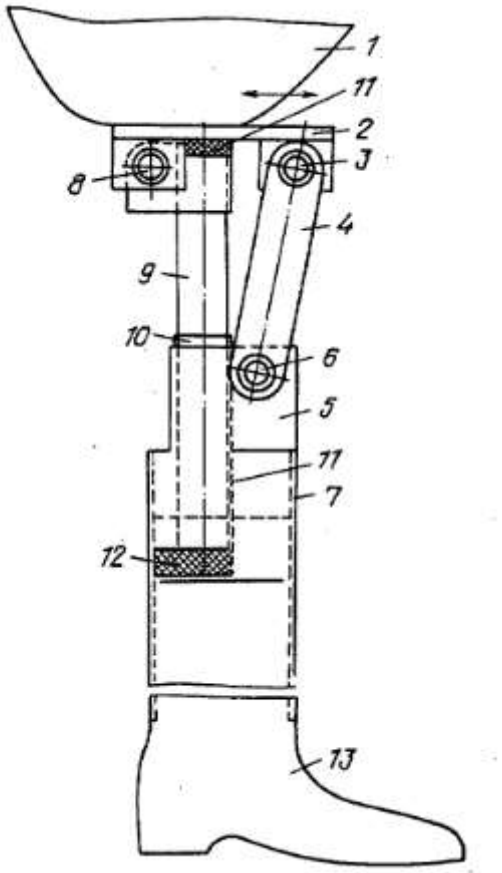
n – число подвижных звеньев механизма

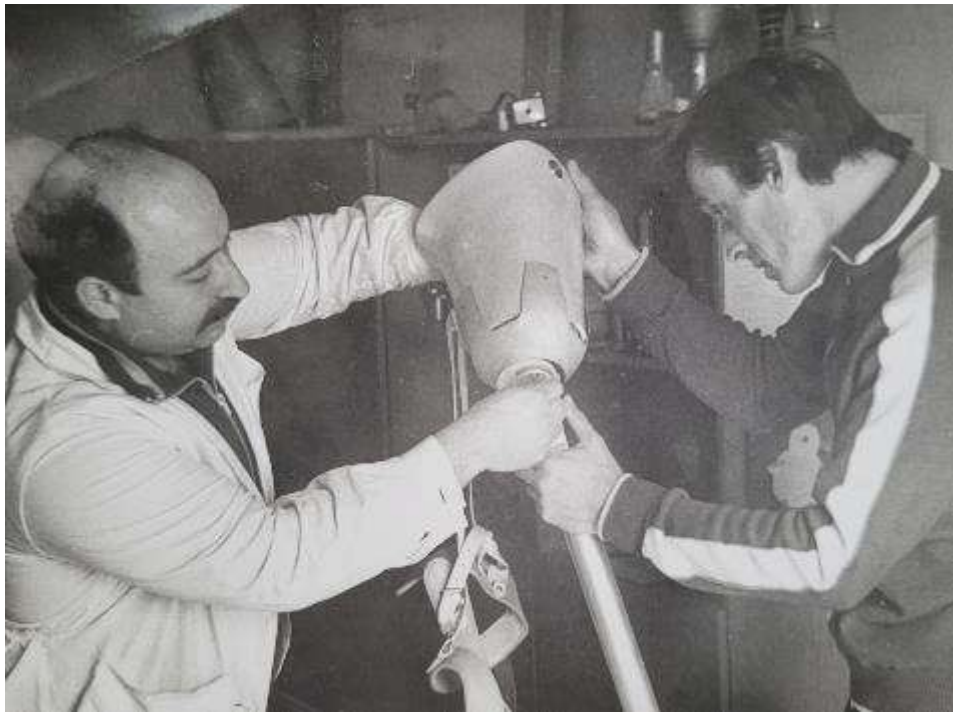
$W=6n-5p_5-4p_4-3p_3-2p_2-p_1$

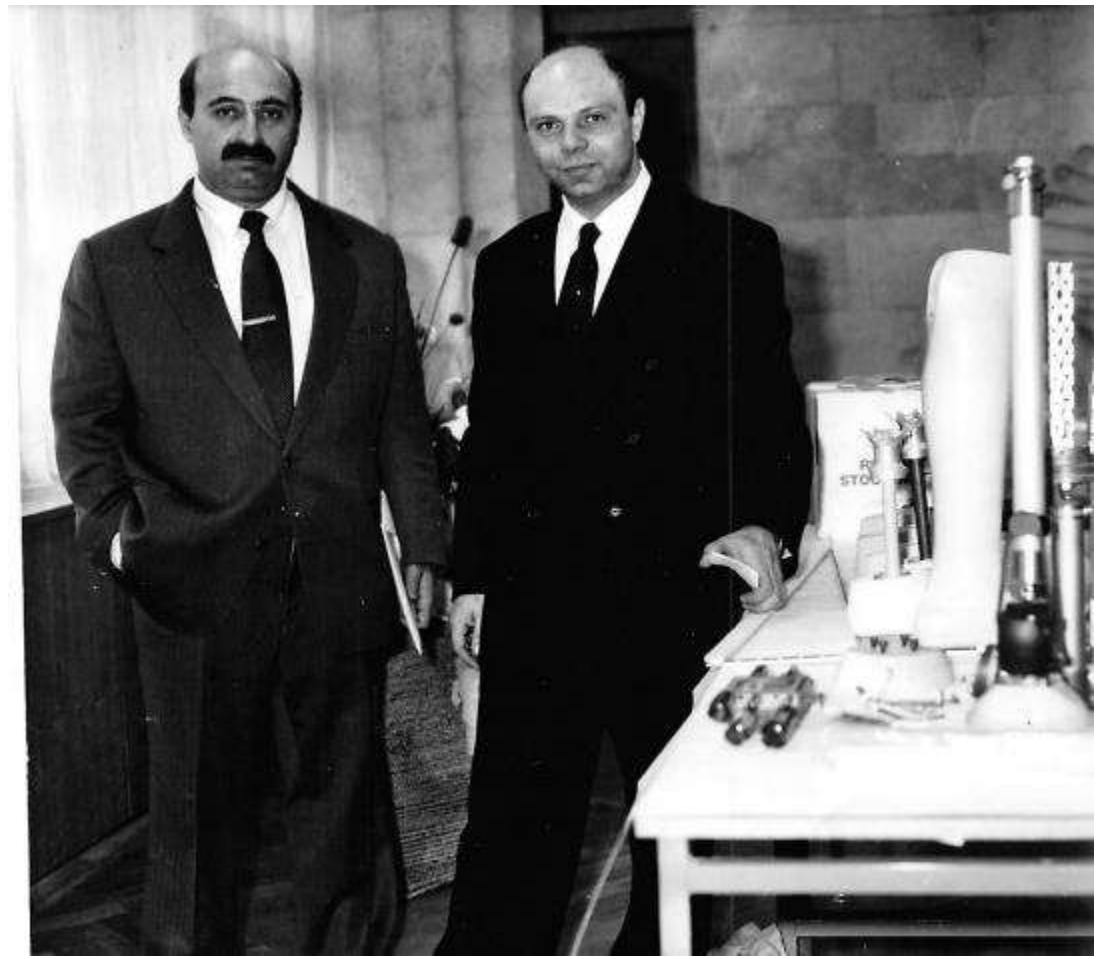
$W=6x3-5x4=-2$

$W=6x3-5x2-4x1-3x1=+1$

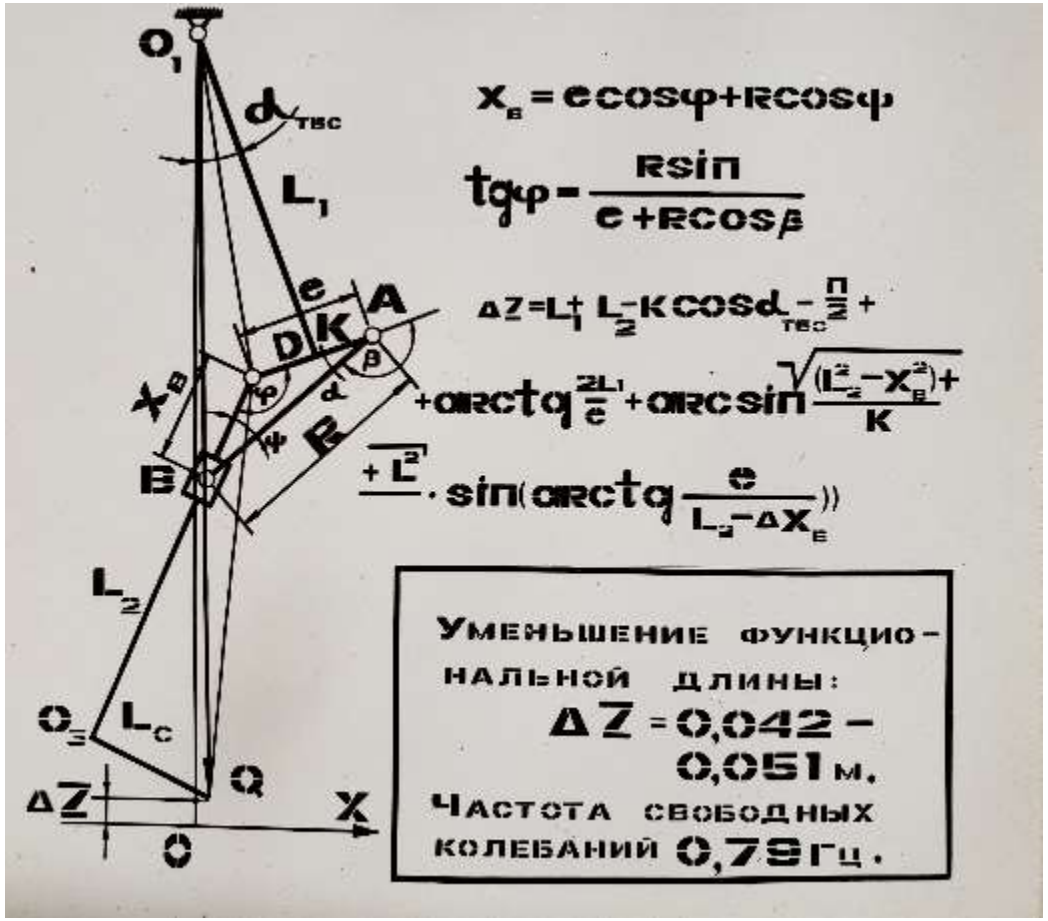
The first in the World Guide Knee Units with pairs of 4th & 5th classes: Farber B. et al., Guide Rocker Knee Patent # 1138151 and Guide Self adjusted Knee Units with pairs of 3rd ,4th & 5th classes: Farber B. et al., Patent #2062073

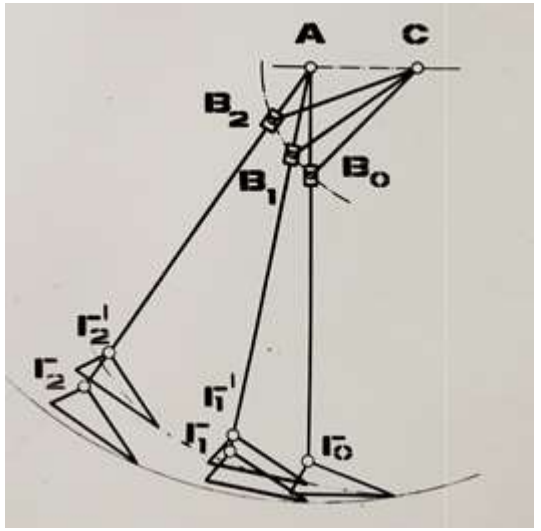


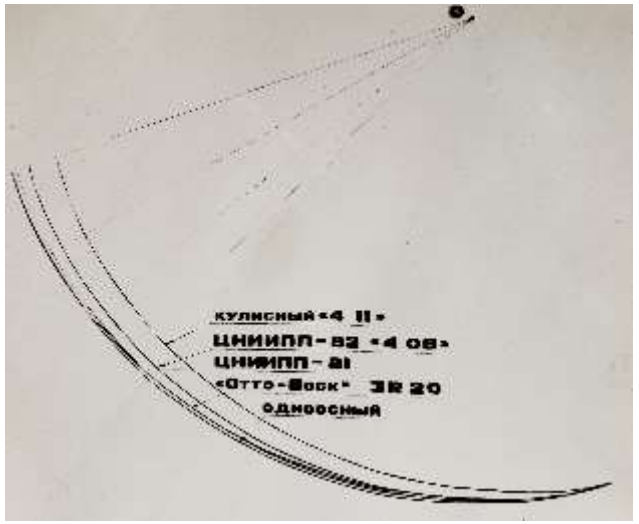


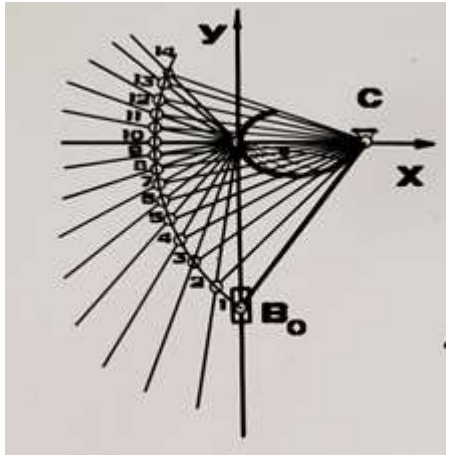


Farber B. et al., adjustable model of guide knee mechanism Patent #1138151
Swing phase: guide rocker knee mechanism

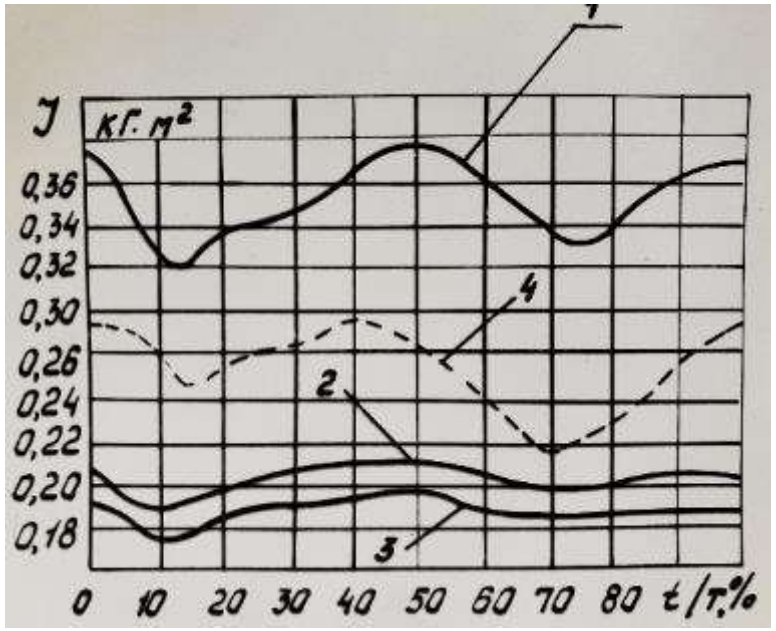


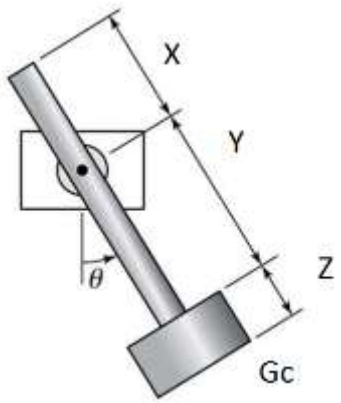


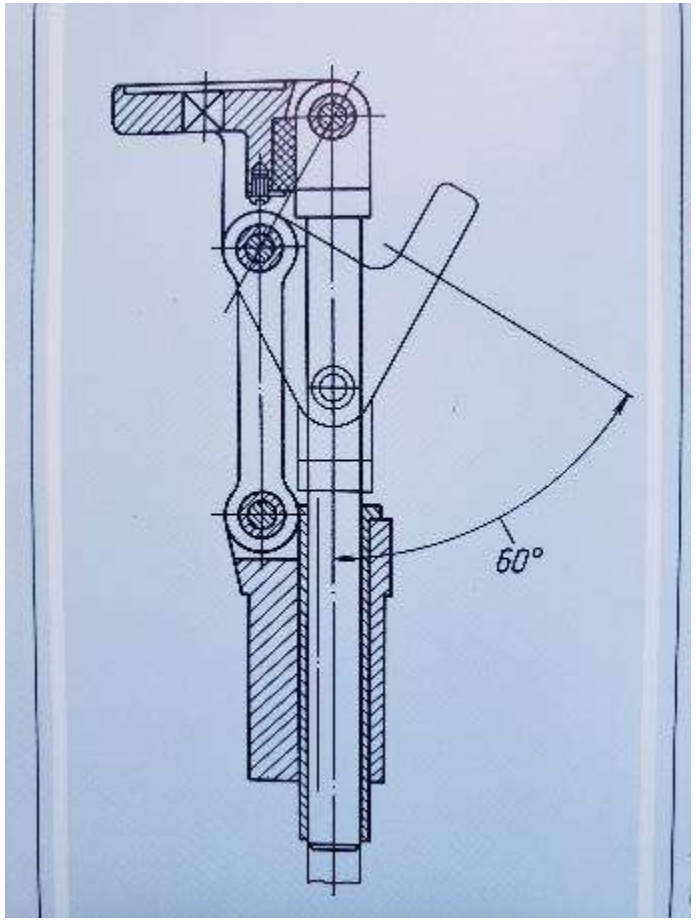


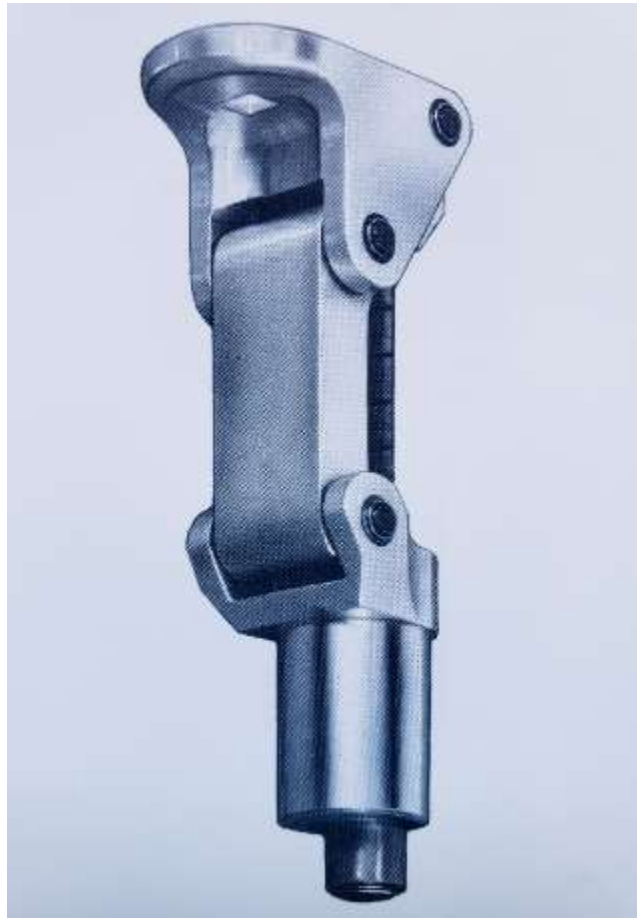


Farber B. et al., Rocker Knee mechanism D16T
Patent # 1138151 Producing by Semashko Plant
Moment Inertia as a function of time (knee angle) in a swing phase

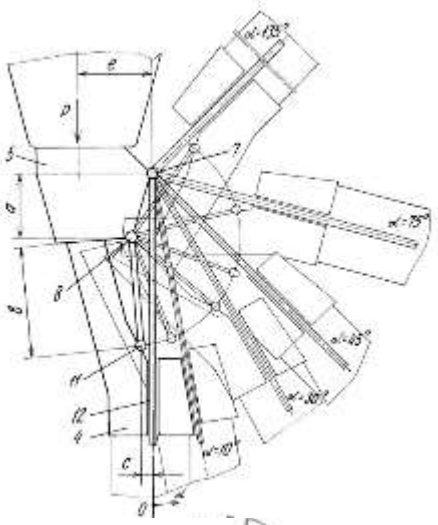


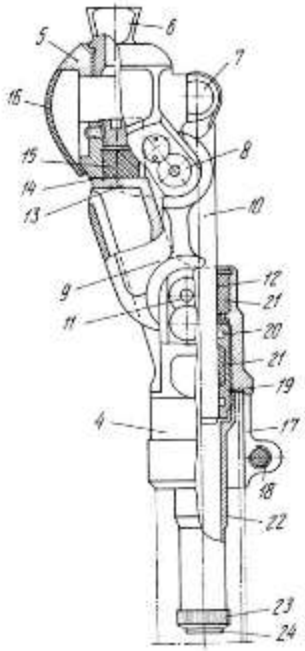


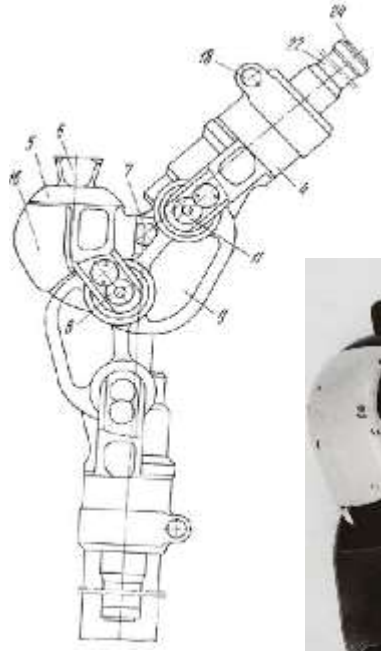


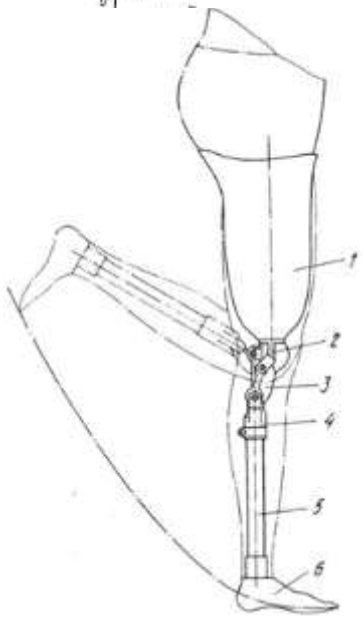


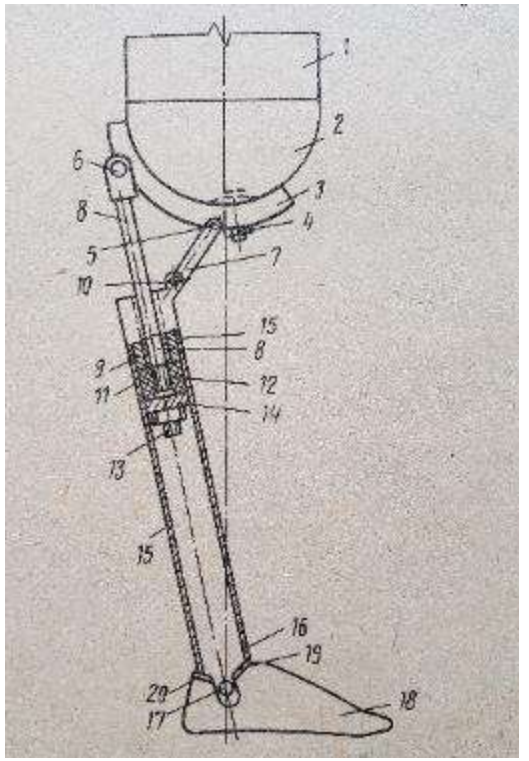
Farber B. et al., Above knee prosthetics with guide rocker unit Patent #2062073 ,Patent # 1466738 guide rocker unit for knee disarticulation







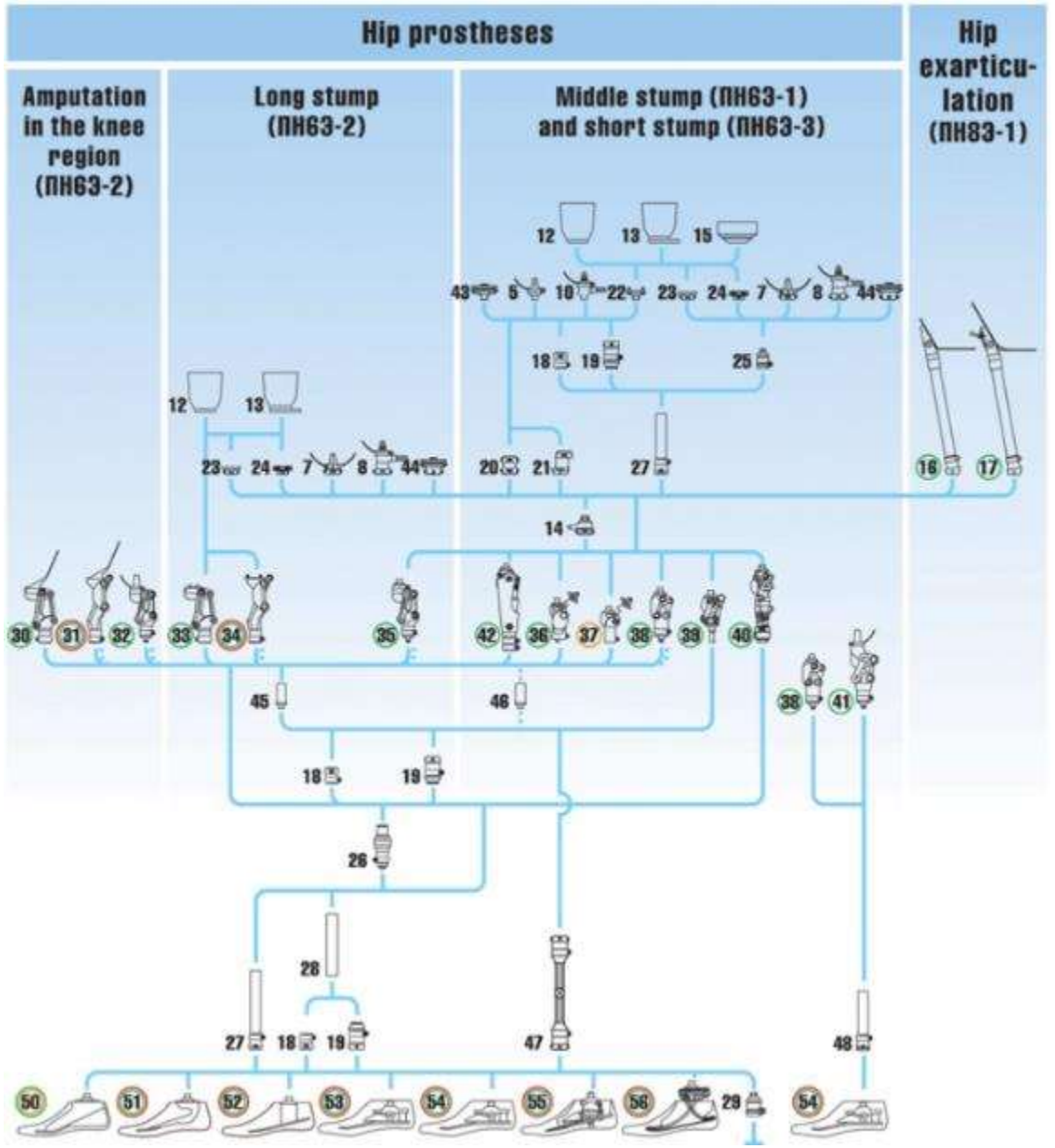




MODULAR SYSTEM OF LOWER LIMB PROSTHETICS

Rocket and Space Corporation RKK “Energiya”, is a Russian manufacturer of ballistic missile, spacecraft and space station components, prime developer and contractor of the

Russian manned spaceflight program.

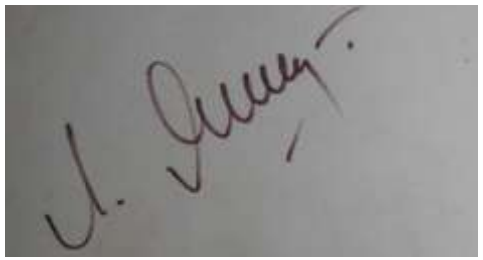


Knee units system produced by “Energia”. Gold Medal World Exhibition of Innovation, Research and New Technologies “Brussels INNOVA”

Advantages of our knee unit :

- 1 Combined all positive features of A,B,C-main existing knee units
- 2. Increased ideality
- 3. Trimmed extra links
- 4. Trimmed extra weight by structural synthesis (IFR)
- 5. Trimmed crank mechanism, but maintained its action (IFR)
- 6. Improved durability and resources
- 7. Improved trajectory
- 8. Improved centroids
- 9. Improved momentum of inertia without extra weight(IFR)
- 10. Improved kinematic & dynamic
- 11.Improved application of dissipative element

Lev Yashin the "Black Panther" considered by as the greatest goalkeeper in the history of the sport



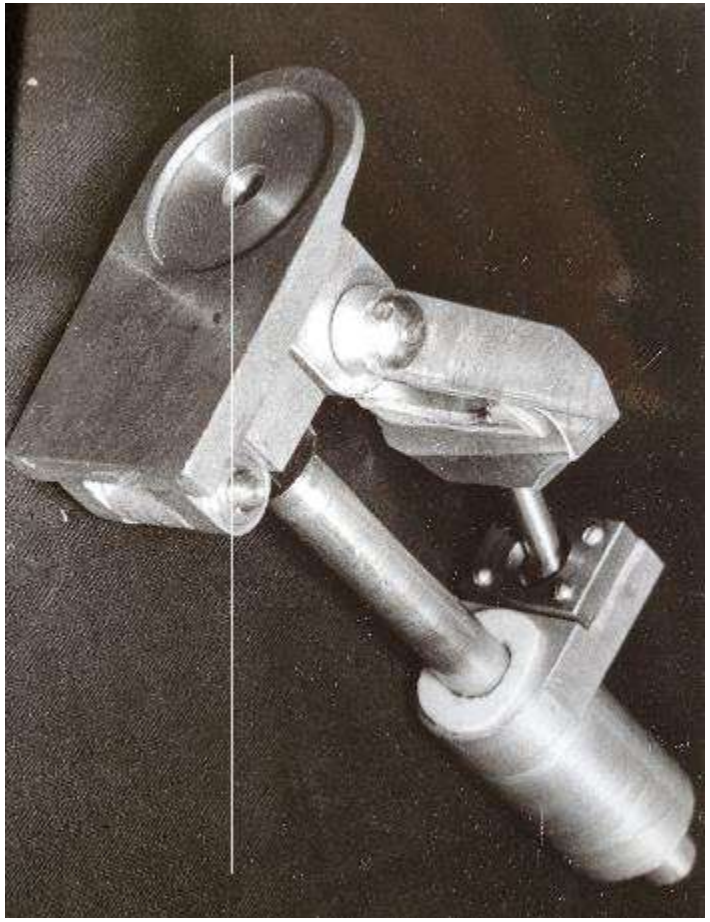
Tatyana Kuznetsova (above knee amputation) World Champion in NY Marathon

МОЛОДАЯ ДАМА НА ПРОТЕЗЕ

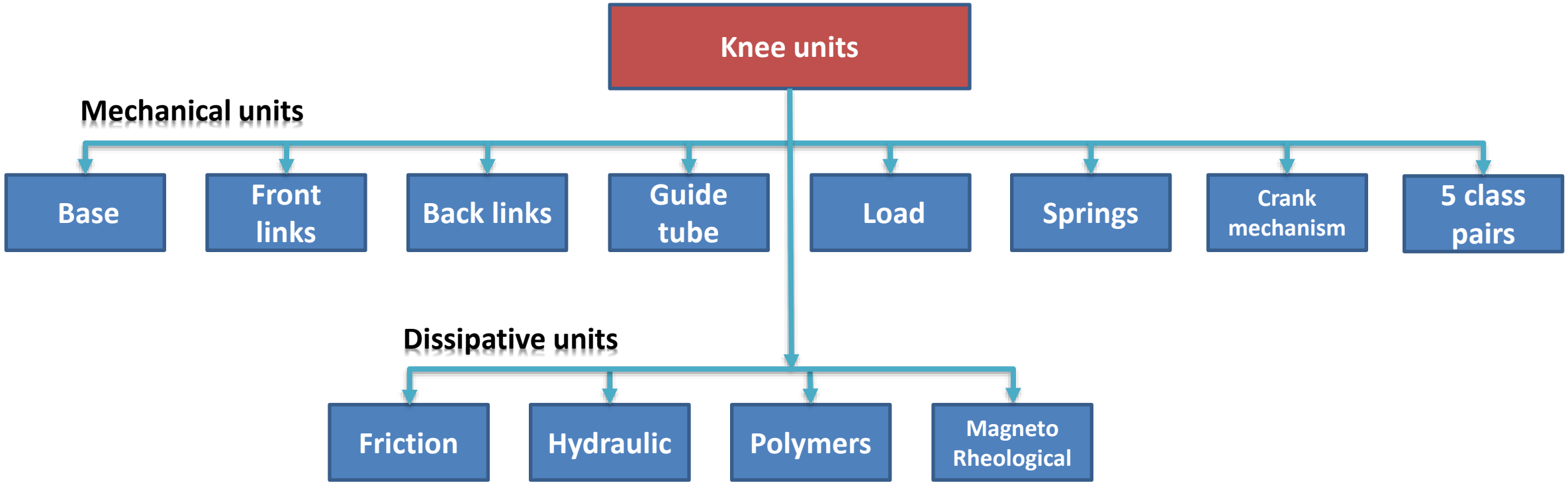
Представляем нашу собеседницу:
Тани Кузнецова, студентка Челябинского государственного института физической культуры и спорта; с 1988 года регулярно участвует в соревнованиях по бегу на длинные дистанции и в нашей стране, и за рубежом. Чемпионка мира в беге на марафонскую дистанцию (42 км 195 метров), обворожительная дама ... на протезе. Ее последнее достижение - победа в знаменитом Нью-Йоркском марафоне. Ее протез – отечественной конструкции изготовлен в подмосковном Калининграде на заводе, где рождались первые искусственные спутники Земли, где и сегодня создается отечественная космическая техника.

ИНТЕРВЬЮ С ЧЕМПИОНКОЙ МИРА

The first in the World Guide Self adjusted Knee Units with pairs of 3rd ,4th & 5th classes: Farber B. et al.,



Levels of abstraction of knee units Swing phase



S- curve for Prothesis Knee Units

АКАДЕМИЯ НАУК СССР
СИБИРСКОЕ ОТДЕЛЕНИЕ

Институт истории, филологии и философии
СО АН СССР

Философское общество СССР

Западно-Сибирское отделение

Новосибирский государственный университет
им. Ленинского комсомола

МЕТОДОЛОГИЯ И МЕТОДЫ ТЕХНИЧЕСКОГО ТВОРЧЕСТВА

Тезисы докладов и сообщений к научно-практической конференции 30 июня — 2 июля 1984 г.

Новосибирск
1984

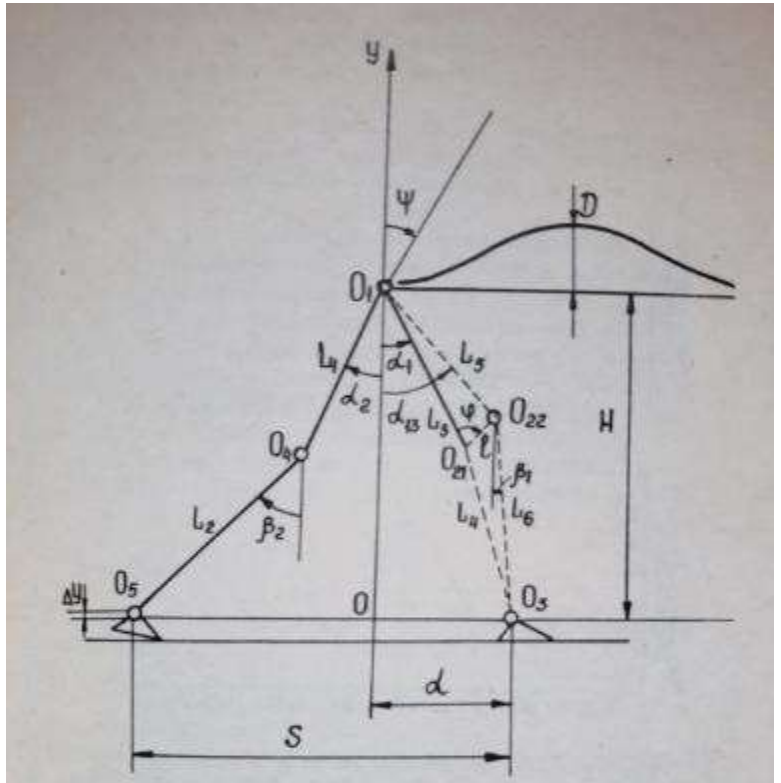


Рис. 1. Модель тела человека

жения. Качество оценивалось с помощью функционала энергозатрат Белецкого – Чудинова /1/:

$$E = \int_0^{2T} \sum_{i=1}^{2} \{[|p_i \dot{\beta}_i| + |q_i(\dot{\psi} - \dot{\alpha}_i)| + |u_i(\dot{\alpha}_i - \dot{\beta}_i)|]\}\, dt$$

где:

p_i, q_i, u_i – моменты в суставах;

β_i, ψ, α_i – углы отклонения сегментов модели от вертикали.

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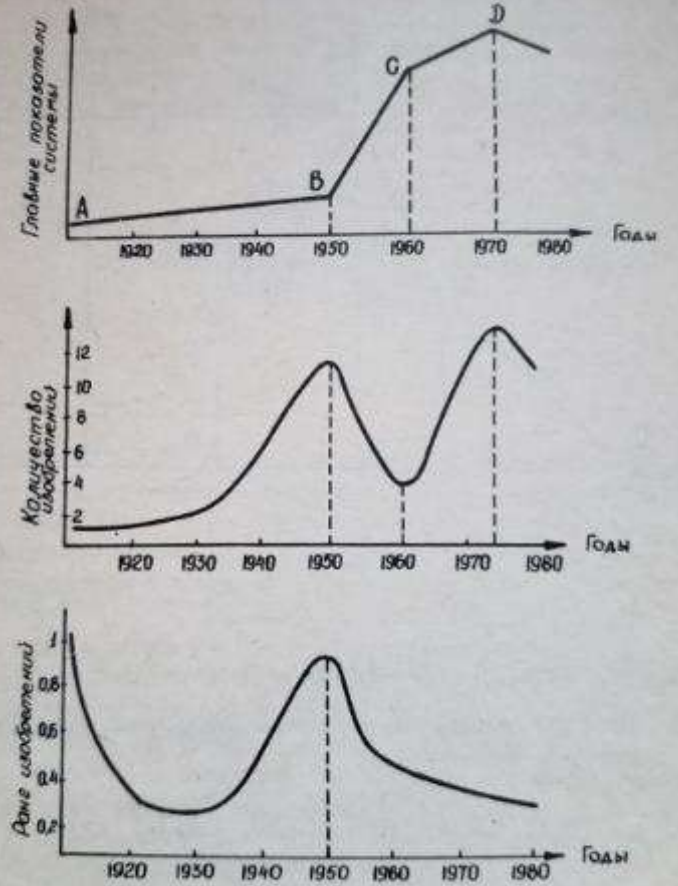

Рис. 2. Динамика патентования коленных механизмов

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“ Micro-Macro Level” Transition
Problem solving

чивающем наибольшую эффективность процесса. В задаче "о приеме радиоволн" наибольшую эффективность обеспечивает отсутствующий молниеотвод: не затеняет радиоволны. Модель задачи: отсутствующий молниеотвод – молния.

Такой подход позволяет выделить главную модель задачи и, следовательно, – основное физическое противоречие данной технической системы.

В докладе также рассматриваются вопросы разрешения физических противоречий.

Литература

1. Альтшуллер Г.С., Селицкий А.Б. Крылья для Икара. – Петрозаводск: Карелия, 1980.

2. Альтшуллер Г.С. Творчество как точная наука. – М.: Сов. радио, 1979.

Б.С.Бербер

МЕТОДИКА РЕШЕНИЯ "МАКРОУРОВНЕВЫХ" ЗАДАЧ В ТРИЗ

Противоречие есть критерий истины, отсутствие противоречия – критерий заблуждения.

Гегель

Одним из объективных законов развития технических систем является переход с макроуровня на микроуровень.

Но как поступить, если для практического осуществления такого перехода еще не разработаны "микроуровневые" условия? Предположим, нужно использовать свойство жидкости изменять вязкость под действием магнитного поля, а жидкости с требуемыми свойствами пока не синтезированы? Получается, что физэффект известен (в данном случае – реологический эффект) – а жидкостей с конкретными свойствами пока нет. Вопрос создания магнитных жидкостей с требуемыми свойствами является не простым. А как же быть, если практика требует незамедлительного решения поставленной задачи?

Если обратиться к мировому фонду патентной и научно-техни-

ческой литературы, то нетрудно обнаружить, что на сегодняшний день разработано и описано огромное количество остроумнейших механизмов (от Кулибина до Артоболевского /3/) на макроуровне, которые в сочетании с решениями на микроуровне представляют собой эффективные решения /1, 2/. (Например, поднятичивание стальных деталей макроуровневых механизмов Альтшуллер Г.С.))

Проблема состоит в том, чтобы из этого огромного массива механизмов выбрать наиболее подходящий или разработать новый.

Для этой цели предлагается использовать методику, базирующуюся на ТРИЗ. (Для сокращения изложения укажем, что переход с "микро" на "макроуровень" начинается после составления вепольной формулы решения задачи.)

Предполагается разработать таблицу "микро- макроуровневых" аналогов, а точнее, таблицу соответствия физических эффектов и механических устройств. Рассмотрим фрагмент таблицы.

Таблица

№№ пп	Входное воздействие на систему	Реакция системы на воздействие	Физический эффект (на микроуровне)	Макроуровневый аналог физэффекта
1.	Магнитное (или электростатическое) поле воздействует на жидкость	Изменение вязкости жидкости	Реологический эффект	Взаимодействие между молекулами заменить взаимодействием между шариками
2.	Механическое поле, а конкретнее крутящий момент воздействует на стальной образец	Диаметр при закручивании уменьшается, образец удлиняется, объем увеличивается	Эффект Пойнтинга	Взаимодействие между молекулами заменить взаимодействием между слоями молекул, использовать спиральную стальную ленту

Из таблицы видно, что между эффектами на "микро" и на "макроуровне" наблюдается некоторая аналогия. В случае спиральной

ленты это зависимость Эйлера $P = Qe^{\varphi\alpha}$

где P – усилие, действующее на один из концов ленты, которое можно удержать с помощью силы Q, приложенной к противоположному концу ленты, при условии что она навита вокруг барабана с углом обхвата α, а коэффициент трения между материалом барабана и ленты φ.

Так, при разработке управляемого коленного механизма был использован макроуровневый аналог эффекта Пойнтинга.

Литература

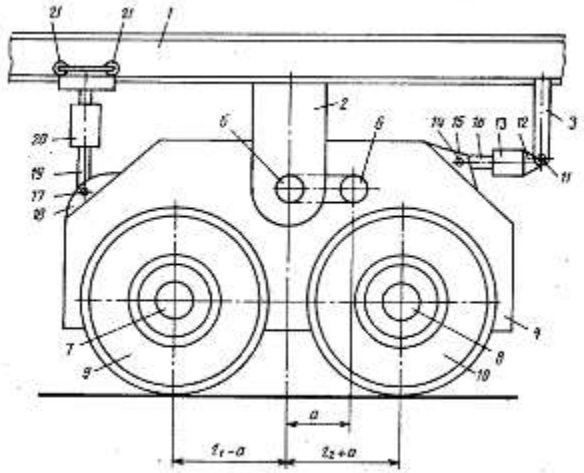
1. Альтшуллер Г.С. Творчество как точная наука. – М.: Сов. радио, 1979,-172 с.

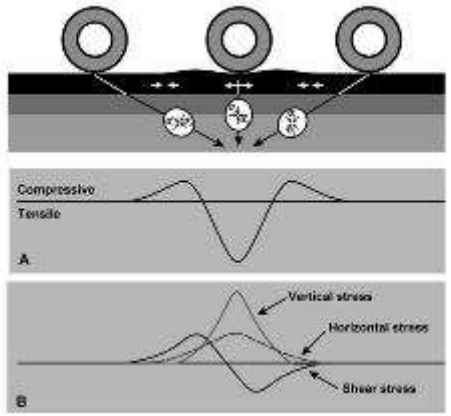
2. Альтшуллер Г.С., Селицкий А.Б. Крылья для Икара. – Петрозаводск: Карелия, 1980. – 223 с.

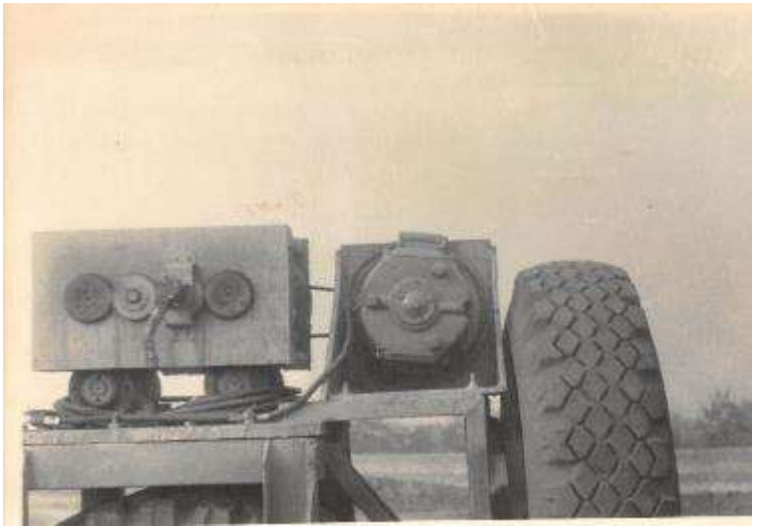
3. Артоболевский И.И. Механизмы в современной технике. Т. I – УI. – М.: Наука, 1973.

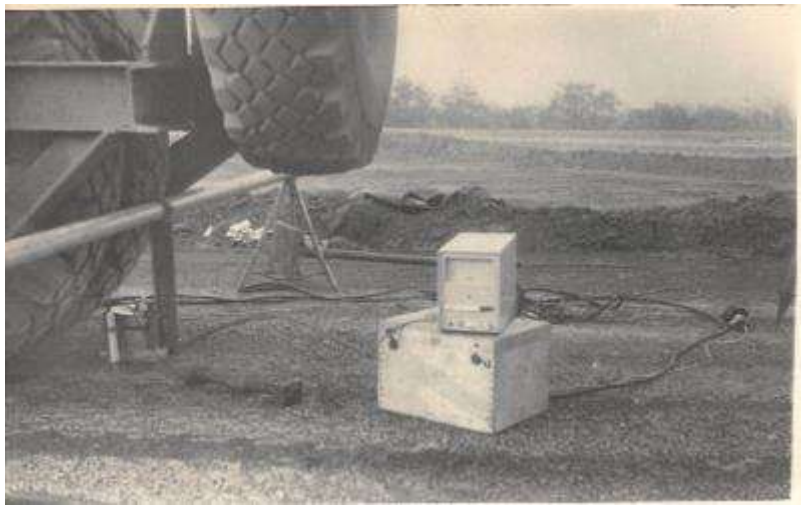
TRIZ Principle 15. Dynamicity

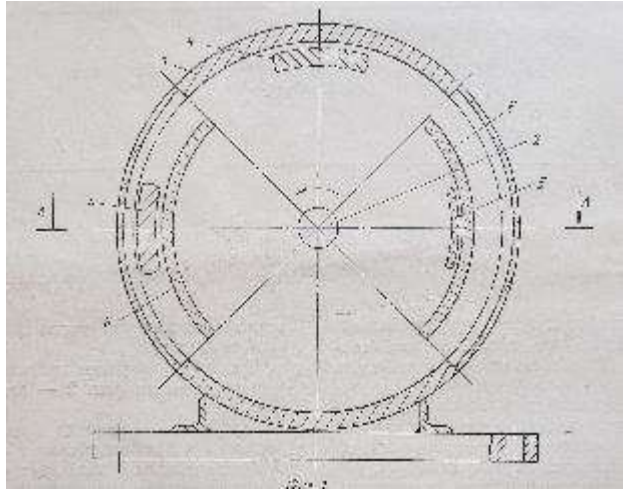
Farber B. et al., Multi axes Dynamic Vehicle Patent #1199885 Farber B. et al., Unbalanced Vibrator Patent # 649478





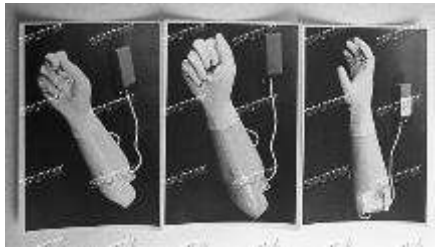






Part1.3

CNIIPP: The First Myoelectric Hand In the World



PART 2: Vibrobiomechanics **Golovchenko G.G: Pine Needle Rust -is great example of Nature Wisdom**

Analogy with Music of Forest (Rustle of the Forest M.K.Ciurlionis-G.G.Golovchenko)

HYPOTHESIS-vibro tactile contact a foot with ground suppose to be used by Nature

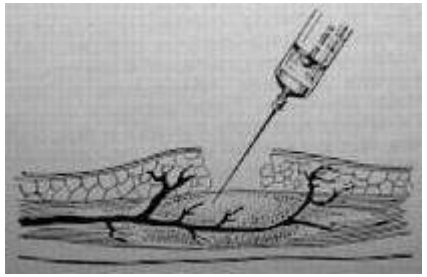
Wind is mechanical energy. The wind that sways the leaves of plants helps them accumulate nutrients. Where the wind does the greatest work - at the junctions of leaves with branches, and branches with a trunk.

MY APPROACH to Wisdom of Nature in Biomechanics

Farber B.et al., An approach to high quality prosthetics through biomechanical data analysis of motion defects. - In: Second World Congress of Biomechanics. Amsterdam, The Netherlands, 1994, v.1, p.285.

Anticipatory Failure Determination2 (AFD2)-anesthesia of the foot with Novocain and study Biomechanics

Anticipatory Failure Determination 1 (AFD 1) in studying lower limbs prosthetics applying “wrong” elasticity



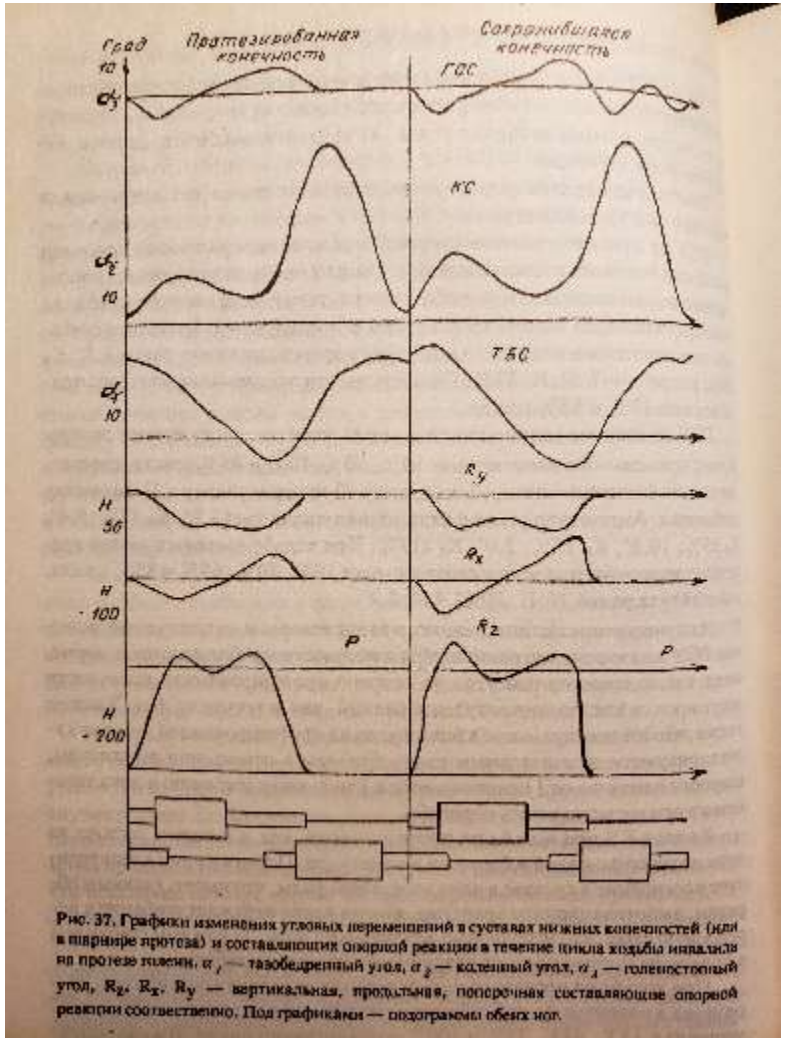
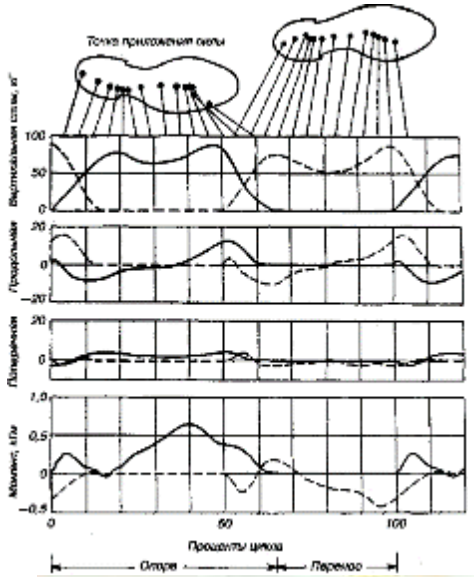
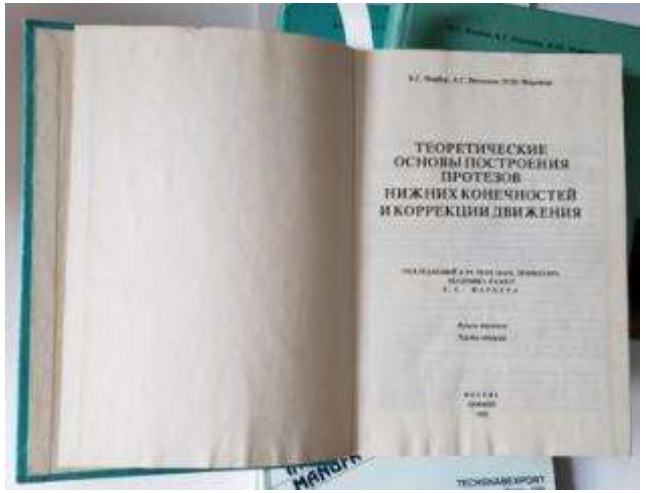


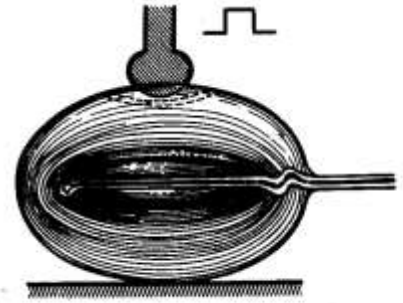
Рис. 37. Графики изменений угловых перемещений в суставах нижних конечностей (для в парнике протеза) и составляющих опорной реакции в течение цикла ходьбы инвалида на протезе голени. α_3 — тазобедренный угол, α_2 — коленный угол, α_1 — голеностопный угол, R_z, R_x, R_y — вертикальная, продольная, поперечная составляющие опорной реакции соответственно. Под графиками — подограммы обеих ног.

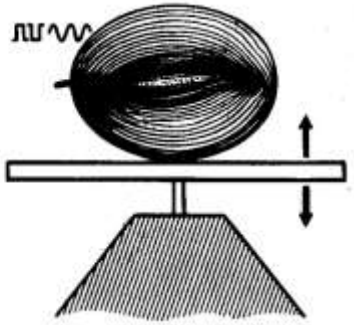


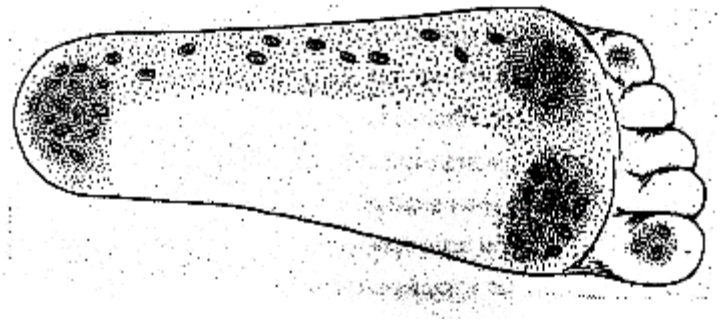


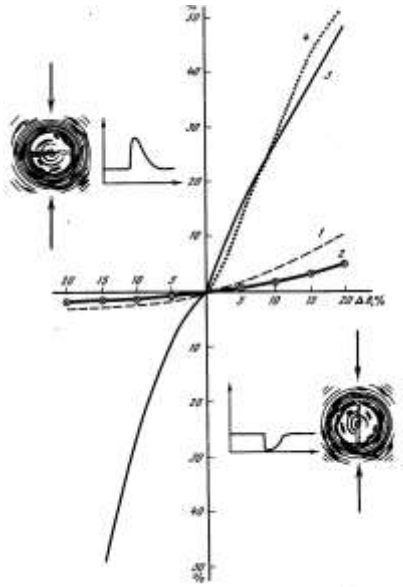
PART 2: Vibrobiomechanics

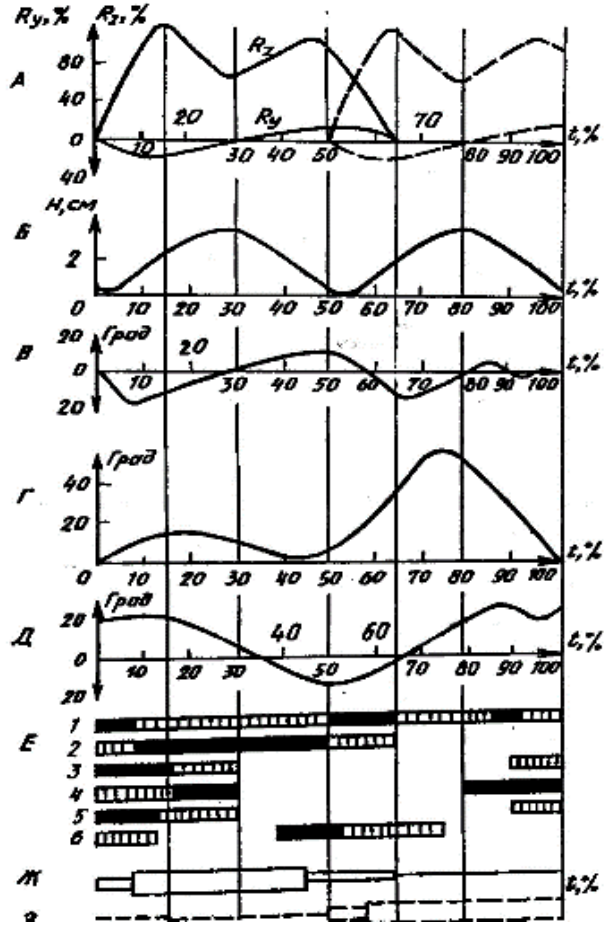
Function-Oriented application for patients after strokes and heart attack: Vater-Pacini corpuscle. Nerve Parameters as a function of pressure & ground reactions





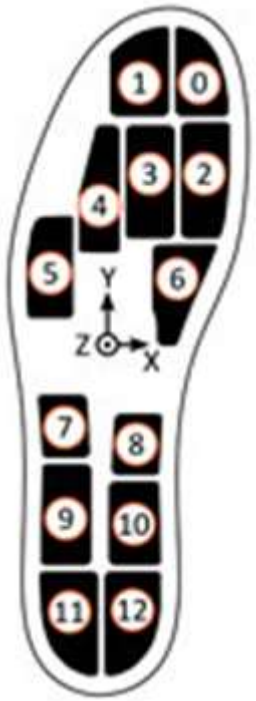




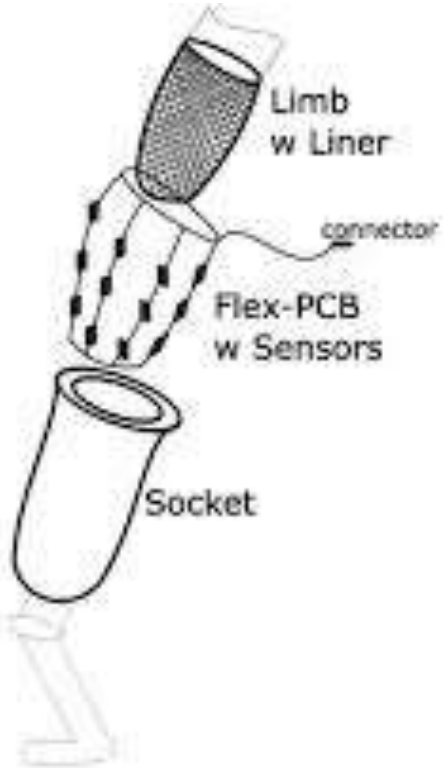


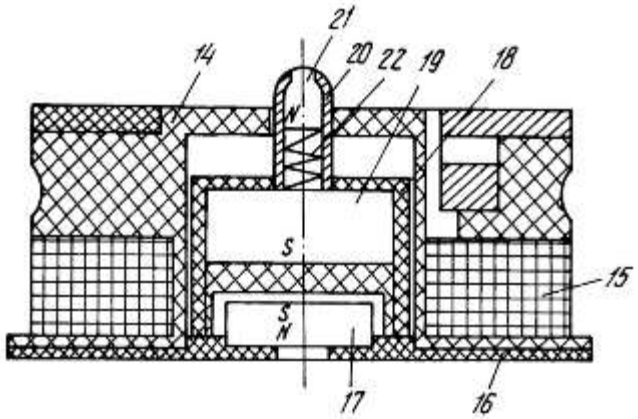
MY APPROACH to Wisdom of Nature in Biomechanics

After studying a subsystem-artificial foot I moved to a Super System - a MAN (Foot Control)



Pressure sensor numbering



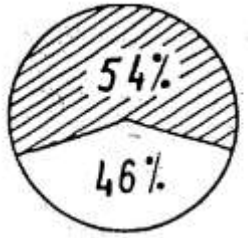


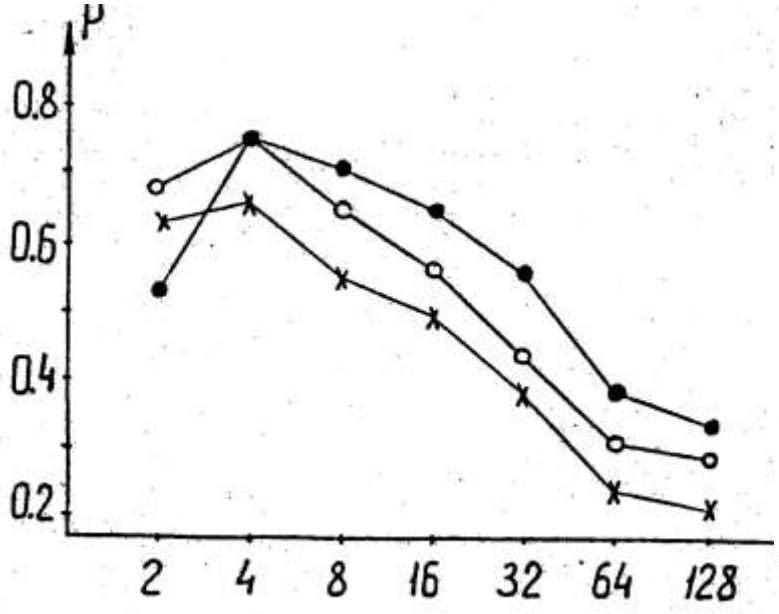
Relative time for visual and vibro tactile sensors reaction

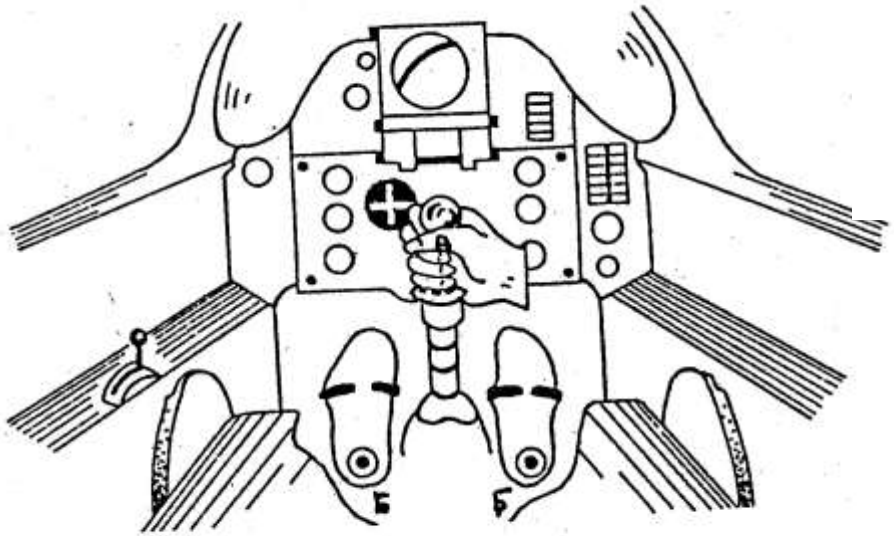
Probability of detecting a vibrating signal on noise background

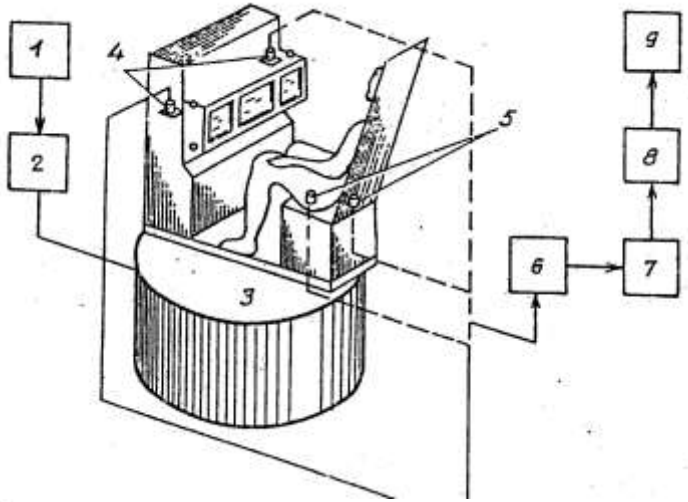
Pilot Cabin with Vibro tactile sensors

Device for studying impact of vibration on human body control









Contradiction: **In order to recover faster, patient should do mild exercises, including walking, but he/she can't walk.**

How to walk without walking?

"Smart Shoes"-Vibro Scanner //Time diagram of vibrator control in Vibro Scanner

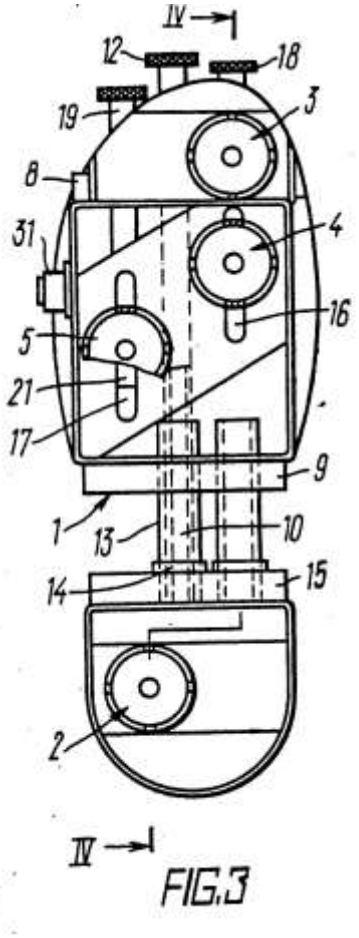


FIG.3

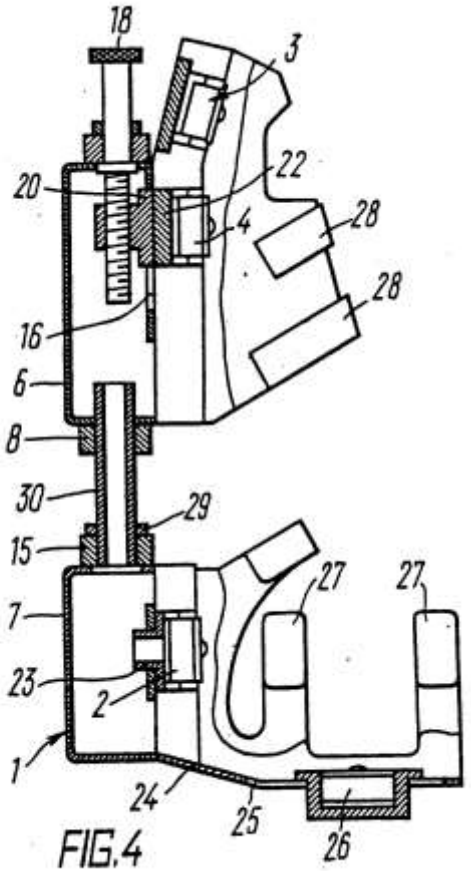
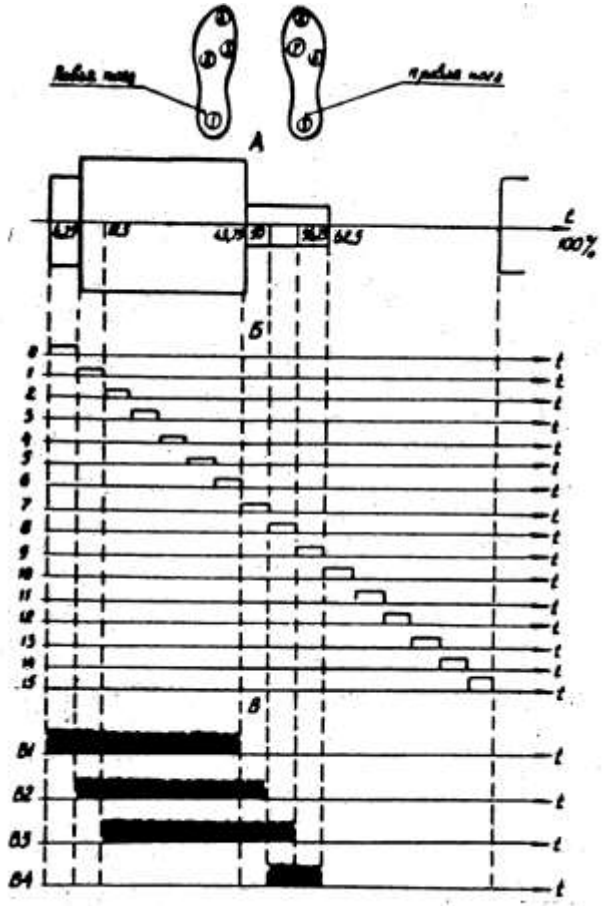


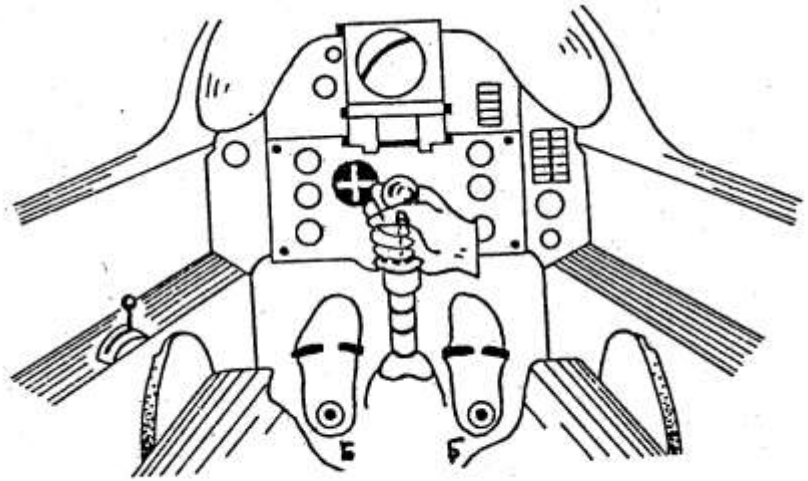
FIG.4

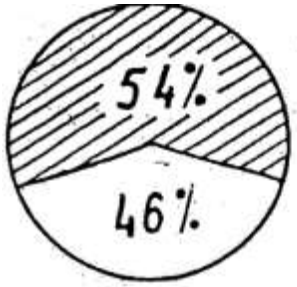


TRIZ Principles #18. Mechanical vibration

Farber B. et al., Transport Control (Pilot Cabin with Vibro tactile sensors) Patent # 2100224

Relative time for visual and vibro tactile sensors reaction. From Earth to Space: Spacemen Sensitivity after flying in spaceship “Saliut-6” (and others) and using vibroscanner

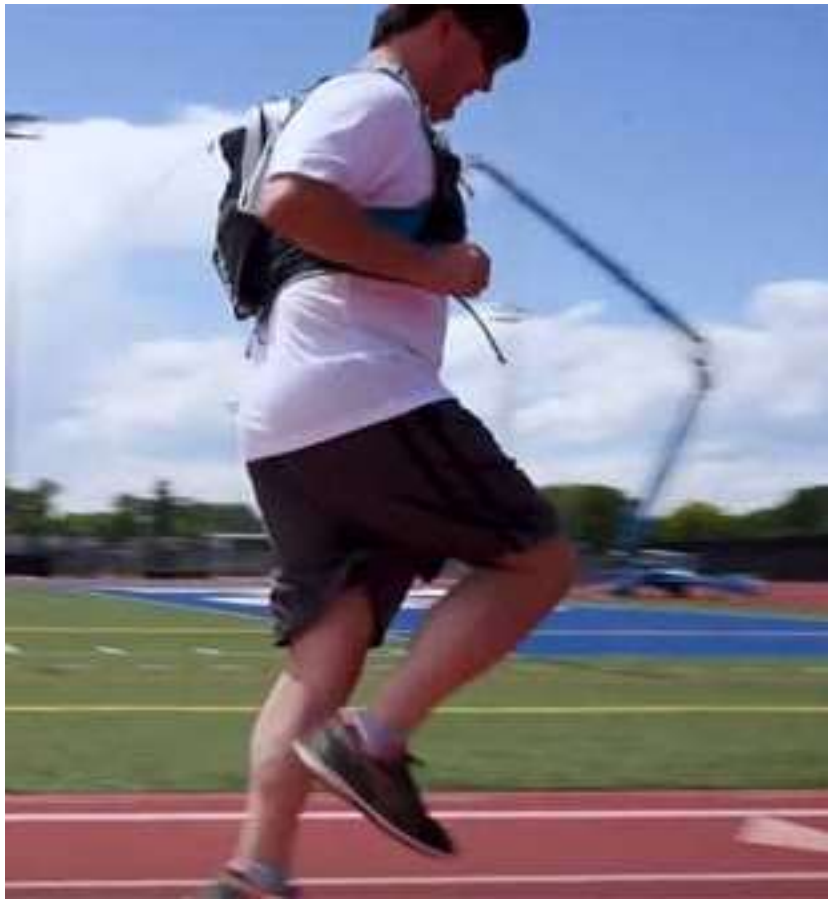




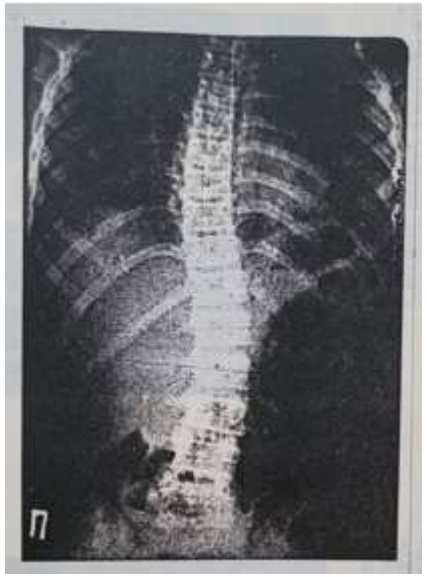
Изменение вибрационной чувствительности после космических полетов

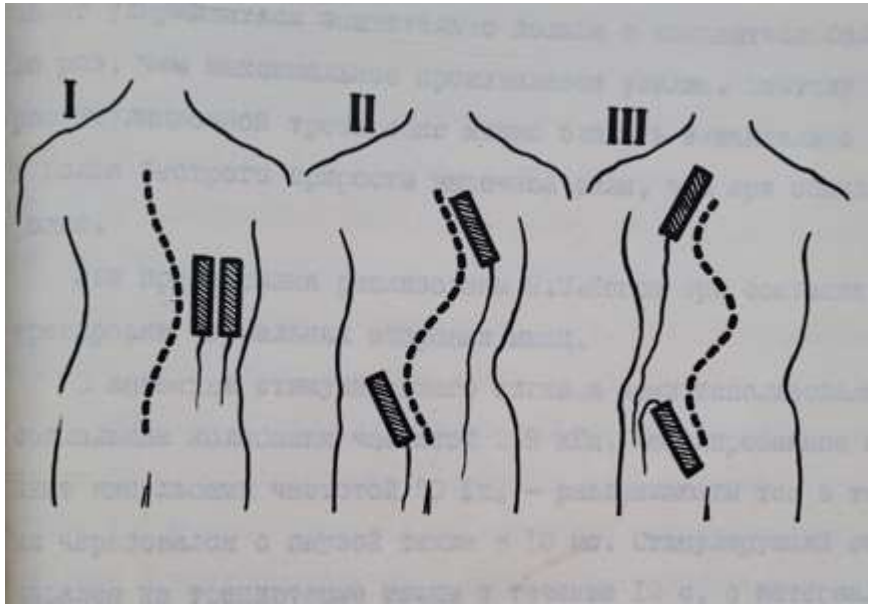
	КОСМОНАВТЫ						
Область измерения	Б-й (к)	И-в (д)	Иен (к)	К-к (д)	Л-в (д)	Р-н (д)	Т-о (к)
Стопа	+10	+6	+6	+2	+2	+3	-3
Пятка	+6	+3	+3	+3	+6	+3	+2

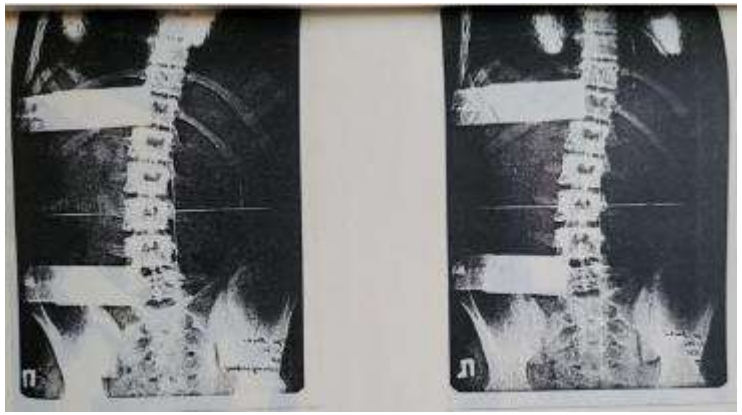
Functional-oriented application for different fields: TRIZ Principle# 23.Feddback #18.Mechanical vibration Blind-Mute-Deaf people running without non blind assistant, based on our “vibro” solution

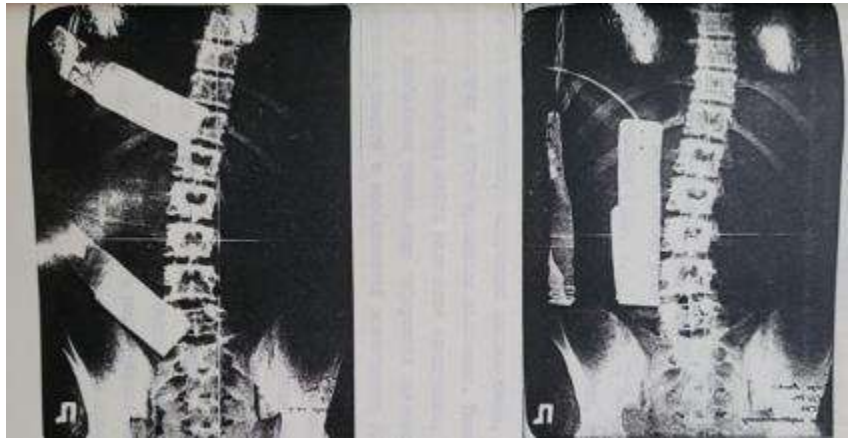


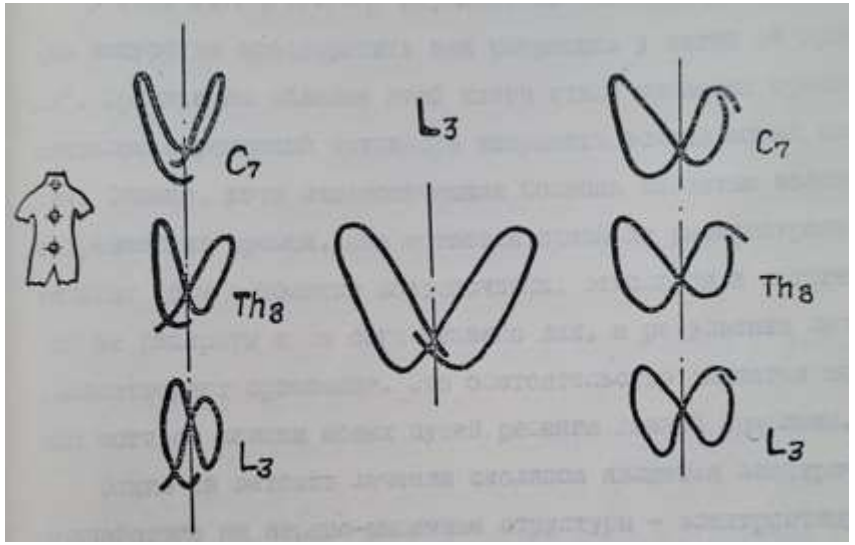
SCOLIOZIS IN CHILDREN: ELECTROSTIMULATION



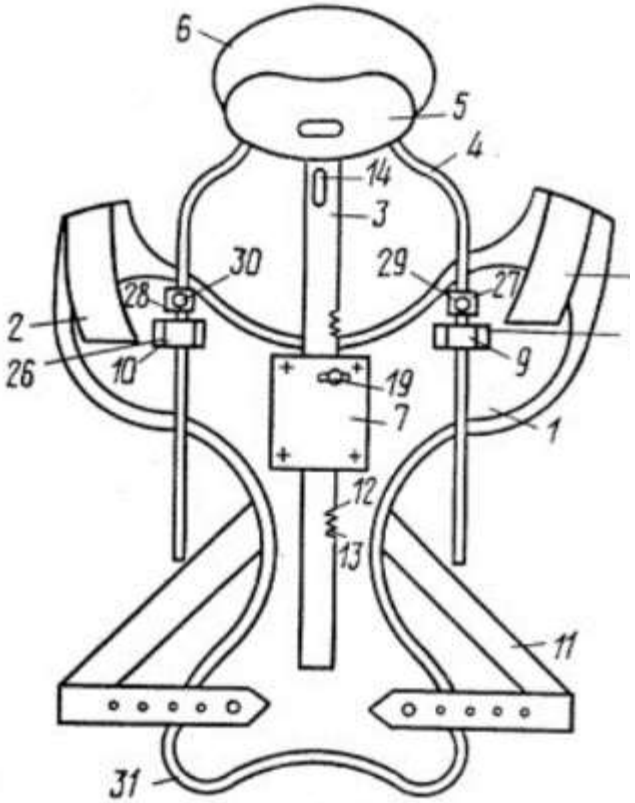


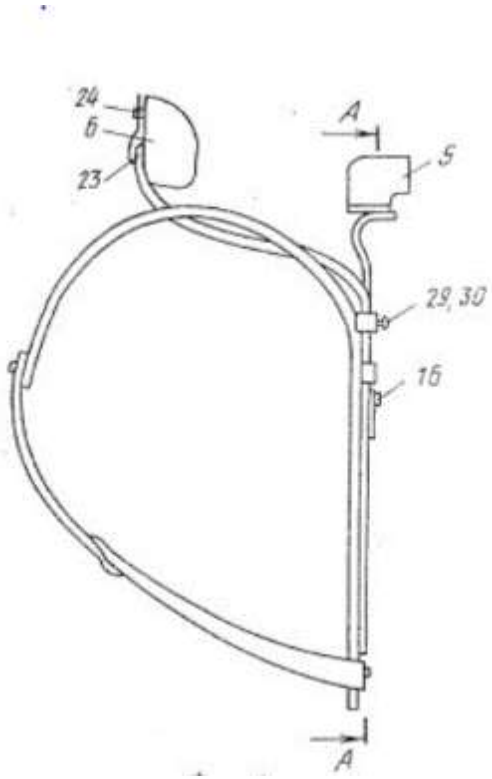


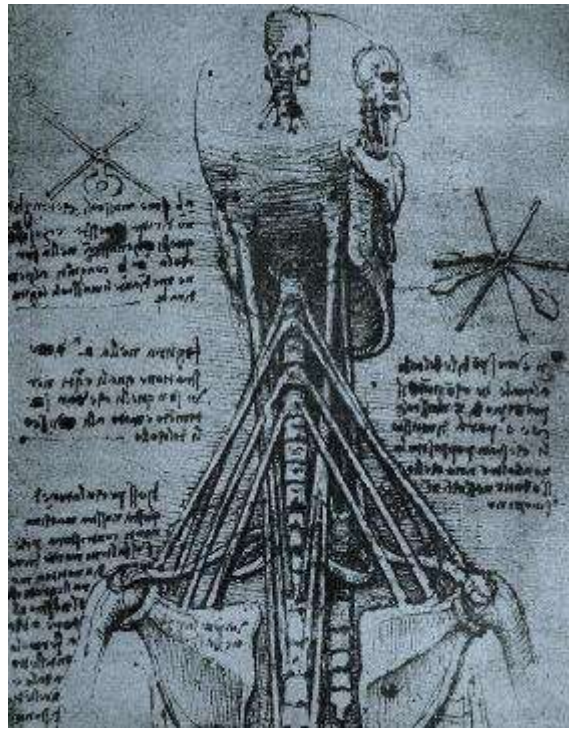




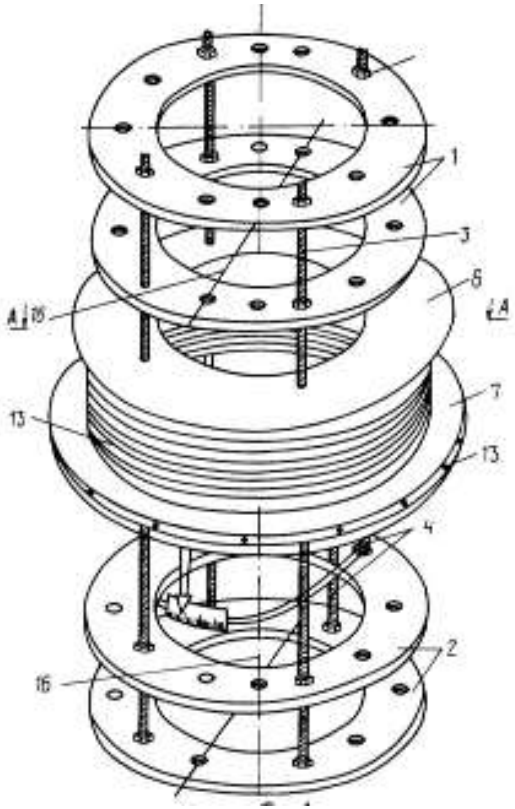
Farber B. et al., Orthotics: Patent # 1584940

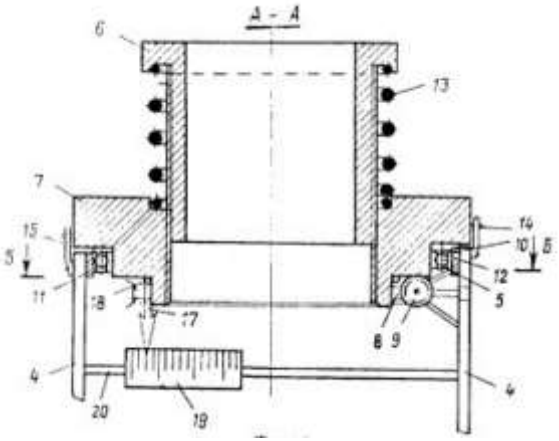


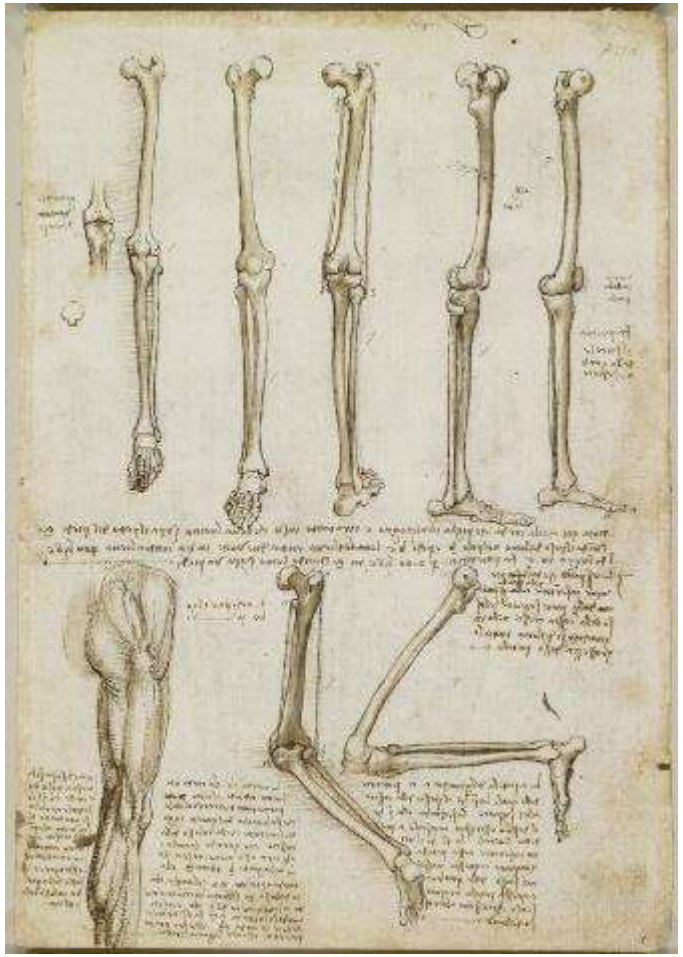




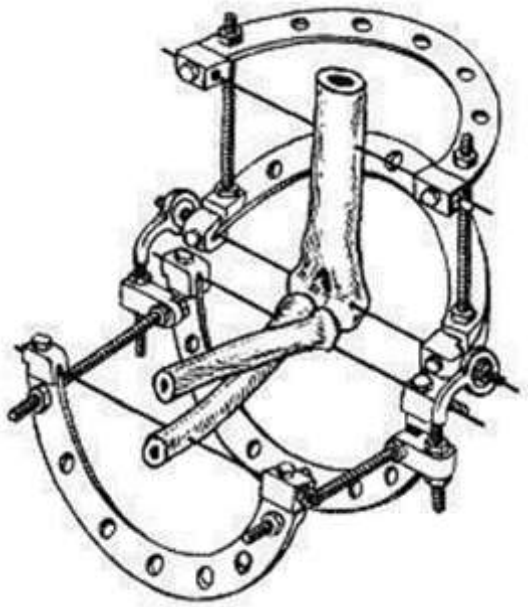
Farber B. et al., Compression-distraction apparatus for osteosynthesis Patent #1553091

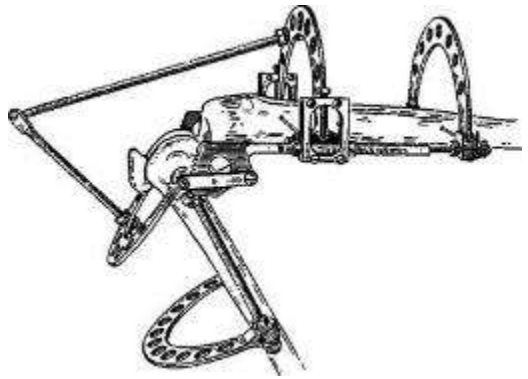






Аппарат Волкова-ОганесянаВолкова — шарнирно-дистракционные аппараты





Устранение контрактуры коленного сустава шарнирно-дистракционным аппаратом Волкова—Оганесяна

ортопедические аппараты для динамической разгрузки сустава при сохранении постоянной дистракции суставных концов, а также для разработки движений в разгруженном суставе, представляющие собой жесткие каркасные конструкции, фиксируемые на спицах, проведенных через суставные концы соответствующих костей, снабженные раздвижными дистракторами с шарнирами, обеспечивающими воспроизведение движений в суставе.

Farber B. et al., Photo elasticity for Foot Studies

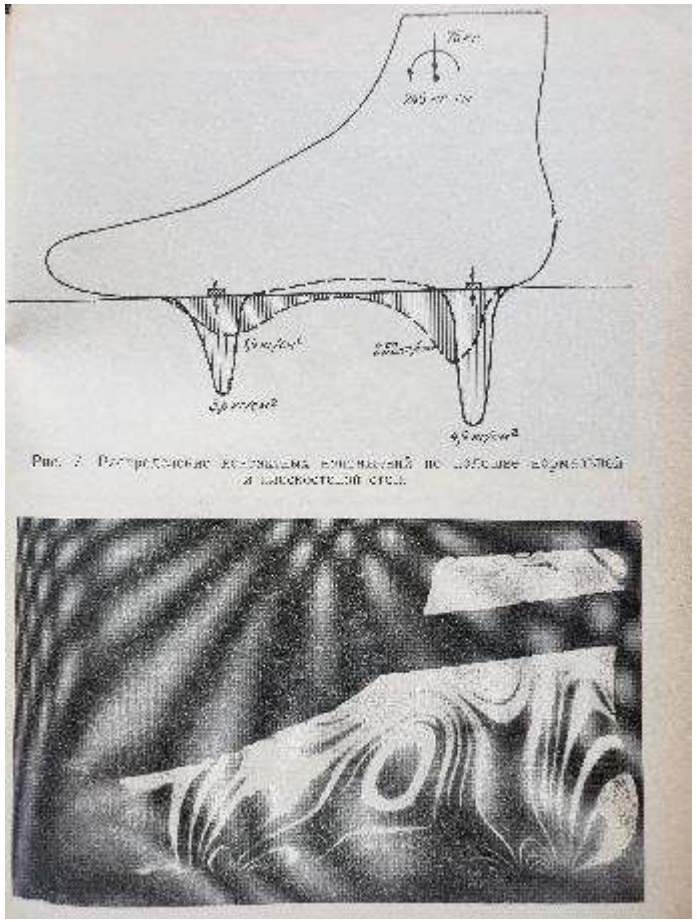
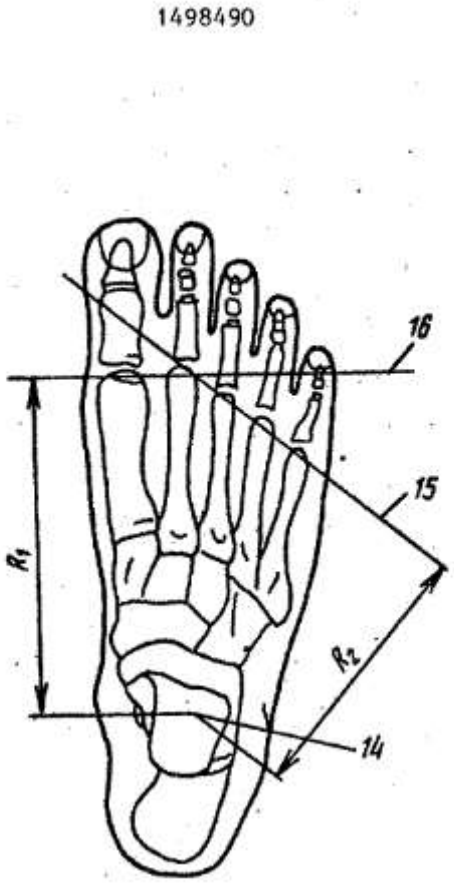
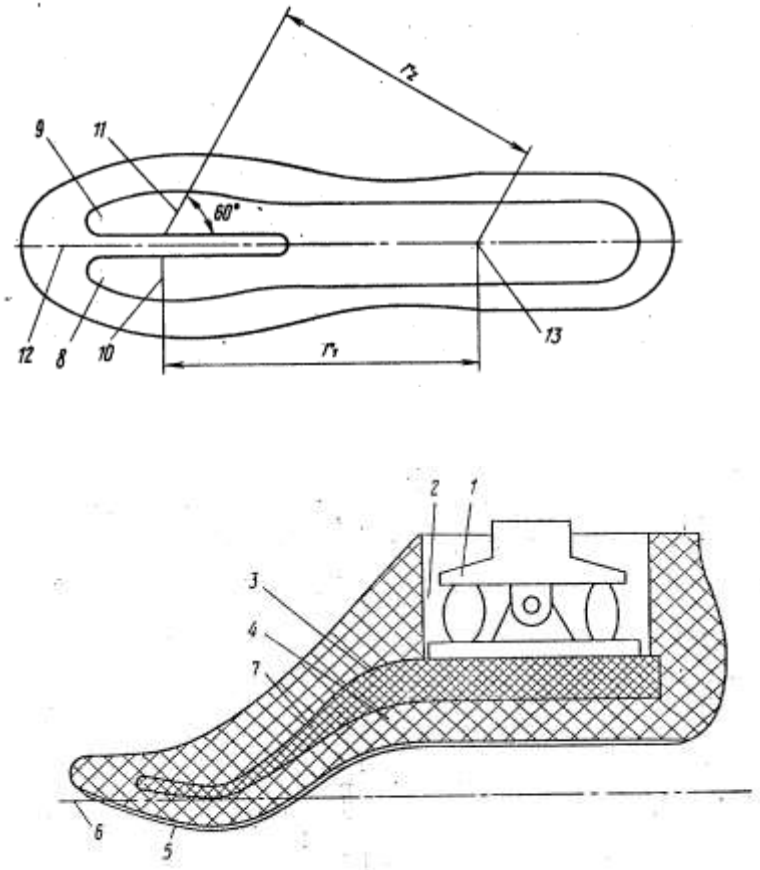
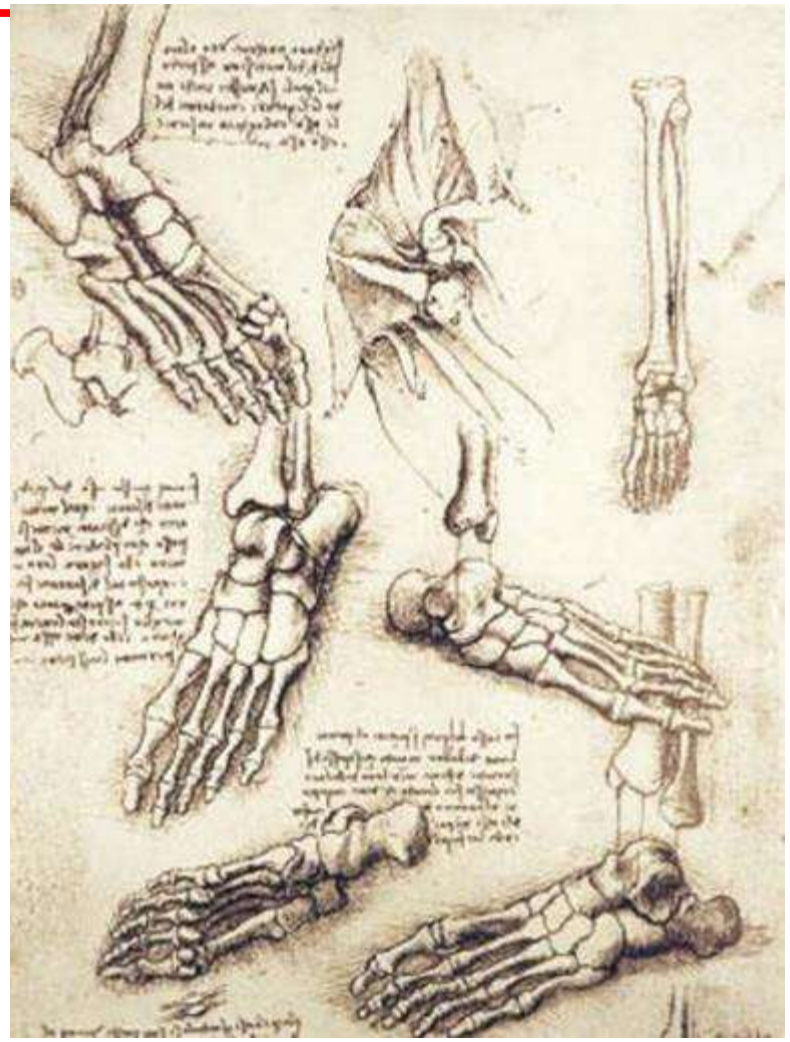


Рис. 2. Картина интерференционных полос в модели плоскостопой стопы.

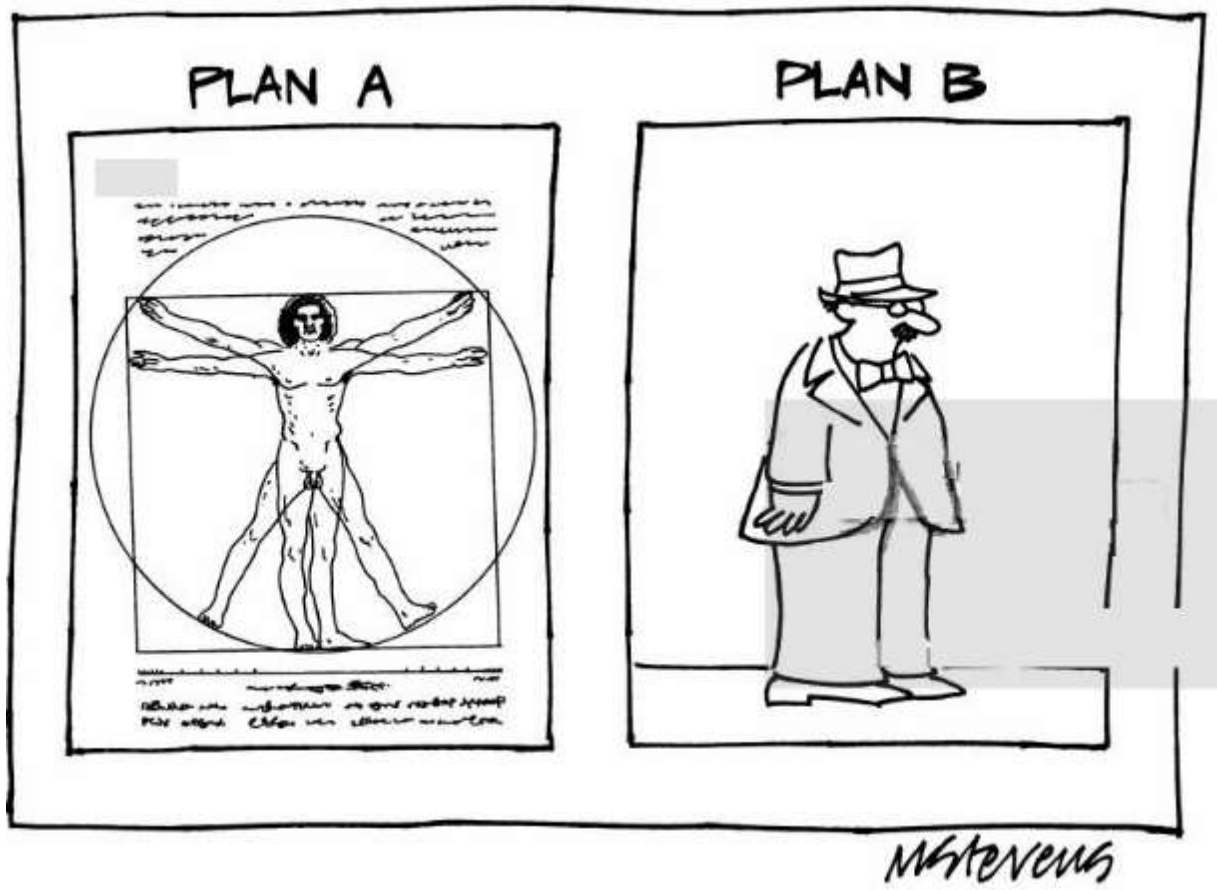
Farber B. et al., Artificial Foot,
2 Patents #1498490, # 133856







My plan was to study a Subsystem (a Foot), but using System operator I decided to move to a System (Lower Limb Prosthesis), where another subsystem –Knee Unit needed serious design



2019 we celebrated 500 years of Leonardo Da Vinci Death.

(presentation in Florence June 16-19, 2019)

55 year-long fascinating experiment inspired By Leonardo Da Vinci

Dr. Boris Farber

TRIZ Biopharma International, Corp; Noigel, LLC New York, NY

http://trizbiopharma.com/ http://nanoigel.com/

INTRODUCTION

Two the most important events happen in my childhood. The first was a present I received from parents for my 10th birthday, a collection of books and coins dedicated to Leonardo Da Vinci, since my father's favorite character was Da Vinci. The second event occurred when I was 11. Father introduced me to TRIZ a new philosophy of system thinking, and year later, he introduced me to Genrich Altshuller. These events inspired me to want to understanding the legacy of Leonardo Da Vinci from different perspectives, including TRIZ. Leonardo's Notebooks became my guide.

In studying Da Vinci's legacy a few facts stood out to me. Firstly, Da Vinci displayed top skills in an unbelievable number of diverse areas. Mankind has never seen such a prolific individual across such a vast array of fields. Secondly Da Vinci, in addition to great scientific brilliance he was one of the greatest artists the world has ever known. As Da Vinci himself said "The human foot is a masterpiece of engineering and a work of art." The last fact that stood out to me was Da Vinci's discovery of the wave nature of light. Specifically, Leonardo studied interference and diffraction in optics and nanotechnology many centuries before they were discovered by the broader scientific community

OBJECTIVE: 5 GOALS

I set five goals for myself:1. To get a deep knowledge and well-rounded education, 2. To study all Da Vinci's fields of knowledge including biomechanics,3. To study optics and nanotechnology,4. To study Leonardo Da Vinci's scientific legacy, 5. Specifically to study the relationship between various fields of Da Vinci's science and his art. I collected a list of Da Vinci's fields of knowledge, based on which created my study path which have been following all my life.

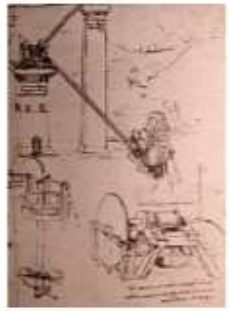
The poster shows some relationships examples between Da Vinci ideas from diverse fields and their impact on our project implementations, related to these fields.

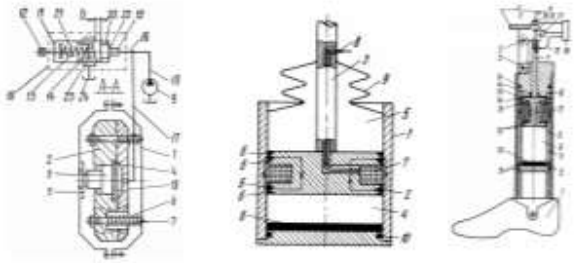
PART A . SYNERGY IN BIOENGINEERING: I have set the task of a fundamental breakthrough in technology and the creation of new ar d upper limb prosthetics and orthotics :

CONCLUSION

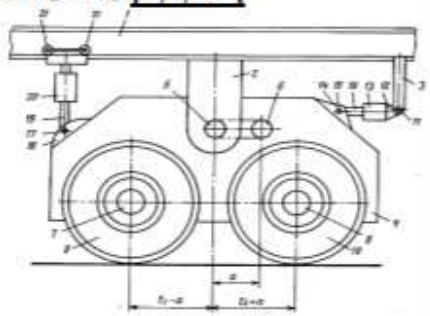
As a result, I pursued a diverse education in 19 institution and post graduate schools, which has helped me in creativity not only in the fields which were collected on the list, but also with overlapping their numerous combinations which have been successfully used for more than 700 hundreds of my projects and inventions and hundreds of publications. Da Vinci ideas from diverse fields made great impact on many of our project implementations related to these fields.

5. HYDRAULICS AND MAGNETO REOLOGICAL LIQUIDS [1,2,9,10,11]





6. MULTI AXES VEHICLES [1,2,12]



7.NANOTECHNOLOGY: 7.1 SFUMATO & ONCOLOGY

OBJECTIVE: 5 GOALS

I set five goals for myself:1. To get a deep knowledge and well-rounded education, 2. To study all Da Vinci's fields of knowledge including biomechanics,3. To study optics and nanotechnology,4. To study Leonardo Da Vinci's scientific legacy, 5. Specifically to study the relationship between various fields of Da Vinci's science and his art. I collected a list of Da Vinci's fields of knowledge, based on which created my study path which have been following all my life.

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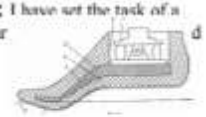

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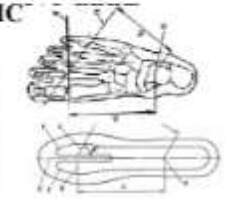
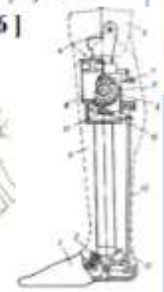


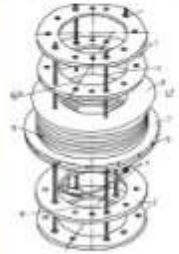
2. KNEE AND ARTIFICIAL KNEE JOINTS [1,2, 5,6]



3. BONES [1,2,7]

4.SKULL AND HELMETS

[1,2,8]



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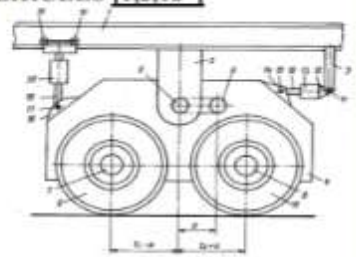
https://www.linkedin.com/in/dr-boris-farber-0309b6121/

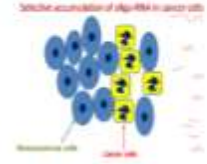
New York, NY phone 1-718-300-0371

6. MULTI AXES VEHICLES [1,2,12]



7.NANOTECHNOLOGY: 7.1 SFUMATO & ONCOLOGY

[1,2,13,14]



7.2 SFUMATO & ANTIVIRAL [1,2,13,14]

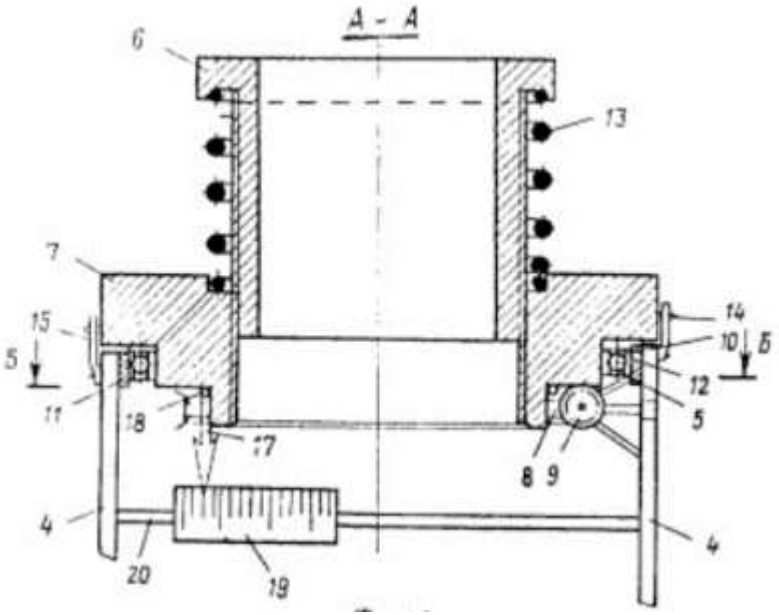
ACKNOWLEDGEMENTS

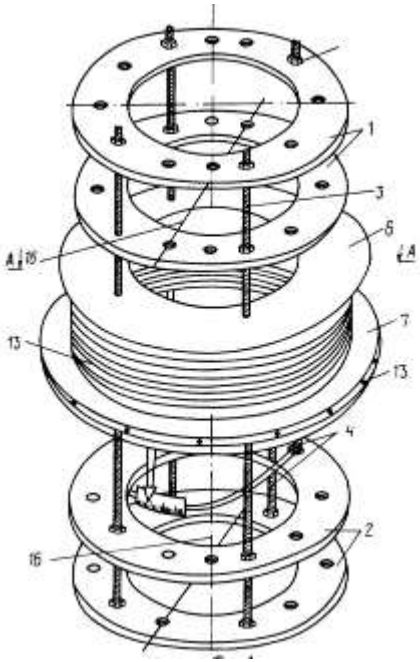
55 years experiment of fascinating Da Vinci road journey approved that educations in his fields gives boost of synergy and sheds light on blind spots in Da Vinci legacy, which is especially important in the 500th anniversary of the death of a great genius.

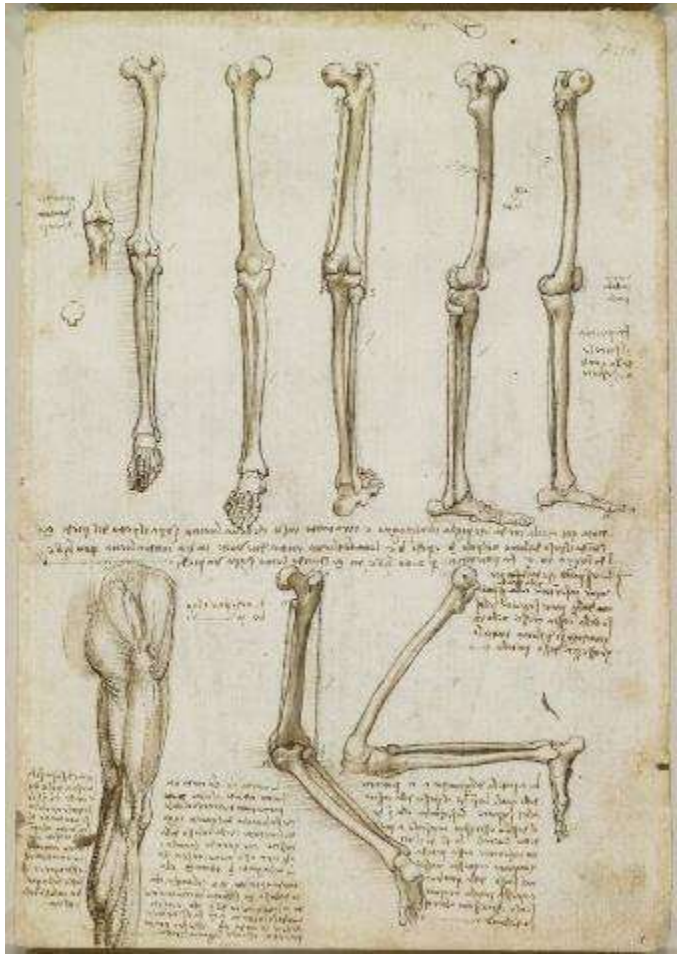
REFERENCES

1.The Notebooks of Leonardo da Vinci,Dover Fine Art, History of Art	8. Method of designing protective helmets Patent 1651834
2.Leonardo da Vinci: Complete Paintings and Drawings, Taschen America, LLC,2012	9. Hydro inertial vibrational unit Patent 1796725
3. Artificial foot Patent 1498690	10. Rheological magnetic hydraulic training device Patent 2081643
4.Artificial ankle Unit Patent 1409258	11. Rheological magnetic hydraulic lower limb prosthesis Patent 2032434
5. Above knee prosthesis Patent 1607799	12. Multi Axes vehicle Patent 1,199,885
6. Above knee prosthesis Patent 1138151	13. Creation of new medical drugs based on TRIZ and computer mathematical modeling https://zenodo.org/record/2547580#.XNVQaHKWE
7. Compression-distraction apparatus Patent 1553051	14. Application of synergetic set of TRIZ principles for developing cAMP - accumulation activators and their influence on multi-drug resistance microorganisms

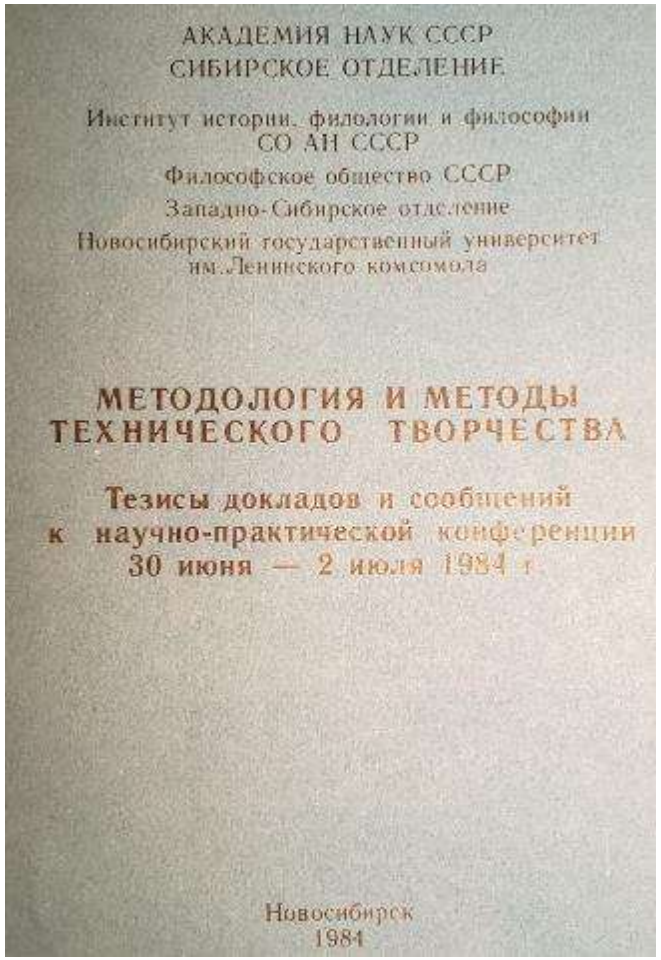
Farber B. et al., Compression-distraction apparatus for osteosynthesis Patent #1553091







S- curve for Prothesis Knee Units



АКАДЕМИЯ НАУК СССР
СИБИРСКОЕ ОТДЕЛЕНИЕ

Институт истории, филологии и философии
СО АН СССР

Философское общество СССР

Западно-Сибирское отделение

Новосибирский государственный университет
им. Ленинского комсомола

МЕТОДОЛОГИЯ И МЕТОДЫ ТЕХНИЧЕСКОГО ТВОРЧЕСТВА

Тезисы докладов и сообщений
к научно-практической конференции
30 июня — 2 июля 1984 г.

Новосибирск
1984

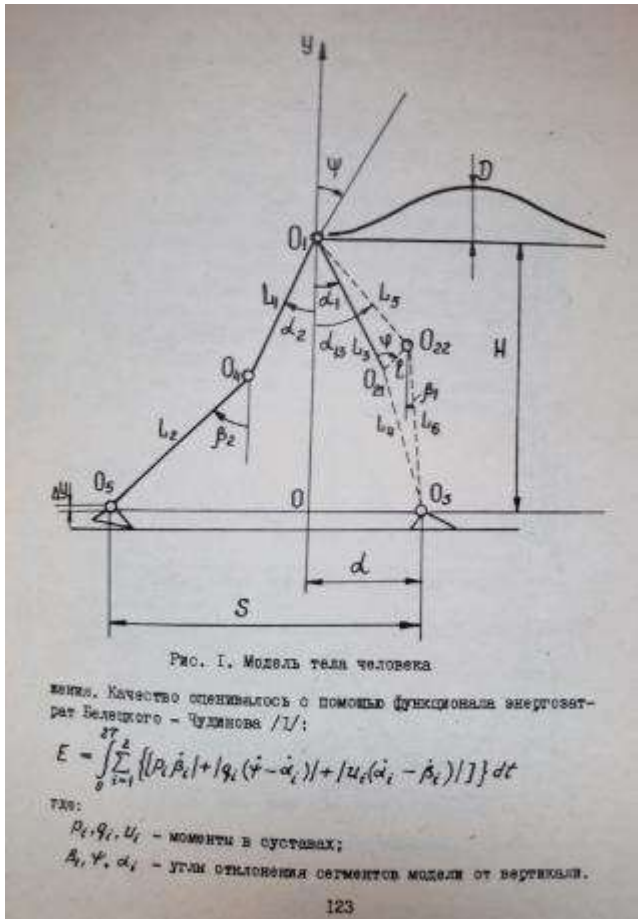


Рис. 1. Модель тела человека

жения. Качество оценивалось с помощью функционала энергозатрат Белецкого – Чудинова /1/:

$$E = \int_0^{2T} \sum_{i=1}^{2} \{|P_i \dot{\beta}_i| + |q_i(\dot{\psi} - \dot{\alpha}_i)| + |u_i(\dot{\alpha}_i - \dot{\beta}_i)|\}\, dt$$

где:

P_i, q_i, u_i – моменты в суставах;

A_i, ψ, α_i – углы отклонения сегментов модели от вертикали.

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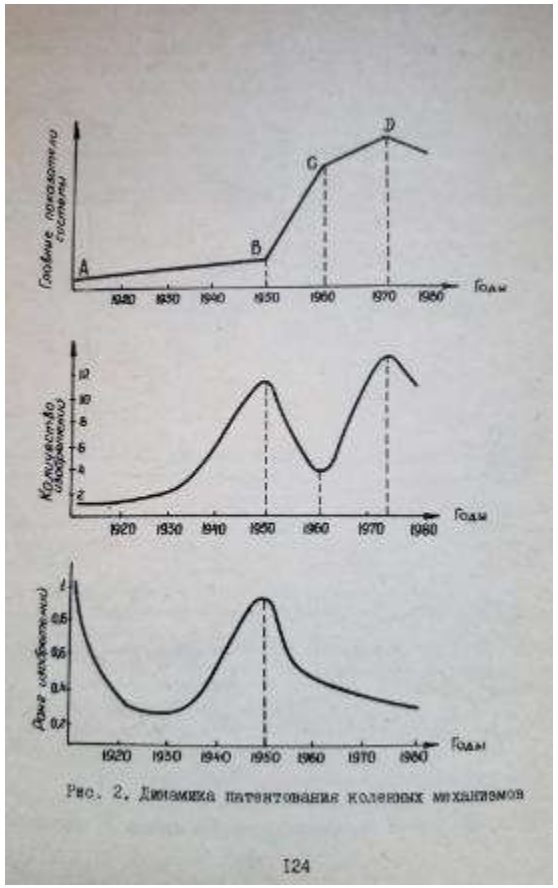

Рис. 2. Динамика патентования коленных механизмов

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" Macro-Level" Problem solving

чивающем наибольшую эффективность пылесоса. В задаче "о прочие радиоволн" наибольшую эффективность обеспечивает отсутствующий молниеотвод: не задевает радиоволны. Модель задачи: отсутствующий молниеотвод – молния.

Такой подход позволяет выделить узкую модель задачи и, следовательно, – основное физическое противоречие данной технической системы.

В докладе также рассматриваются вопросы разрешения физических противоречий.

Литература

1. Альтшуллер Г.С., Селюцкий А.Б. Крылья для Икара. – Петрозаводск: Карелия, 1980.
2. Альтшуллер Г.С. Творчество как точная наука. – М.: Сов. радио, 1979.

Б.С.Опубер

МЕТОДИКА РЕШЕНИЯ "МАКРОУРОВНЕВЫХ" ЗАДАЧ В ТРИЗ

Противоречие есть критерий истины, отсутствие противоречия – критерий заблуждения.

Гегель

Одним из объективных законов развития технических систем является переход с макроуровня на микроуровень.

Но как поступить, если для практического осуществления такого перехода еще не разработаны "микроуровневые" условия? Предположим, нужно использовать свойство жидкости изменять вязкость под действием магнитного поля, а жидкости с требуемыми свойствами пока не синтезированы? Получается, что физэффект известен (в данном случае – реологический эффект) – а жидкостей с конкретными свойствами пока нет. Вопрос создания магнитных жидкостей с требуемыми свойствами является не простым. А как же быть, если практика требует незамедлительного решения поставленной задачи?

Если обратиться к мировому фонду патентной и научно-технической литературы, то нетрудно обнаружить, что на сегодняшний день разработано и описано огромное количество разнообразных механизмов (от Кулибина до Артоболевского /3/) на макроуровне, которые в сочетании с решениями на микроуровне представляют собой эффективные решения /1, 2/. (Например, полиметаллические стальных деталей макроуровневых механизмов Альтшуллер Г.С.).

Проблема состоит в том, чтобы из этого огромного массива механизмов выбрать наиболее подходящий или разработать новый.

Для этой цели предлагается использовать методику, базирующуюся на ТРИЗ. (Для сокращения изложения укажем, что переход с "макро" на "микроуровень" начинается после составления идеальной формулы решения задачи.)

Предполагается разработать таблицу "макро-микроуровневых" аналогов, а точнее, таблицу соответствия физических эффектов и механических устройств. Рассмотрим фрагмент таблицы.

Таблица

№№ пп	Входное воздействие на систему	Реакция системы на воздействие	Физический эффект (на микроуровне)	Макроуровневый аналог физэффекта
1.	Магнитное (или электростатическое) поле воздействует на жидкость	Изменение вязкости жидкости	Реологический эффект	Взаимодействие между молекулами заменить взаимодействием между шарами
2.	Механическое поле, а именно крутящий момент воздействует на стальной образец	Диаметр при закручивании уменьшается, образец удлиняется, объем увеличивается	Эффект Пойнтинга	Взаимодействие между молекулами заменить взаимодействием между слоями молекул, использовать спиральную стальную ленту

Из таблицы видно, что между эффектами на "микро" и на "макроуровне" наблюдается некоторая аналогия. В случае спиральной

ленты это зависимость Эйлера

$$P = Qe^{\varphi\alpha}$$

где P – усилие, действующее на один из концов ленты, которое можно удержать с помощью силы Q, приложенной к противоположному концу ленты, при условии что она навита вокруг барабана с углом обхвата α, а коэффициент трения между материалом барабана и ленты φ.

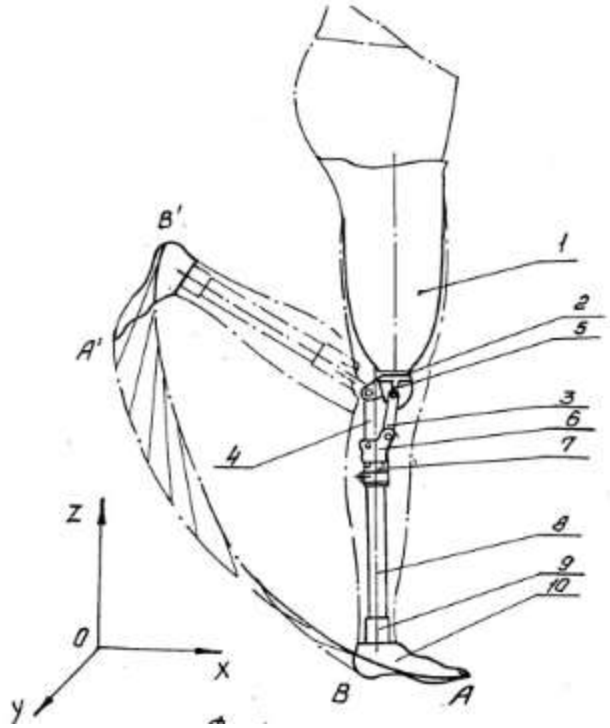
Так, при разработке управляемого коленного механизма был использован макроуровневый аналог эффекта Пойнтинга.

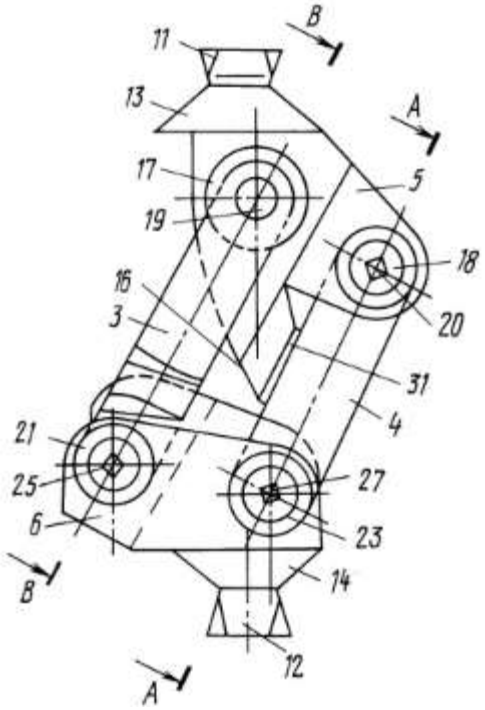
Литература

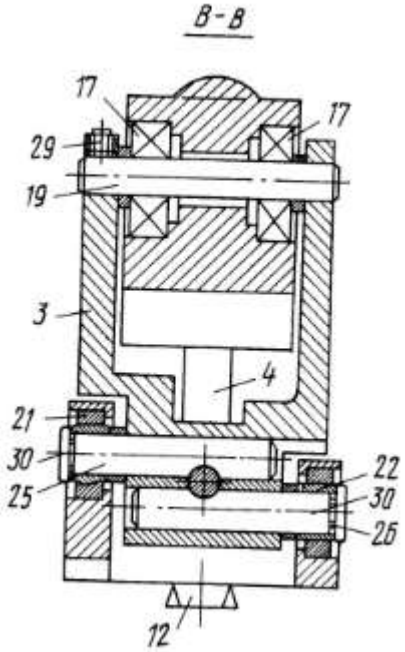
1. Альтшуллер Г.С. Творчество как точная наука. – М.: Сов. радио, 1979.-172 с.
2. Альтшуллер Г.С., Селюцкий А.Б. Крылья для Икара. – Петрозаводск: Карелия, 1980. – 223 с.
3. Артоболевский И.И. Механизмы в современной технике. Т. I – VI. – М.: Наука, 1973.

TRIZ Principle #17. Farber B. et al., Patent # 2049446

IMPLEMENTATION OF THE FIRST 3D MOVEMENT KNEE UNIT







жения, связывающие координаты точки в двух системах X O Y и XOY представляют собой известные зависимости и здесь не приводятся.

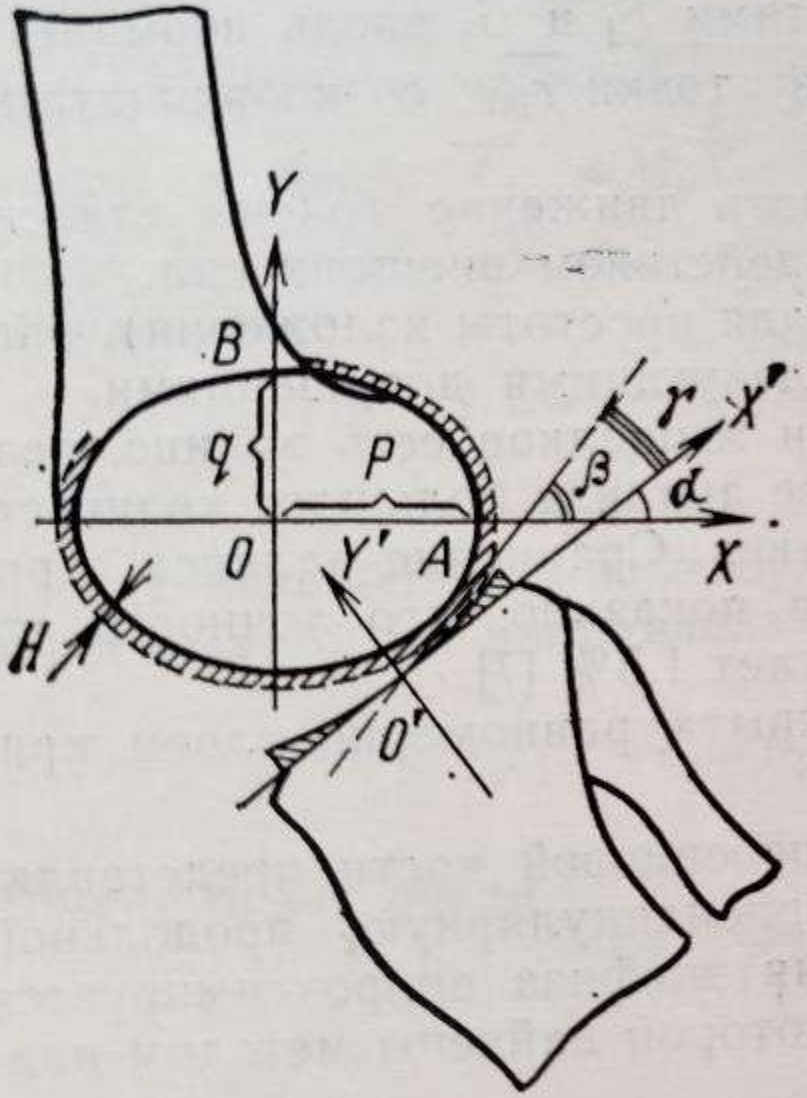


Рис. 2. Кинематическая схема

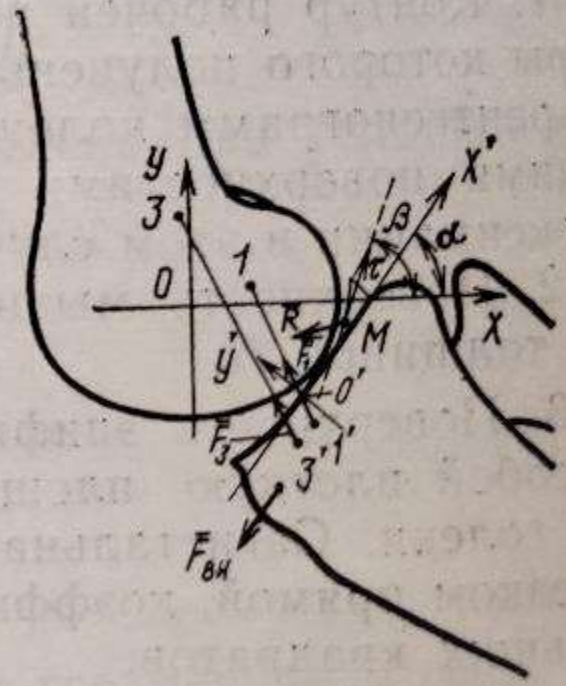
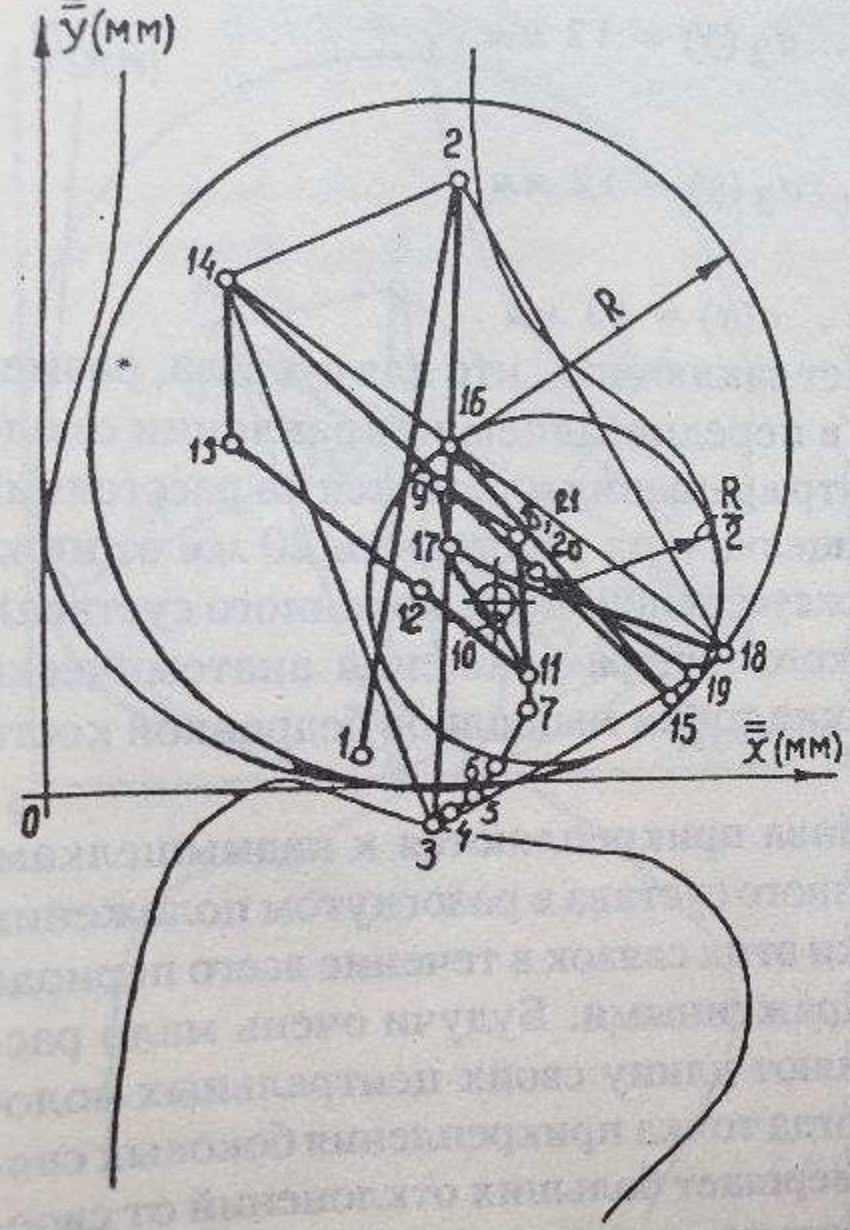


Рис. 3. Точки приложения сил, действующих в коленном сус-



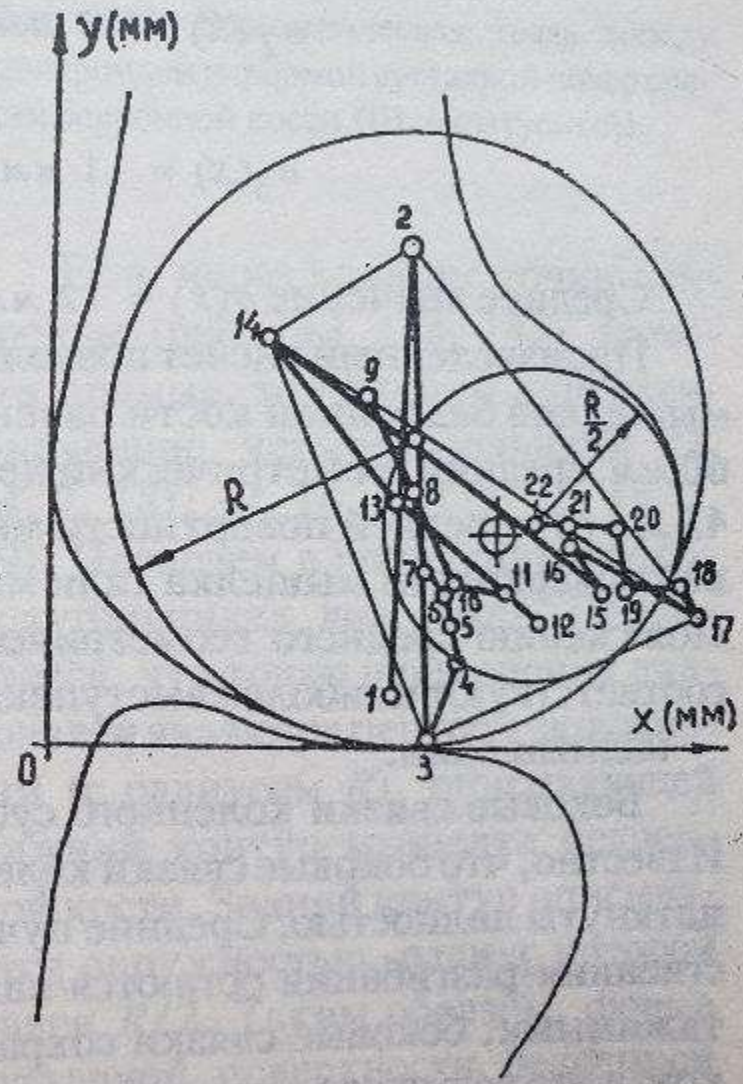


Рис. 144. Геометрическая связь между

за значительного разброса полученных центров вращ
поставимого с размером контура мыщелков бедренной
удалось проанализировать форму самой центроиды. П

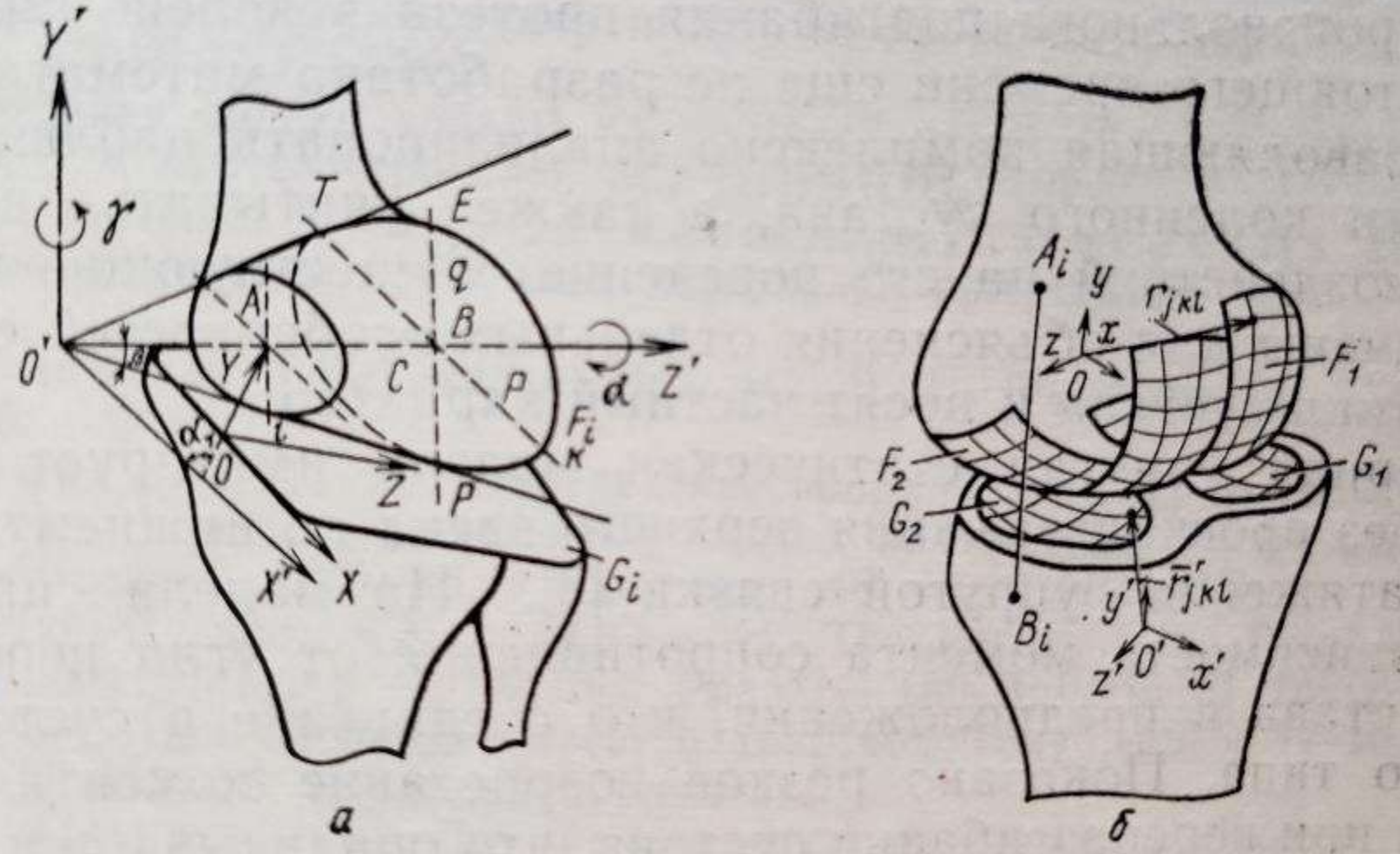
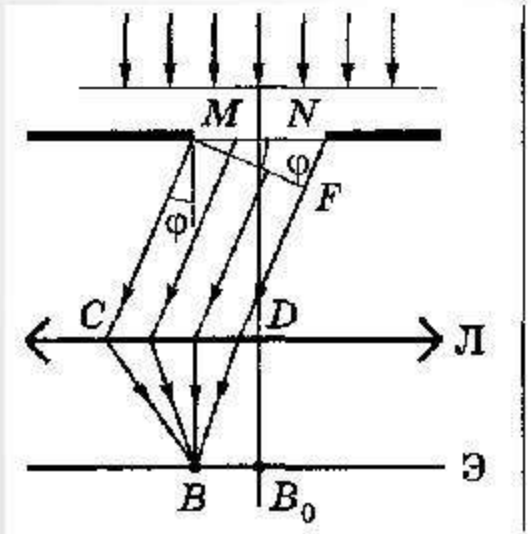
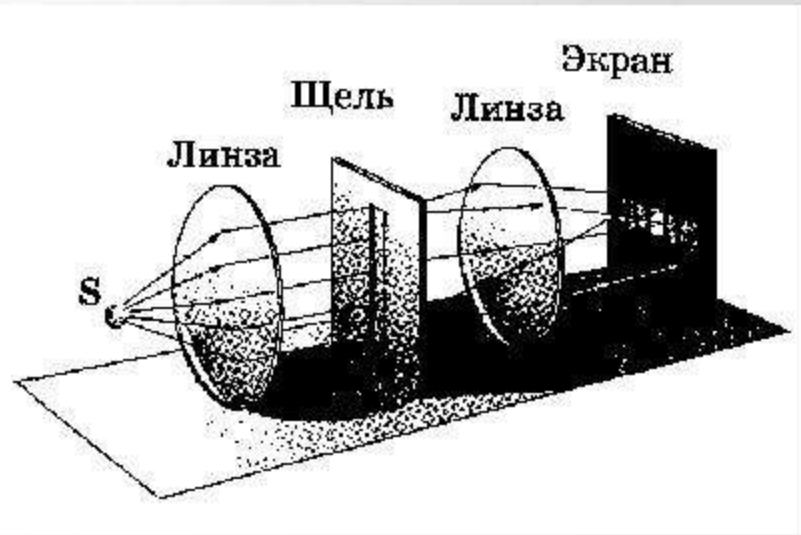


Рис. 1. Трехмерная модель коленного сустава.
а — мыщелки — эллиптический конус, мениск — плоскость,

Дифракция Фраунгофера на щели

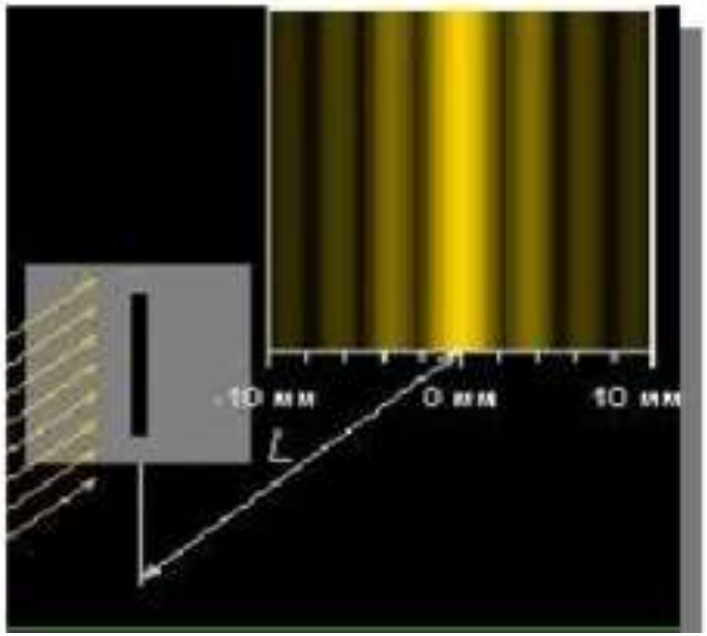
Плоская монохроматическая световая волна падает нормально плоскости щели шириной а. Параллельные пучки лучей, выходящие из щели в произвольном направлении ф (ф — угол дифракции), собираются линзой в точке В.





Дифракционные картины от цели

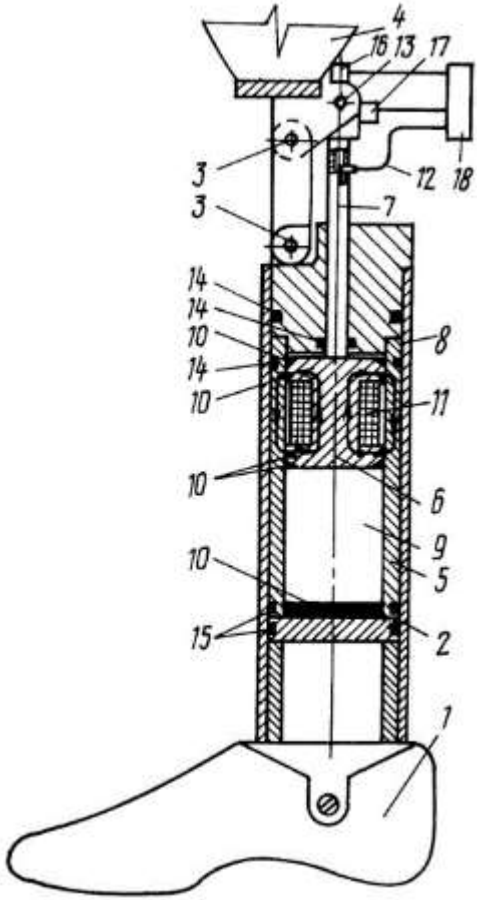
Особенности дифракционной картины	Объяснение
В центре картины возникает светлая полоса	Вторичные волны в направлении, перпендикулярном щели, имеют одинаковую фазу. Поэтому при их наложении амплитуда колебаний увеличивается

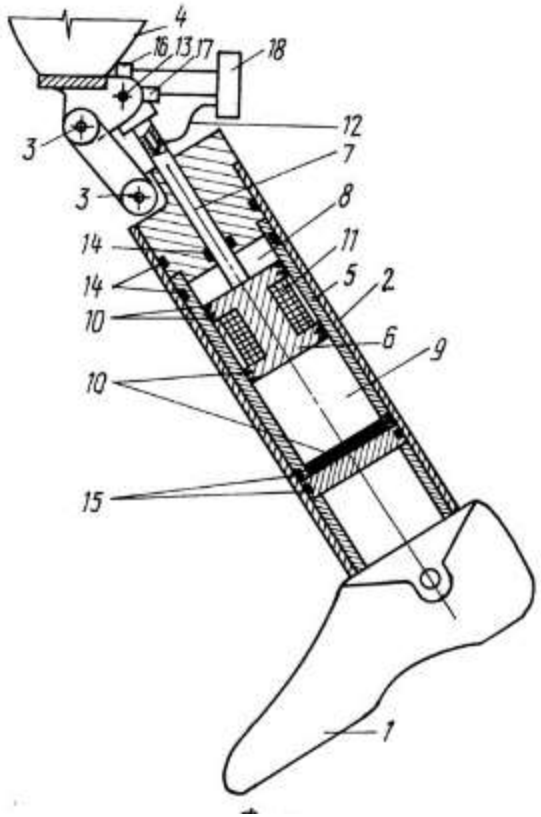


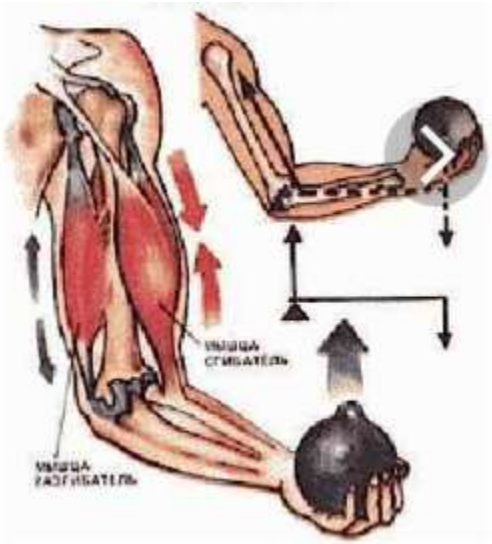
PART 4: Magnetic fluids in medicine

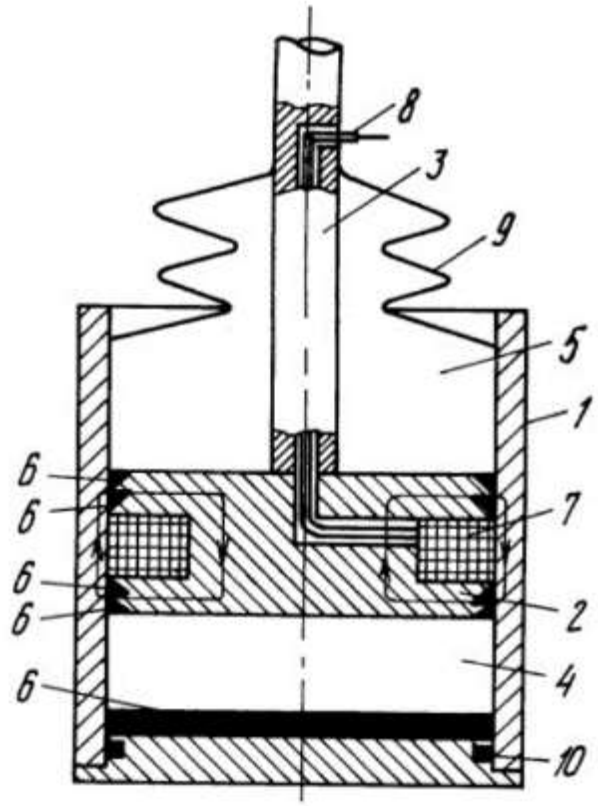
Farber B. et al., Patent 2032434, 1993

Magneto rheological device and method of control Farber B. et al., Rheomagnetic training device Patent 2081643,1993

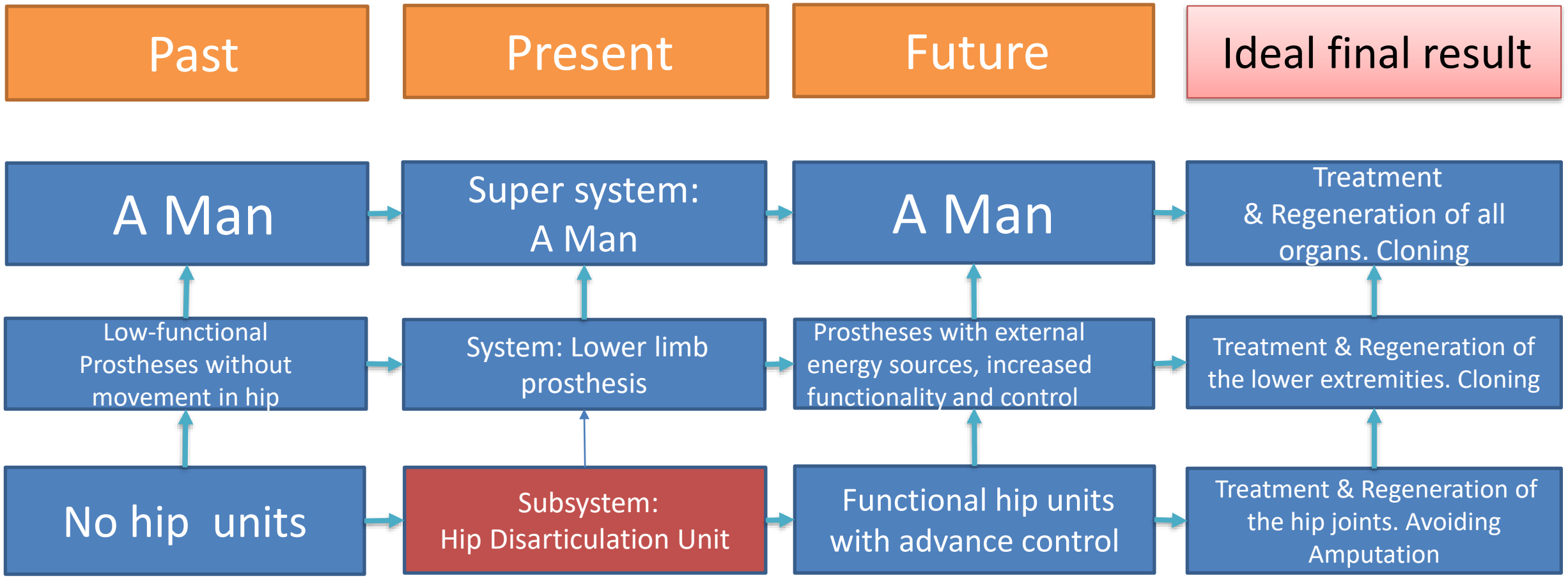






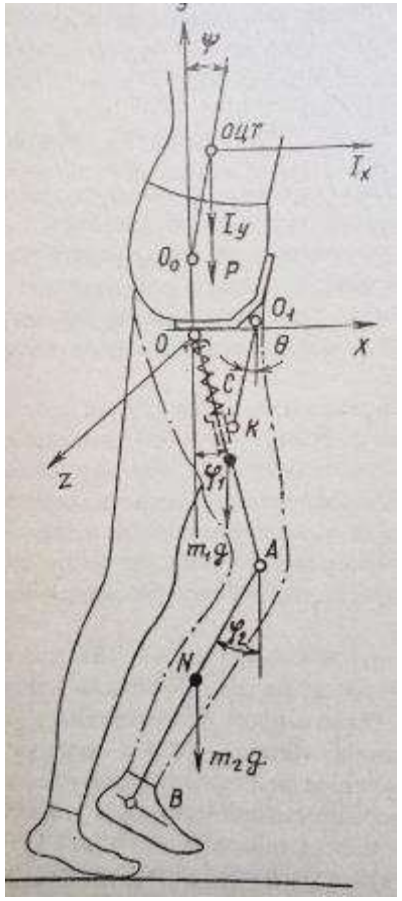


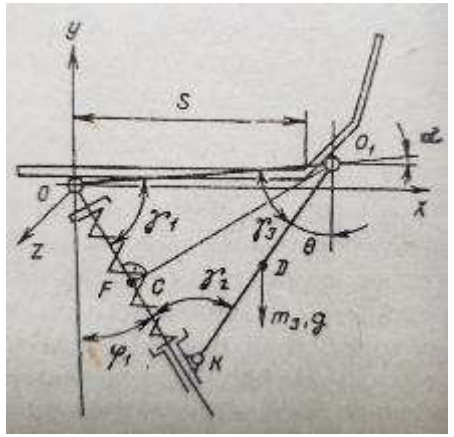
System Operator for The First Hip Disarticulation Lower Limb Prosthetics Hip Unit Design

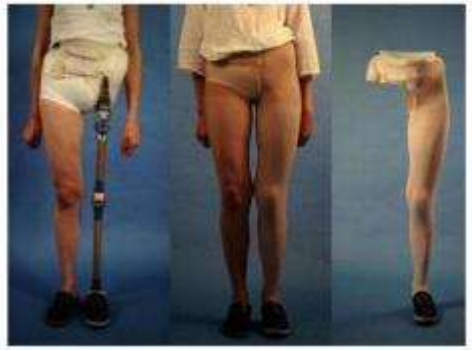


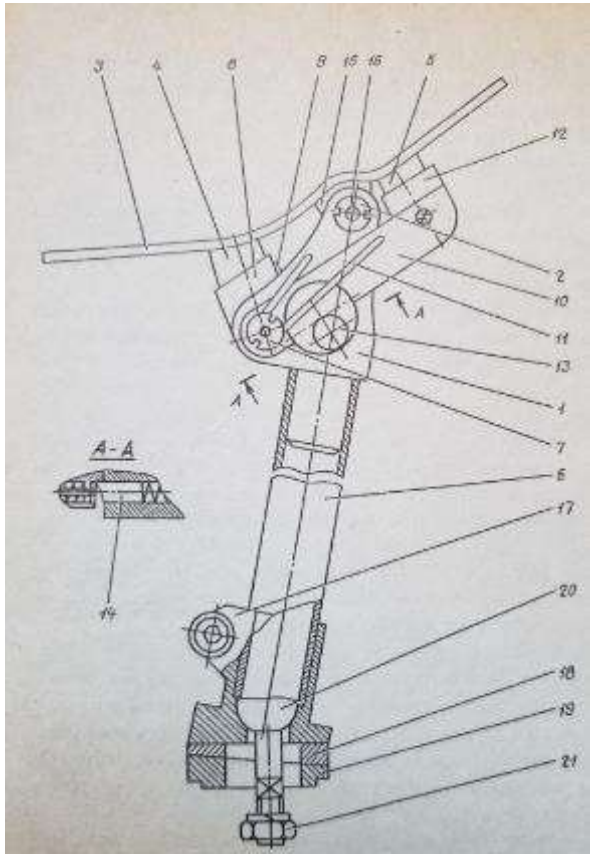
Subsystem2-Supersystem-Subsystem3

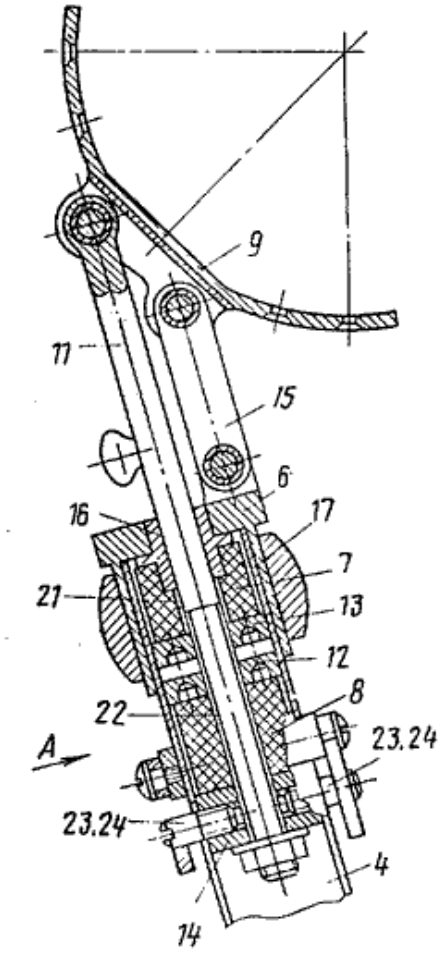
Farber B. et al., The First Hip Disarticulation Lower Limb Prosthetics with guide element Patent #1600758





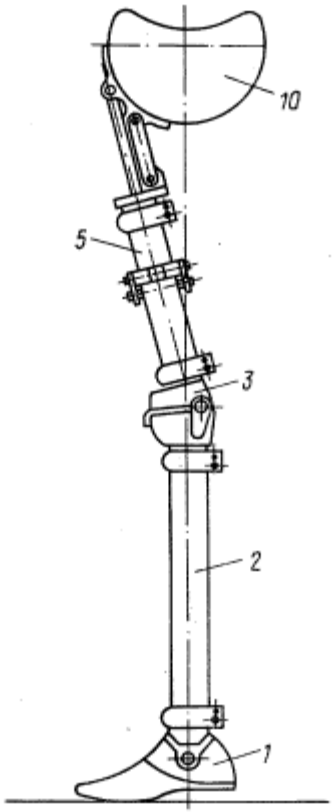


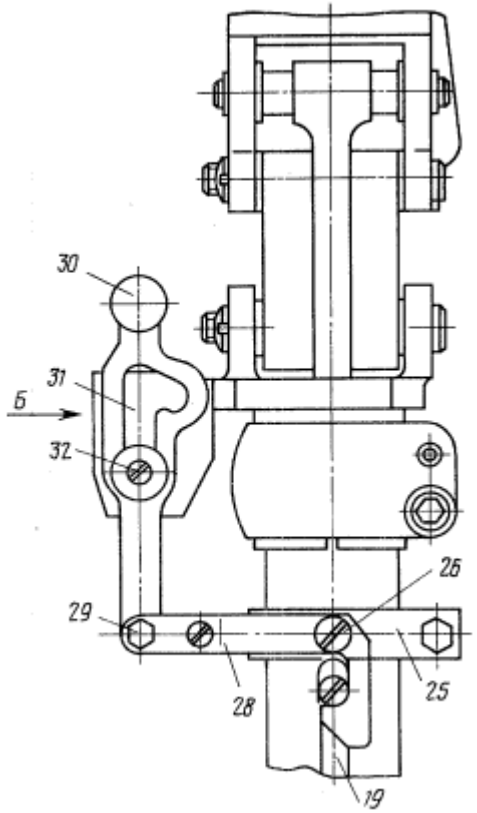


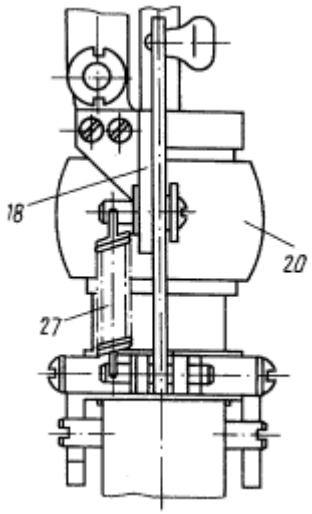


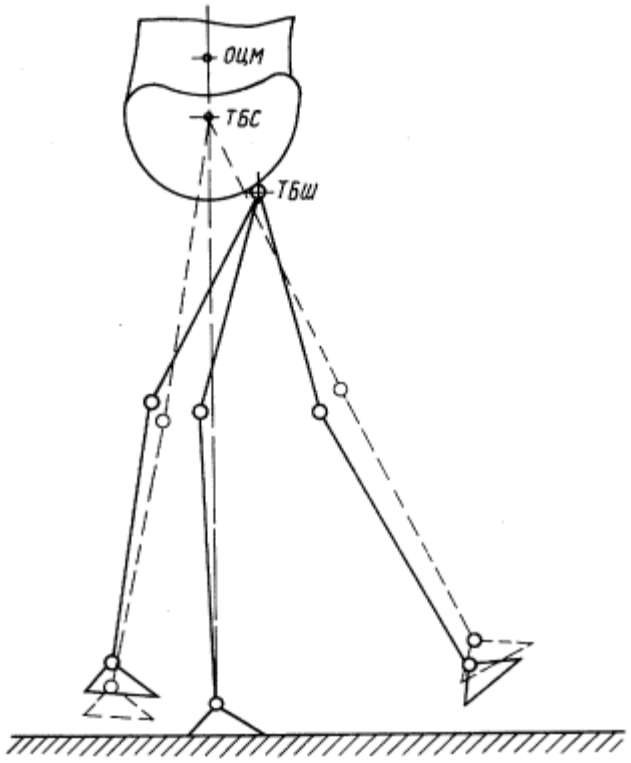
Farber B. et al., The First Hip Disarticulation Lower Limb Prosthetics with guide element Patent #1600758

- **Subsystem2-Supersystem-Subsystem3**

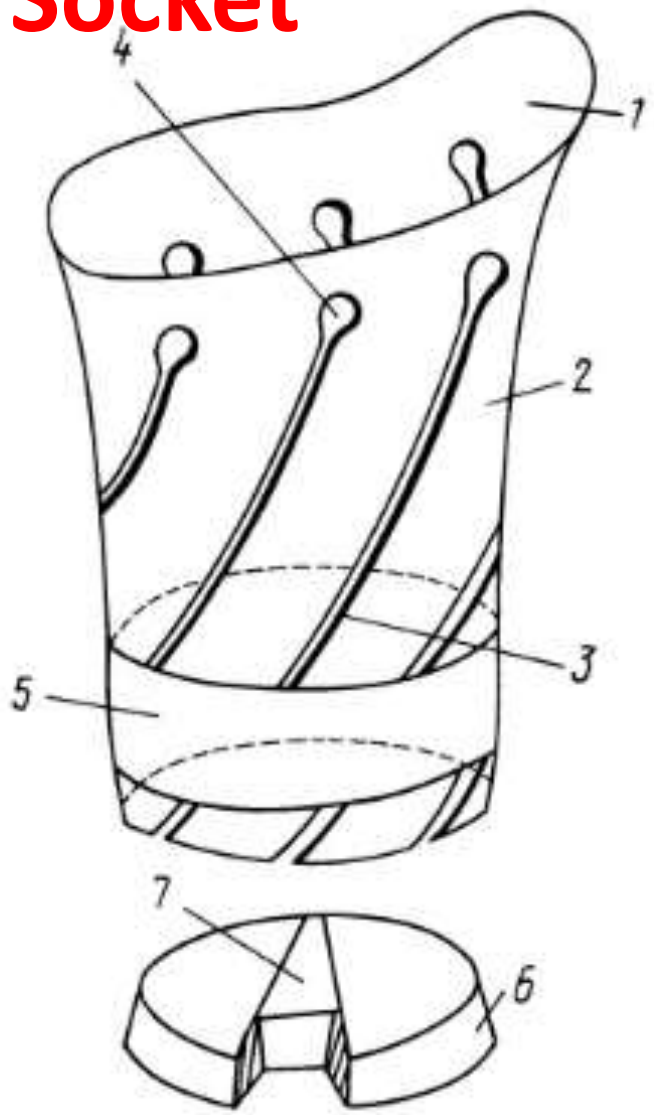






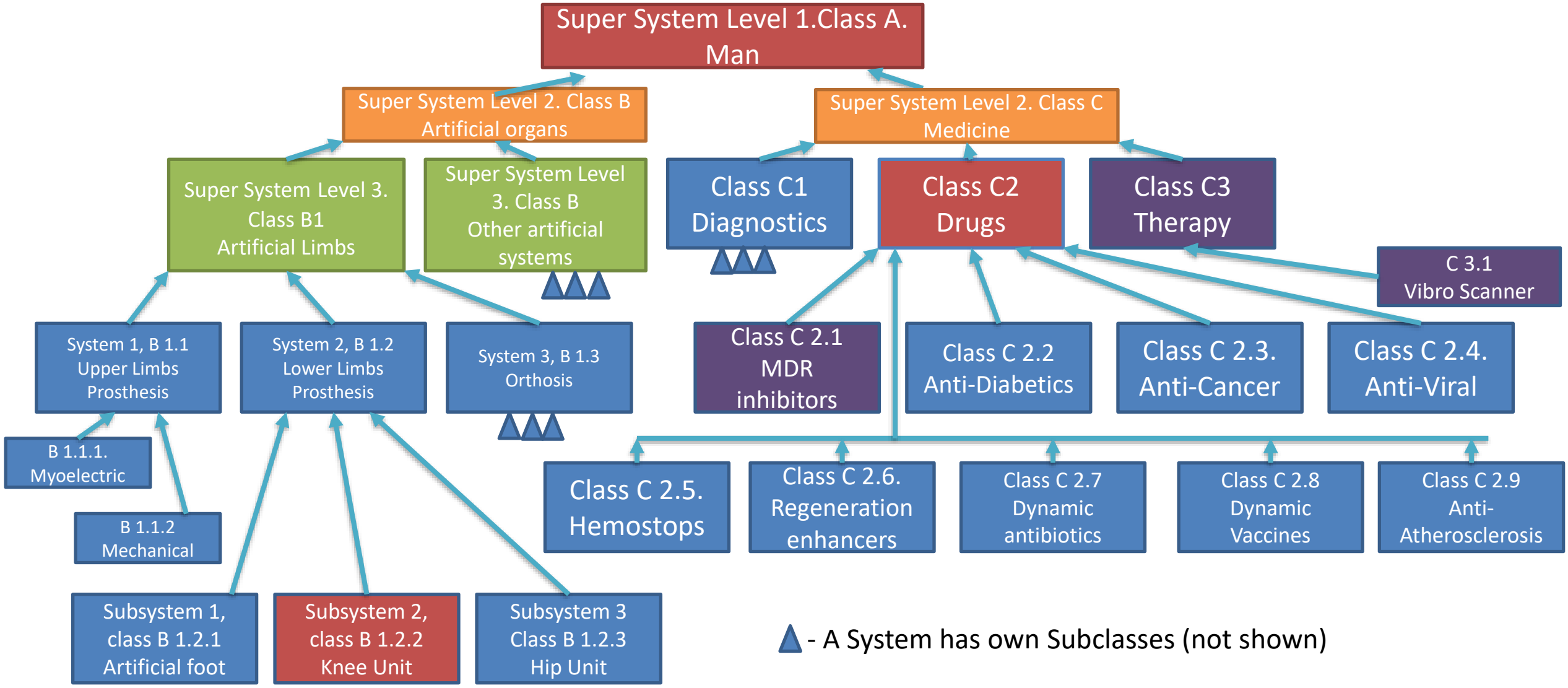


Farber B. et al., Patent # 2012286 “Spiral Poynting effect” Socket

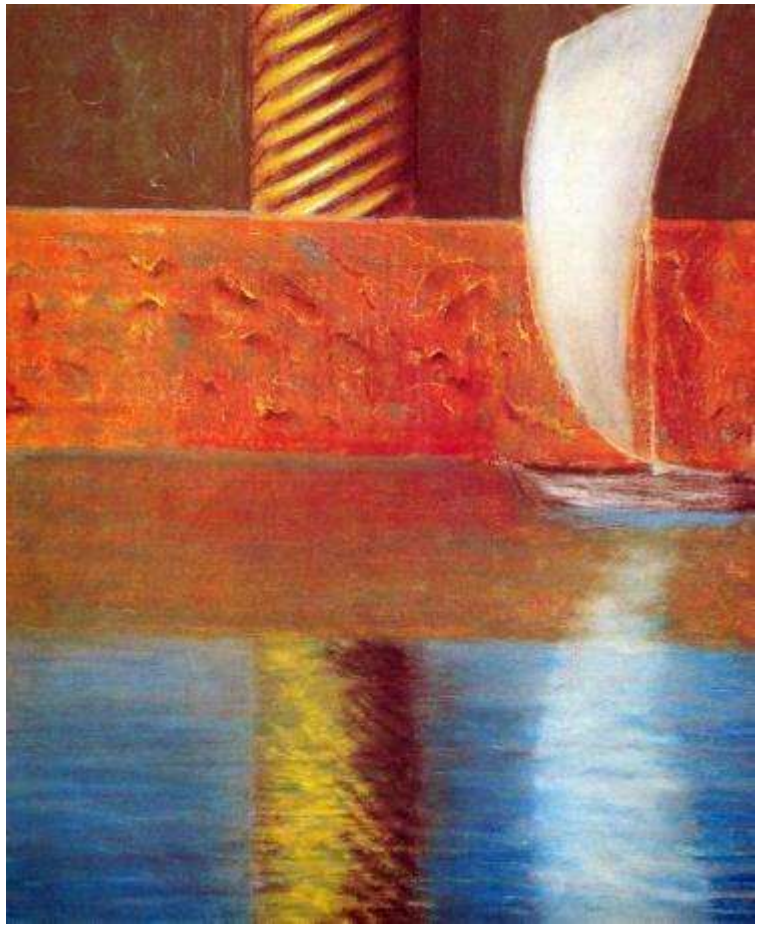


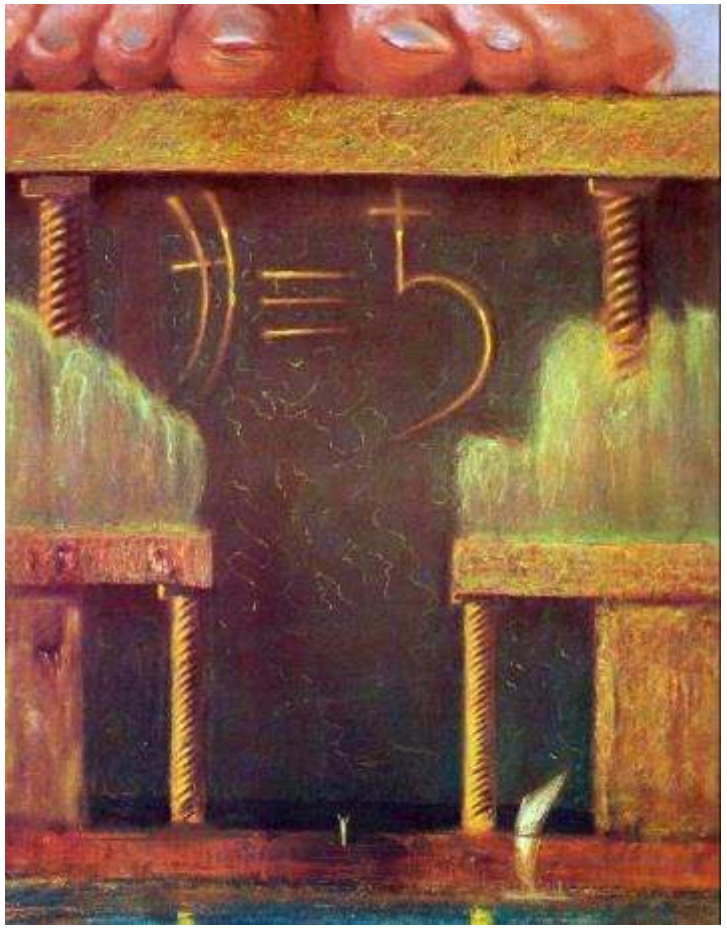
Inheritance of System

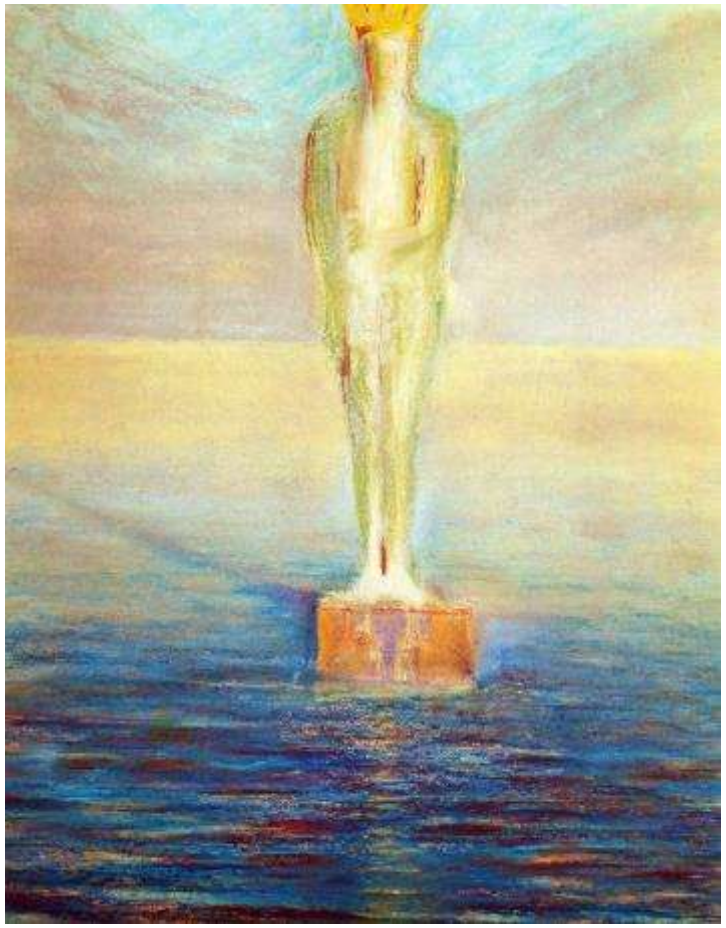
"man-artificial organs-medicine-environment"



М. Чюрленис "Рекс"







The Key to NOIGEL's breakthrough

Line 1. Repurposing FDA approved generic drugs .

1: Multiple drug resistance bacteria (MDR) new paradigm to fight MDR.
2: Polymyxin Nephroprotectors to reduce polymyxin nephrotoxicity.
3: Composition stimulating autologous stem cells and activate tissue regeneration
4: Medical Device, Binary hemostatic, biocompatible and biodegradable.
5: New approach of Metformin use with reduced Gastrointestinal side effects.
6: Anti-TB drugs based on stimulants of complete phagocytosis

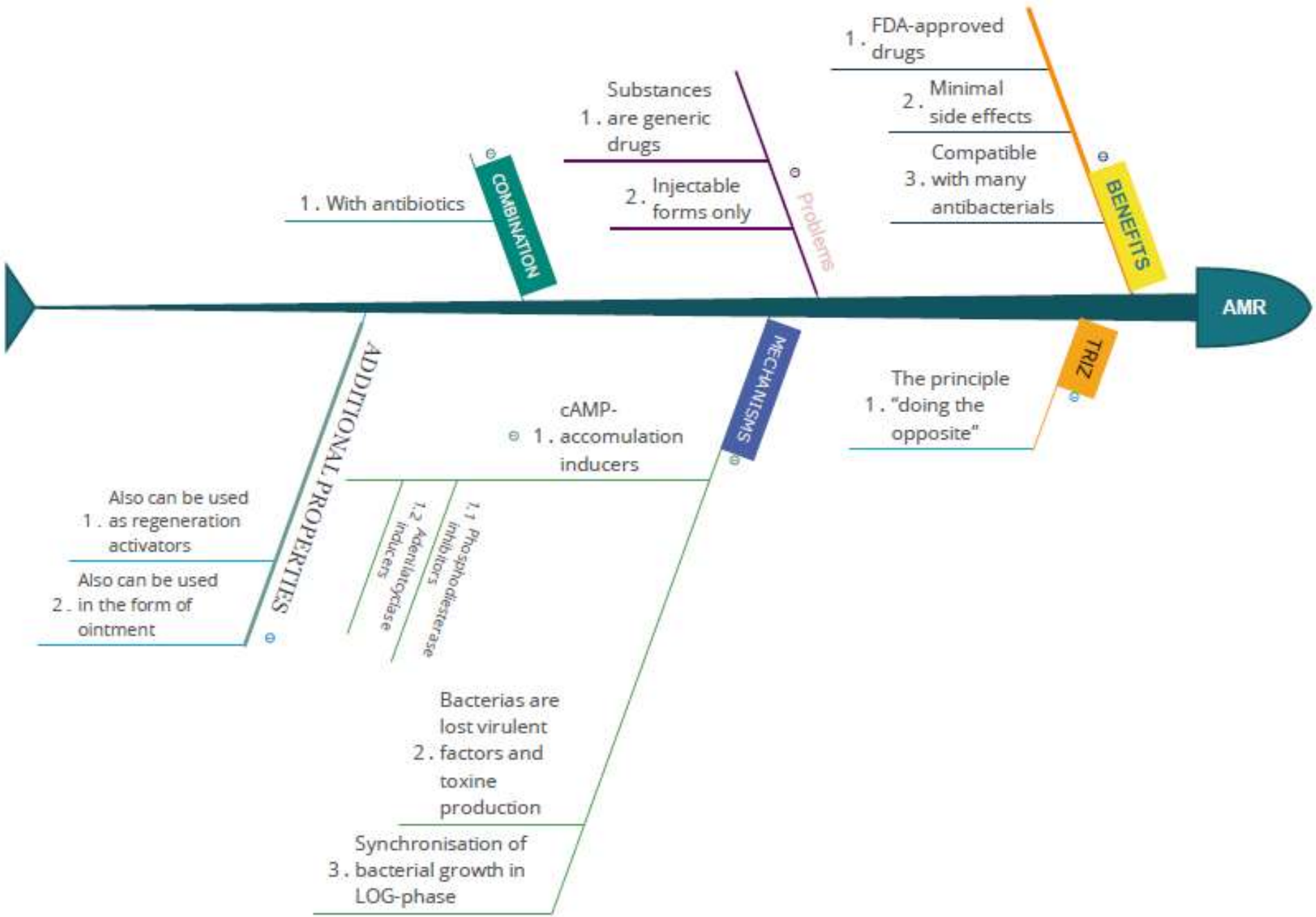
Line 2. Novel drugs generation "dynamic drugs" vs "static" drugs.

1. Anticancer agent based on RNA fragments (fRNA- fractionated)
2. Vaccines Supramolecular nanostructures on the basis of phospholipids modified peptides.
3. Antiviral drug based on modified peptides
4. Oral insulin based on self-organizing modified peptides

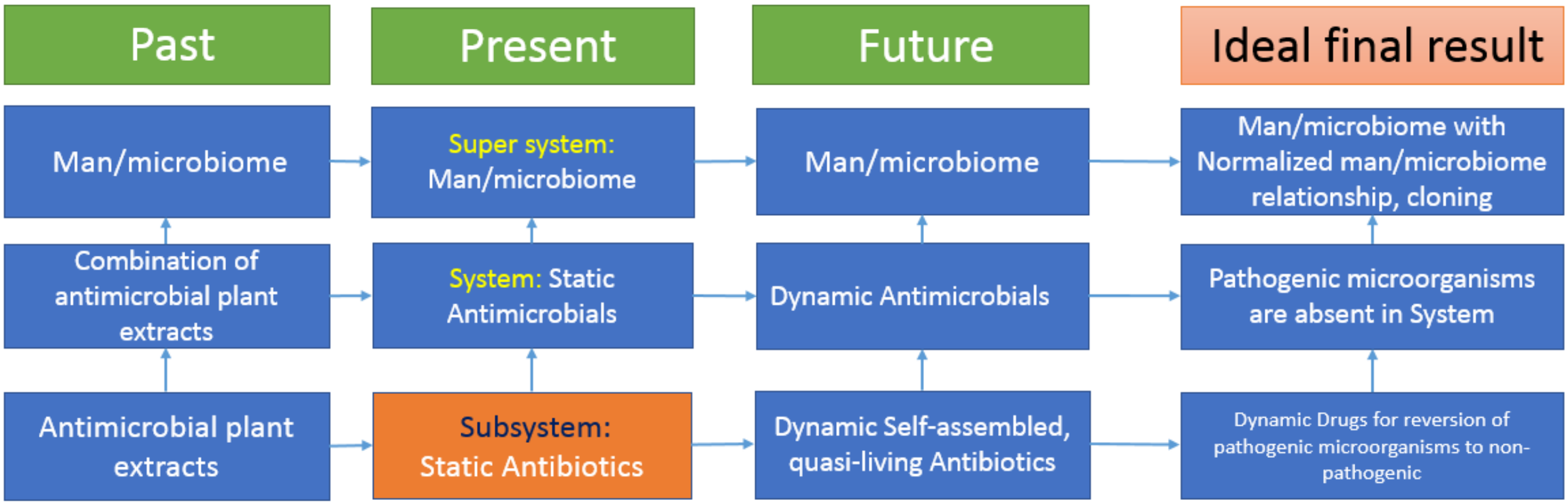
Line 3. New diagnostic approach for early cancer and early vascular atherosclerosis detection.

NOIGEL, LLC

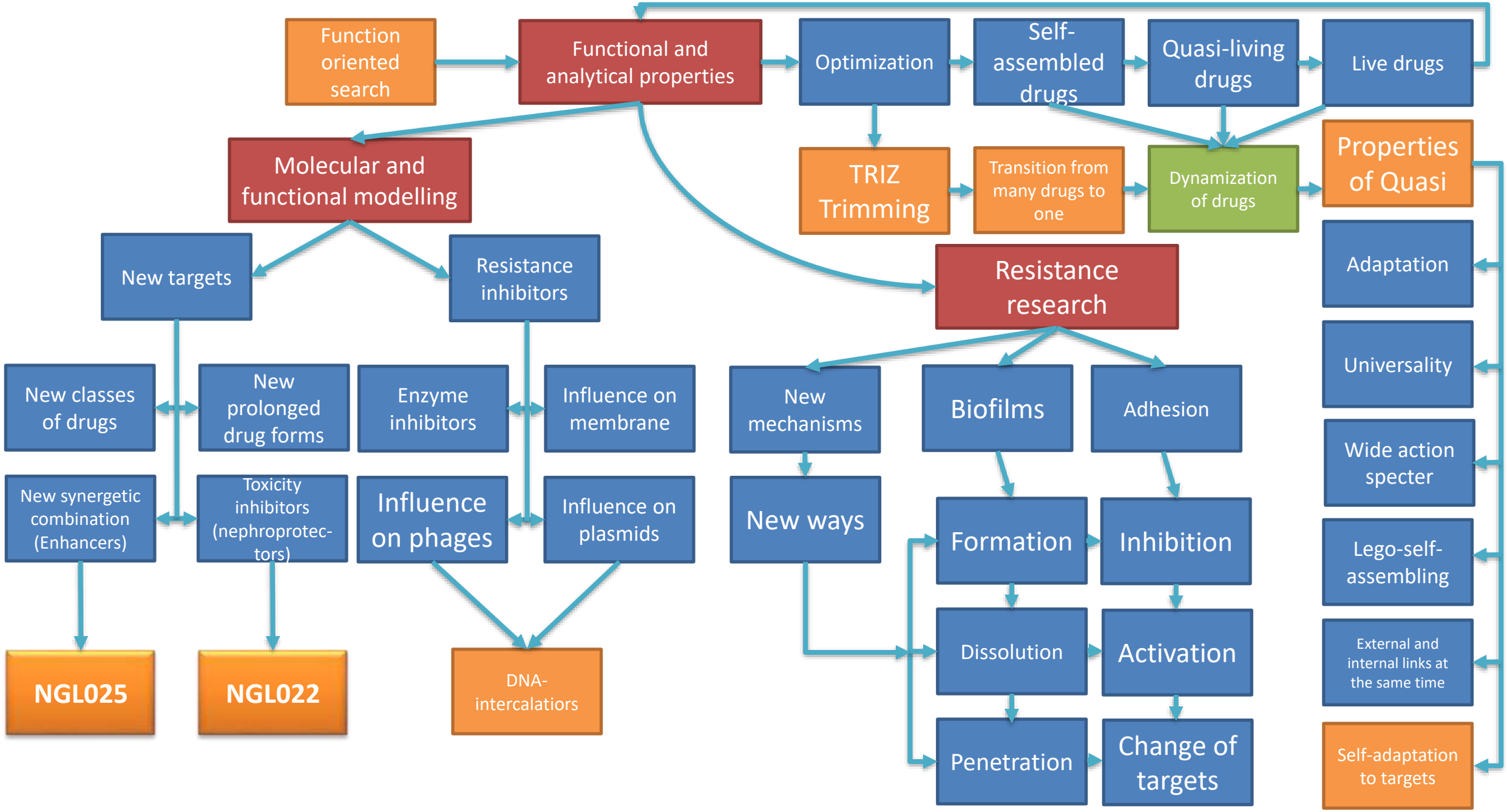
ISHIKAVA DAIAGRAM FOR AMR-FIGHTING



System Operator for Pathogenic Microorganisms Fighting

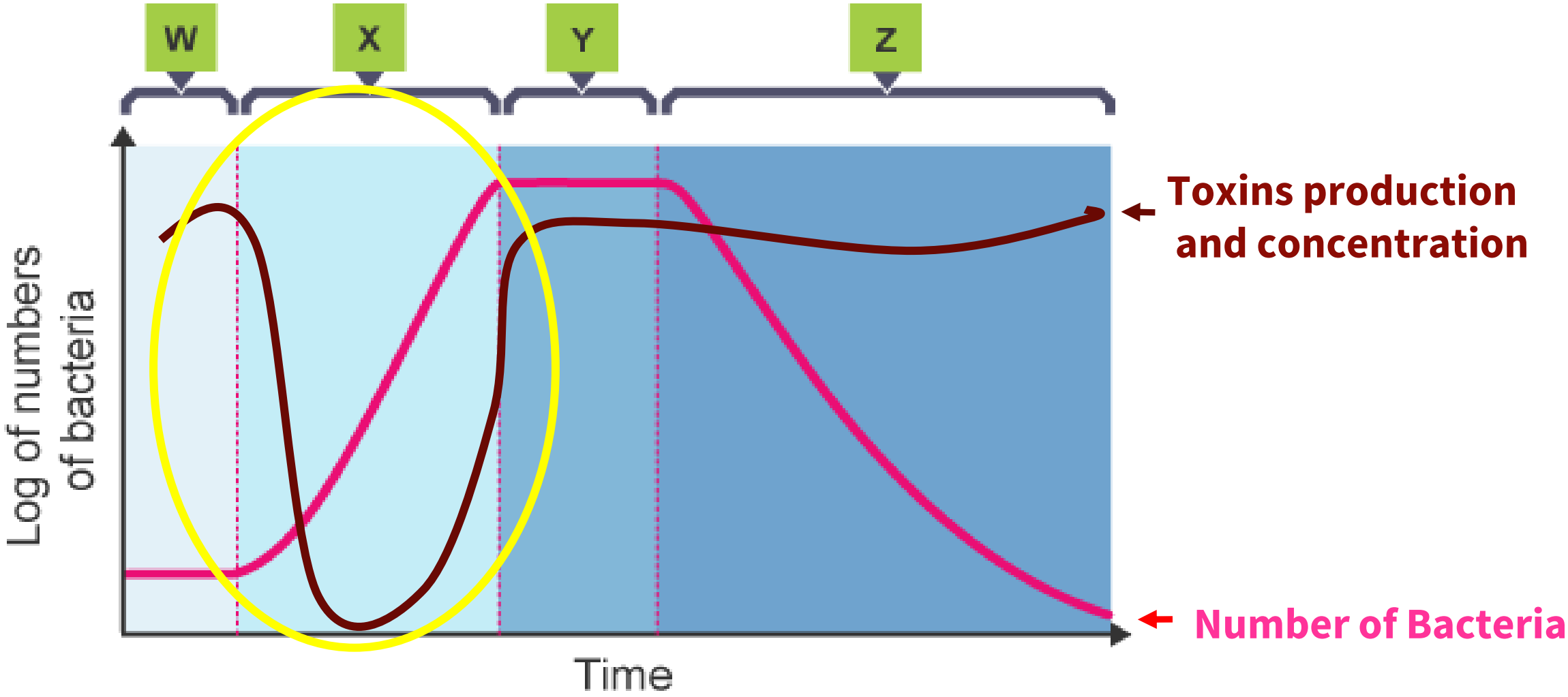


TRIZ structure of the functional-analytical method of improving the system “man - microbiome- environment”



"Don't forget to take a handful of our complimentary antibiotics on your way out."

Virulence factors dynamics



Sivonen, K. (1990). Effects of light, temperature, nitrate, orthophosphate, and bacteria on growth of and hepatotoxin production by Oscillatoria agardhii strains. *Applied and environmental microbiology*, *56*(9), 2658-2666.

Herbert, D., Elsworth, R., & Telling, R. C. (1956). The continuous culture of bacteria; a theoretical and experimental study. *Microbiology*, *14*(3), 601-622.13

New TRIZ paradigm to fight MDR bacteria

In a suitable environment Log phase, bacteria will stop virulent factors, toxins production. At log phase MDR resistant bacteria regains sensitivity to the antibiotic. Instead of killing bacteria, our composition will synchronize bacteria growth in Log phase

To fight and conquer in all your battles is not supreme excellence; supreme excellence consists in breaking the enemy's resistance without fighting.

Sun Tzu

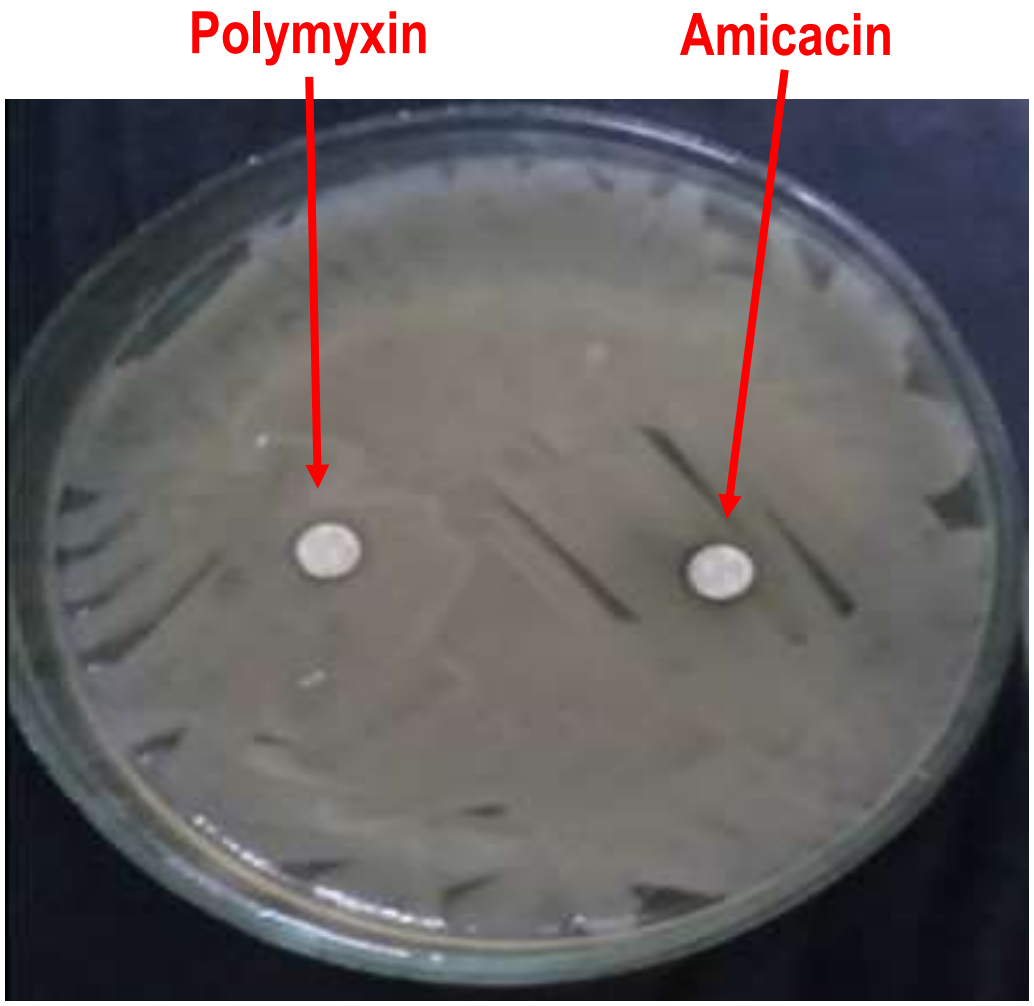
For to win one hundred victories in one hundred battles is not the acme of skill. To subdue the enemy without fighting is the acme of skill.

Sun Tzu

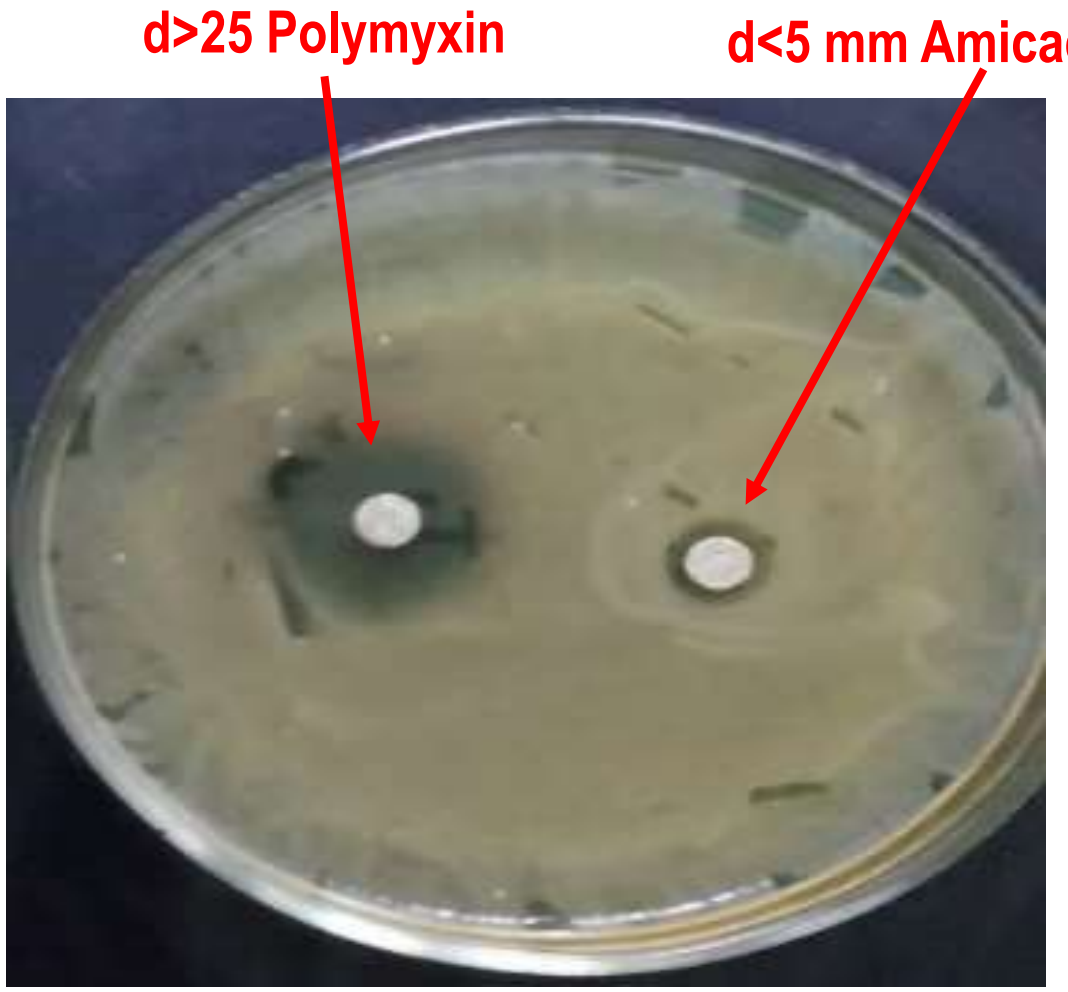
You must not fight too often with one enemy, or you will teach him all your art of war.

Napoleon Bonaparte

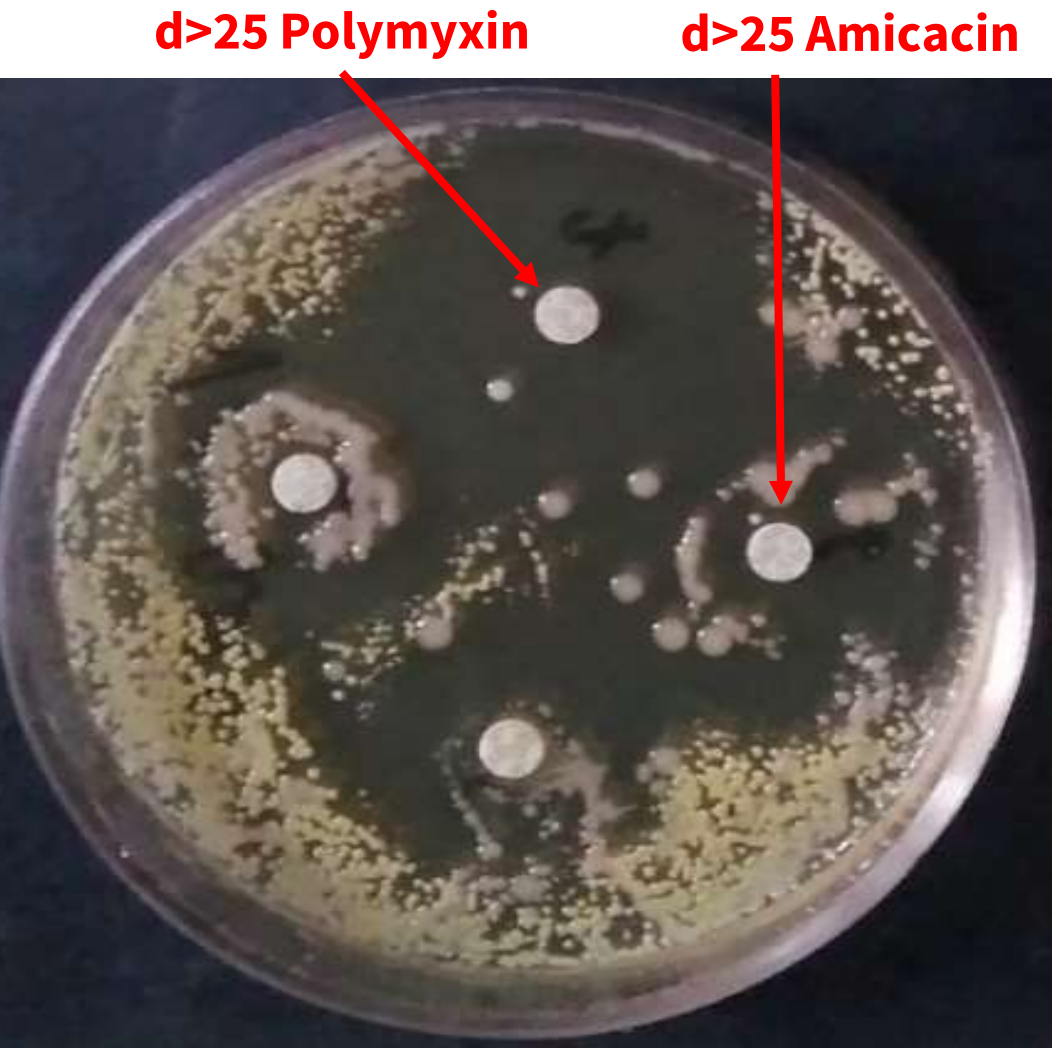
- **Noigel developed the composition based on generic drugs and based on expertise in synergistic combination substances.**



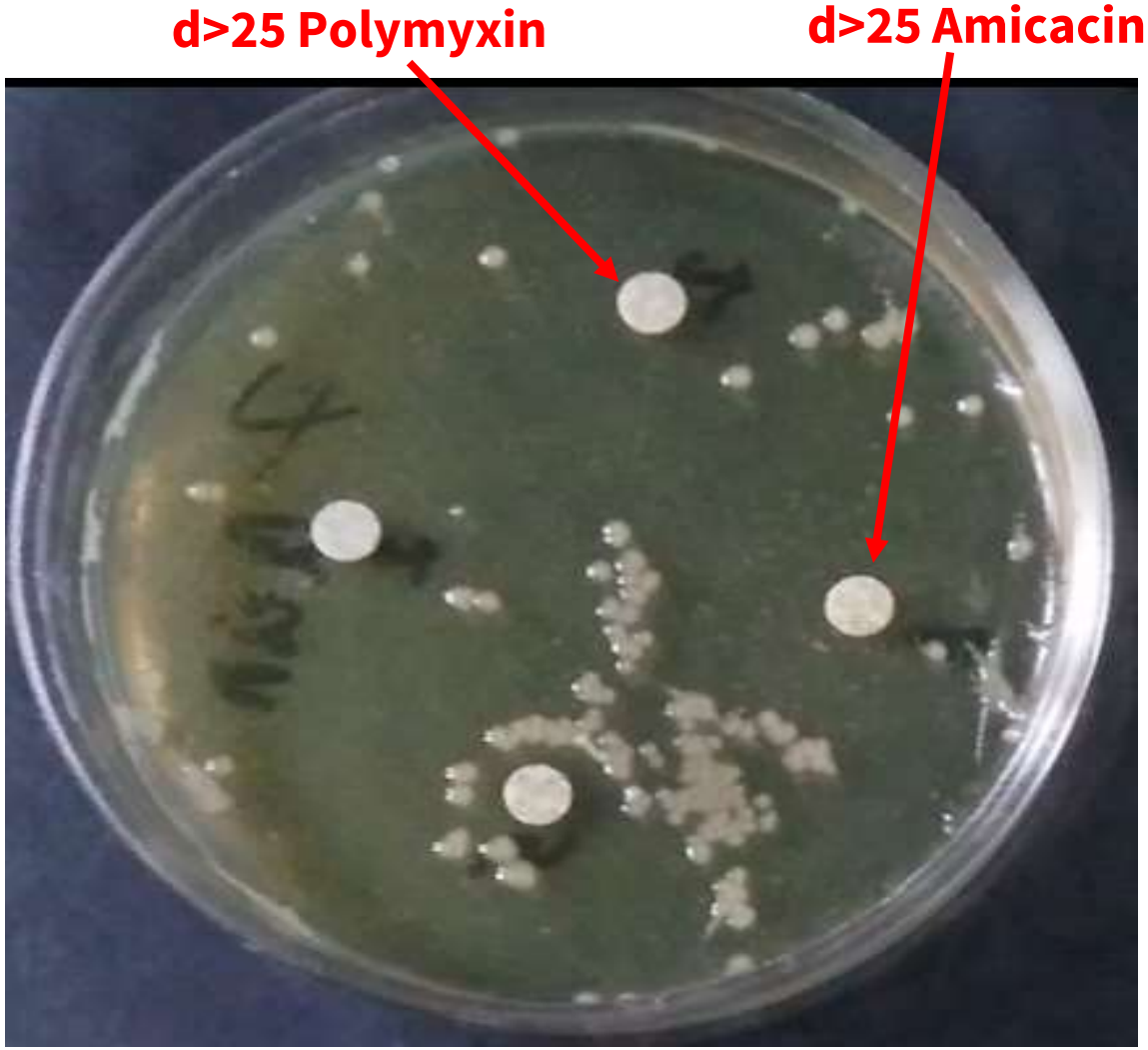
MDR *A.baumannii* growth **without NGL025:** 6 day growth, 2nd passage.



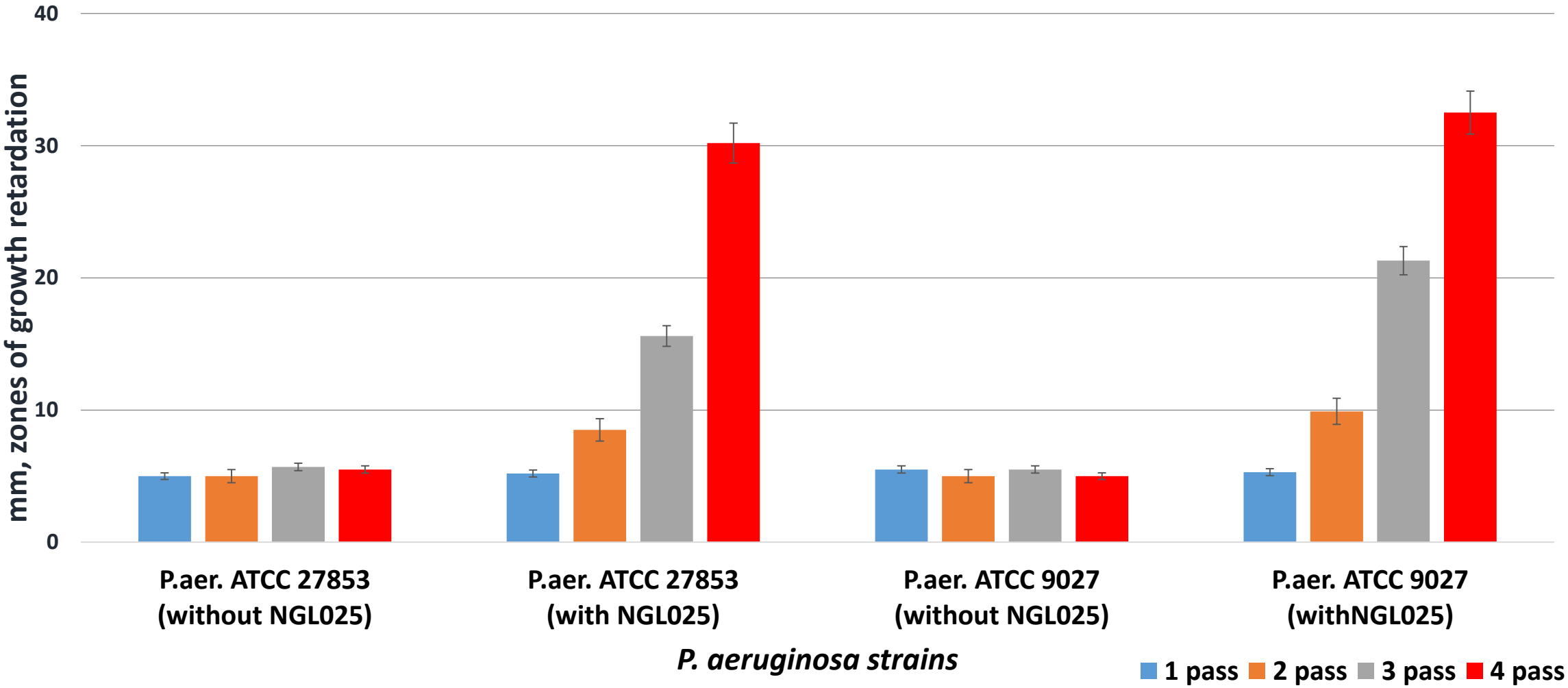
MDR *A.baumannii* growth **with NGL025**: 6 day growth, 2nd passage.



MDR *A.baumannii* growth **with NGL025:**
9 day growth, 3rd passage.

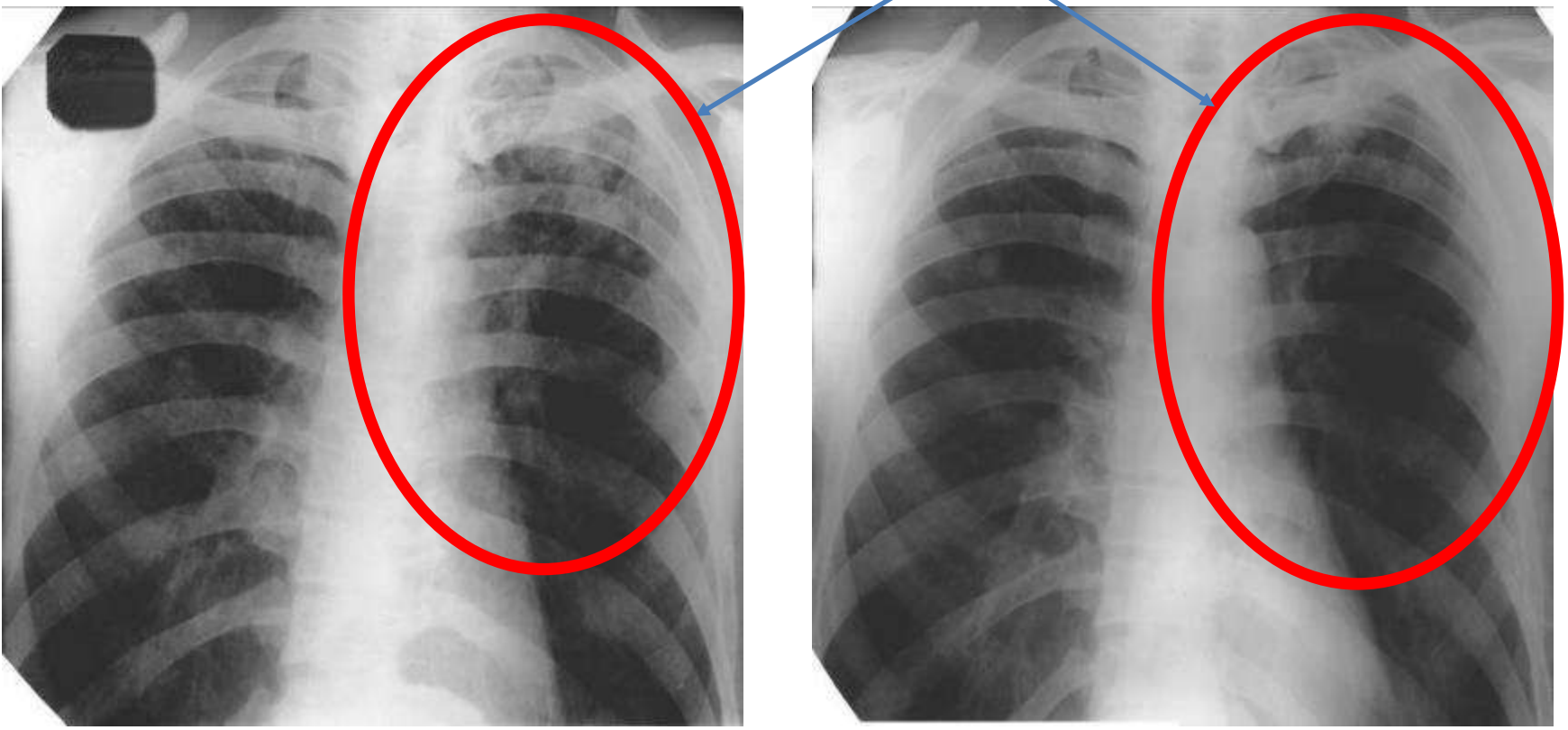


MDR *A.baumannii* growth **with NGL025:**
12 day growth, 4th passage.



Notes: n=6 for each studies, P<0,05. Stat.hypothesis (dispersion analysis) it is differences between *P. aeruginosa* sensitivity to polymyxin at classic medium

Clinical case of active pulmonary TB



There has been a positive result: on the radiograph in the upper parts of both lungs there was a significant resorption of focal and infiltrative shadows cavity of the lung tissue decay is not detected.

Patient 42 years old male was diagnosed with active multidrug resistant pulmonary tuberculosis.
Patient received first and then second-line drugs therapy **according to WHO criteria :** (HRZE) , streptomycin (S) and second line later generation quinolones, ethionamide etc. He had poor response on standard therapy.
Patient was given enhancers intravenously in 500cc 0.9%NS once a day for 3 days and then he continued HRZE therapy. After 15 day of therapy cough, SOB and low grade fever subsided, patient's symptoms improved. CXR was done and compared prior to enhancers therapy as shown above . Patient had clinical and radiological improvement. Patient followed by general practitioner for a year with no recurrence.

Polymyxin: Pros and Cons

Pros: Polymyxin and Nephrotoxicity

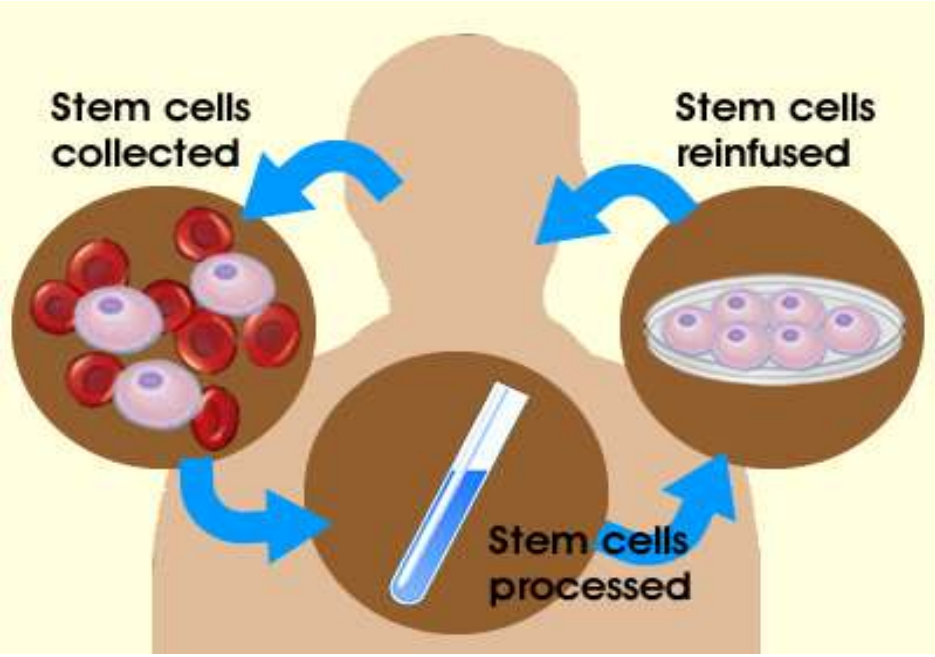
- **Strong antimicrobial activity** against the most common gram negative nosocomial pathogens.
- The majority of gram-negative bacteria are sensitive to polymyxin, and the resistance to these cationic lipoproteins develops slowly and occurs rarely compare to others antibiotics.

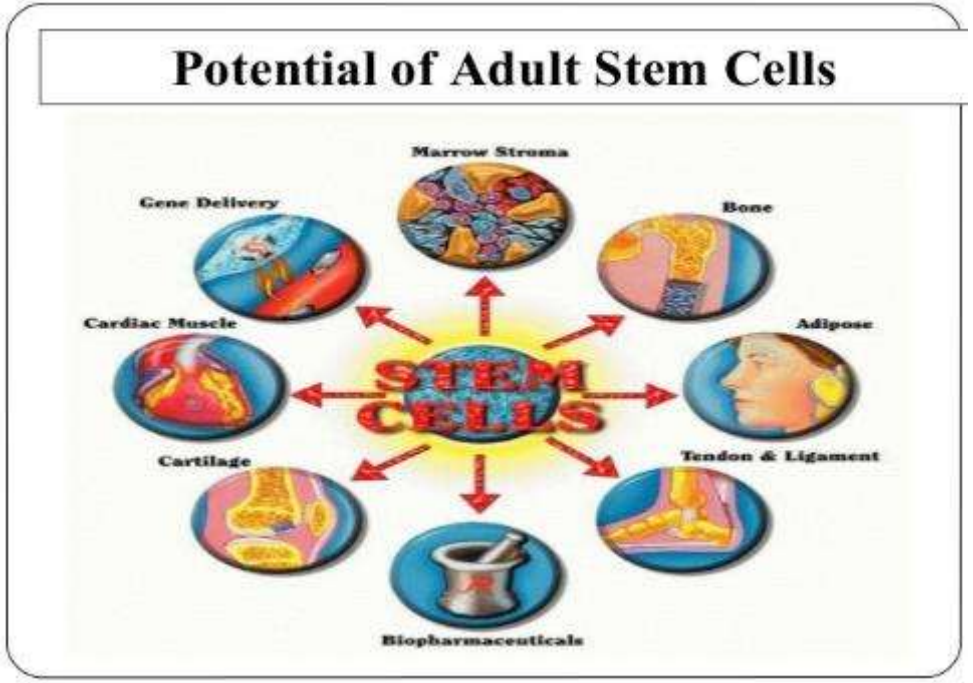
Cons:

- **Significant nephrotoxic side effect** since it has high affinity to the lipoprotein **megalin,** localized in the kidney.
- Blocking this lipoprotein megalin leads to the **disruption of renal function, renal failure and electrolytes imbalance.**

Current stem cells development

- Peripheral blood stem cells transplantation is a standard procedure after its first successful transplantation more than 35 years ago.
- Most prospective studies recognize the stem cell functions, the development of methods for their isolation and harvesting, as well as the application of such developments in medicine.
- Human stem cells are responsible for health maintenance and longevity. Stem cells generated by bone marrow, it present in every organ and human tissue.





STEM CELLS PROJECT PCT WO 2007/021210

(12) МЕЖДУНАРОДНАЯ ЗАЯВКА, ОПУБЛИКОВАННАЯ В СООТВЕТСТВИИ С ДОГОВОРОМ О ПАТЕНТНОЙ КООПЕРАЦИИ (PCT)

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(81) Указанные государства *(если не указано иначе, для каждого вида национальной охраны)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NL, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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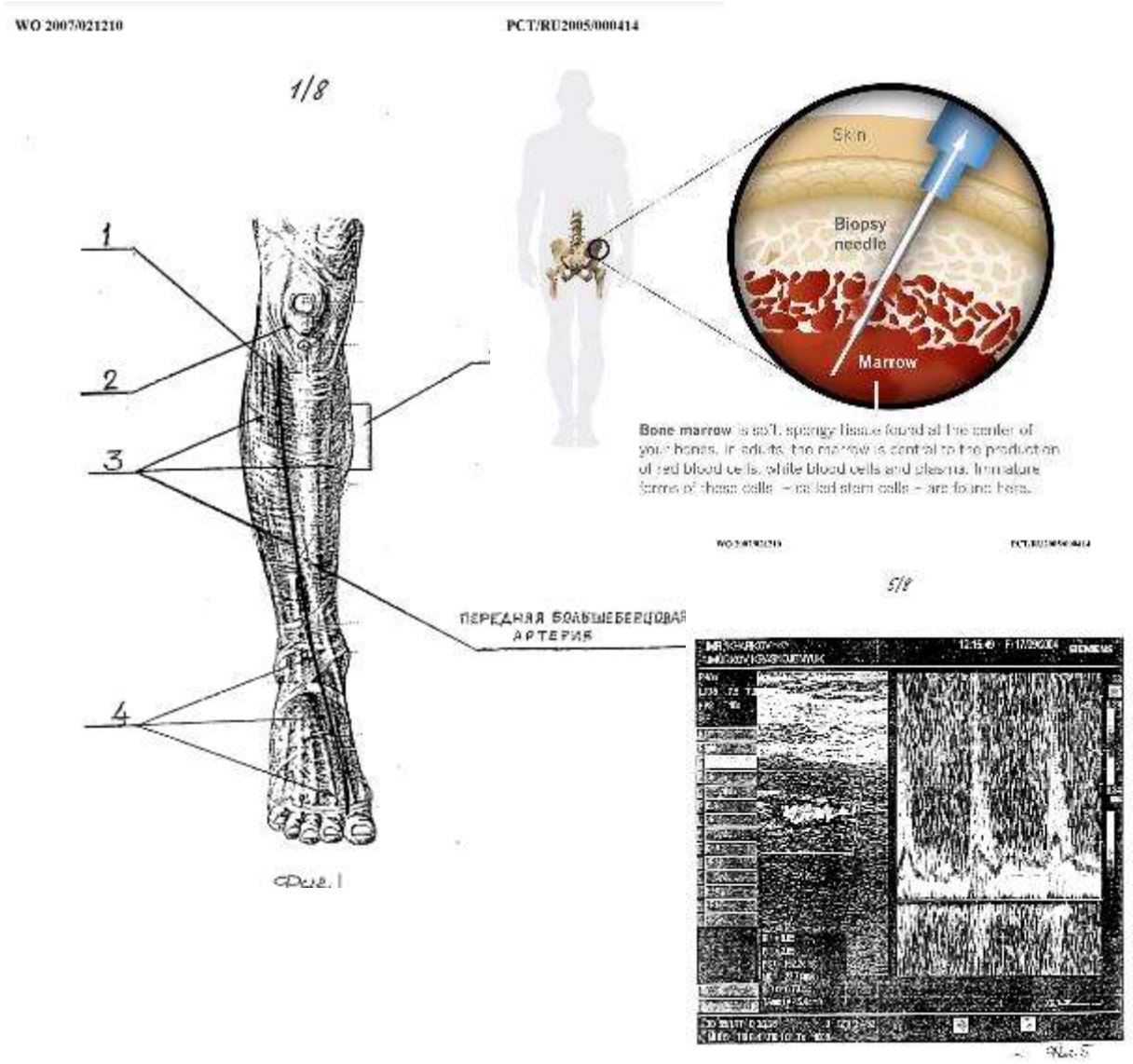
Декларация в соответствии с правилом 4.17:
— *об авторстве изобретения (правило 4.17 (iv))*

Опубликована:
— *с отчётом о международном поиске*

В отношении двубуквенных кодов, кодов языков и других сокращений см. "Пояснения к кодам и сокращениям", публикуемые в начале каждого очередного выпуска Бюллетеня PCT.

(54) Title: METHOD FOR TREATING DISEASES CAUSED BY VASCULAR DISEASES



8 Human volunteers (stage 3 diabetic ulcers)

Drug	Heparin gel	Diclofenac gel 5%	Lidocaine	Dipasol*
Time of onset of effect (pain inhibition and anti- inflammatory effect)	8 h	50 min	30 min	20 min
Effect duration	4-5 h	6-8 h	12 h	12 h

*- to accelerate the healing of wounds and burns (5-6) analogues in the world there is no

Dipasol based on FDA-approved compositions has the ability to selectively stimulate the growth, migration, and differentiation of stem cells in humans.

#1 Dipasol for wounds & pressure ulcers, severe Burns, varicose veins.

- Dipazol is a ointment based composition.
- The 100 gr of ointment contains 1.5 gr of active substances.
- Accelerates healing of wounds, pressure ulcers, severe burns, varicose veins, diabetic trophic ulcers.

Diabetic pressure ulcer

Varicose veins

Burns

Post – op wound healing

Pharmaceutical composition for stimulating stem cell division and suppressing bacterial virulence. PCT/RU2017/ 000851 WO2019098869A1; US 16/772,980

PHARMACEUTICAL COMPOSITION FOR STIMULATING STEM CELL DIVISION AND SUPPRESSING BACTERIAL VIRULENCE

Field of invention

The invention relates to organic and bioorganic combinatorial chemistry and pharmacia, namely to new combinatorial library of dipyridamole derivative and supramolecular structure based on them, which when being used, if not separated in individual components, have high bioactivity as a means of stem cell fission encouragement in the form of pharmaceutical compositions combined with phosphodiesterase inhibitors and histone deacetylase inhibitors, as well as pharmaceutically acceptable excipients. The composition is also designed for bacteria virulence depression and recovery of their sensitivity to anti-infective drugs, as well as for production of medical and veterinary biologics, nutrient additives, probiotics and sour-milk ferments on their basis, vaccine production.

Prior knowledge

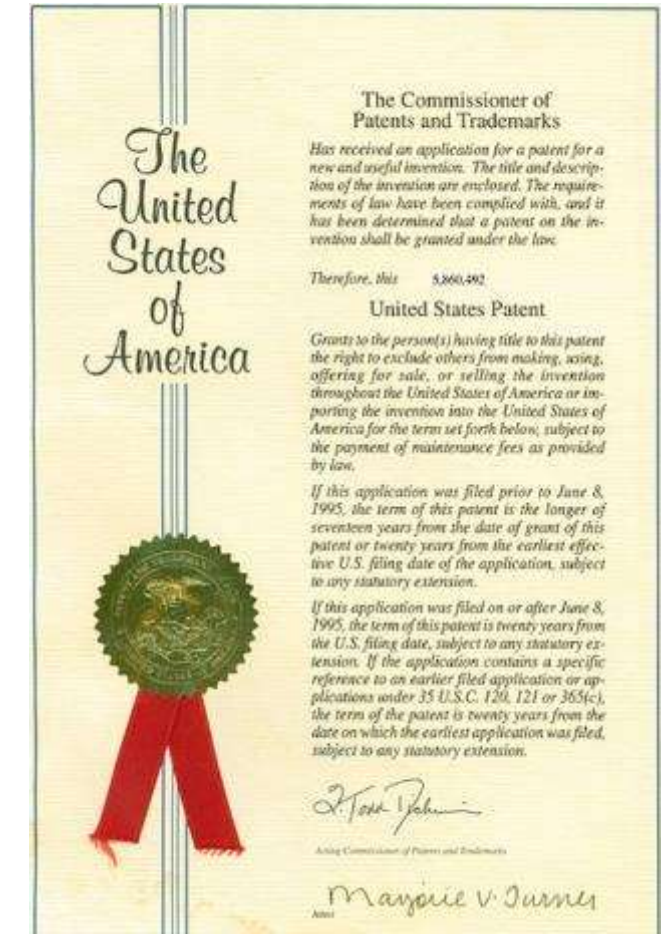
Pluripotent stem cells are currently considered to be the most advanced source of youth; they are responsible for angiogenesis and support physiologically sound immune status. The problem is the decrease of native iPS cells in body with age and correspondingly – ageing. The Japanese scientists (Tanabe *et.al.*, 2013) found the ability of well differential cells to differentiate into pluripotent ones when influenced by genetic vectors. The disadvantage of this avenue is the need for genetic modification of differentiated cells and the hazard of cancer cells formation. The authors managed to find product groups which, in composition, are able to scale up massively the yield percentage stem cells after genetic modification. These are two groups of compounds – cAMP-phosphodiesterase inhibitors and histone deacetylase inhibitors. Though we have not been able to do without genetic modification, the yield of stem cells was increased thousandfold. With this in view, an idea has started up that it is possible to find small-molecule substances able to replace genetic vectors and cause tissue differentiation (reprogramming) into stem ones.

iPS cells maturational stage

Just a small number of cells passes maturational stage successfully shown as low effectiveness of reprogramming in total (Tanabe *et.al.*, 2013). At this stage, epigenetic modifiers allow activating the expression of genes encoding internal pluripotency causes, such as Oct4, Nanog, Sall4, etc. (Feng *et.al.*, 2009).

LIF-STAT signal pathway is essential to iPS cells maturing. For cell culture on a medium free of LIF (leukemia inhibitory factor) serving as an activating ligand of this signal pathway, colonies are formed similar to embryonic stem cells in morphology, but six days later after formation they detach from adhesive surface. Activation of LIF-STAT pathway results in gene promoter demethylation maintaining the pluripotent state. It was demonstrated that transcriptional factor Stat3 blocks directly the DNA and methyltransferase DNMT1 and histone deacylases HDAC2, HDAC3 and HDAC8 (Tang and Tian, 2013).

WNT-signal path way is involved in maturing of iPS cells as adding Wnt3a- activating ligand between the sixth and ninth days after the start of reprogramming increases the number of the formed iPS colonies (Ho *et.al.*, 2013). Such colonies express endogenic Nanog, and maybe the product of this gene is necessary for transition of cells from maturational stage to stabilization stage (Sumavarchi-Tehrani *et.al.*, 2010).



The United States of America

The Commissioner of Patents and Trademarks

Has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this 5,860,492

United States Patent

Grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America for the term set forth below, subject to the payment of maintenance fees as provided by law.

If this application was filed prior to June 8, 1995, the term of this patent is the longer of seventeen years from the date of grant of this patent or twenty years from the earliest effective U.S. filing date of the application, subject to any statutory extension.

If this application was filed on or after June 8, 1995, the term of this patent is twenty years from the U.S. filing date, subject to any statutory extension. If the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121 or 365(c), the term of the patent is twenty years from the date on which the earliest application was filed, subject to any statutory extension.

Acting Commissioner of Patents and Trademarks

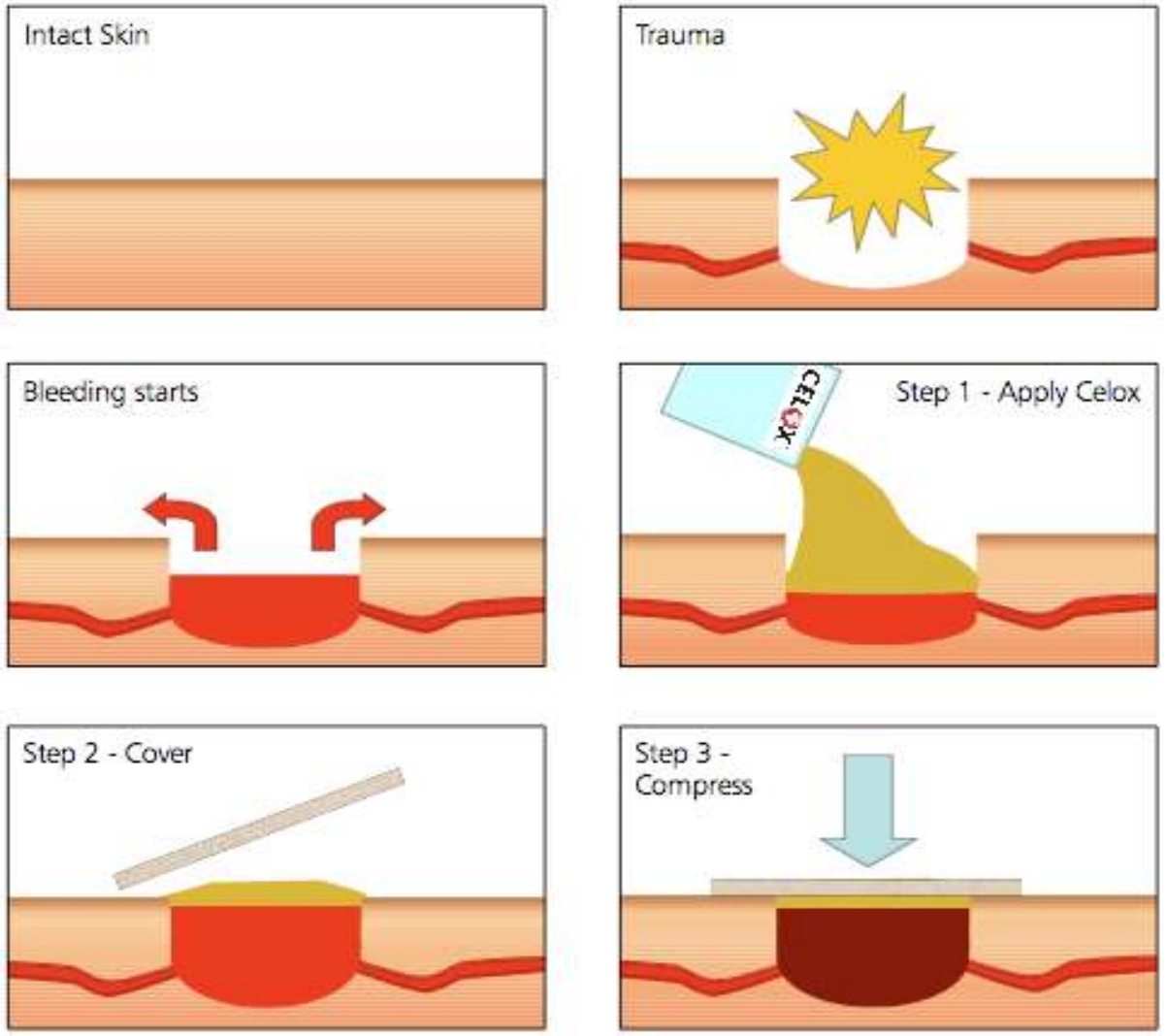
Attest

4 - BINARY HEMOSTATIC "GEMMA"

According to world statistics, since the Second World War up to the present time, the main cause of death up to 60% of the wounded on the battlefield and in emergencies, is a bleeding.

As cited in "Military Times",
"90 percent of the deaths occurred before the injured soldiers reached a medical facility."

Kime, Patricia. "Study: 25% of War Deaths Medically Preventable." Military Times, 29 Mar. 2013. https://www.militarytimes.com/2013/03/29/study-25-of-war-deaths-medically-preventable/

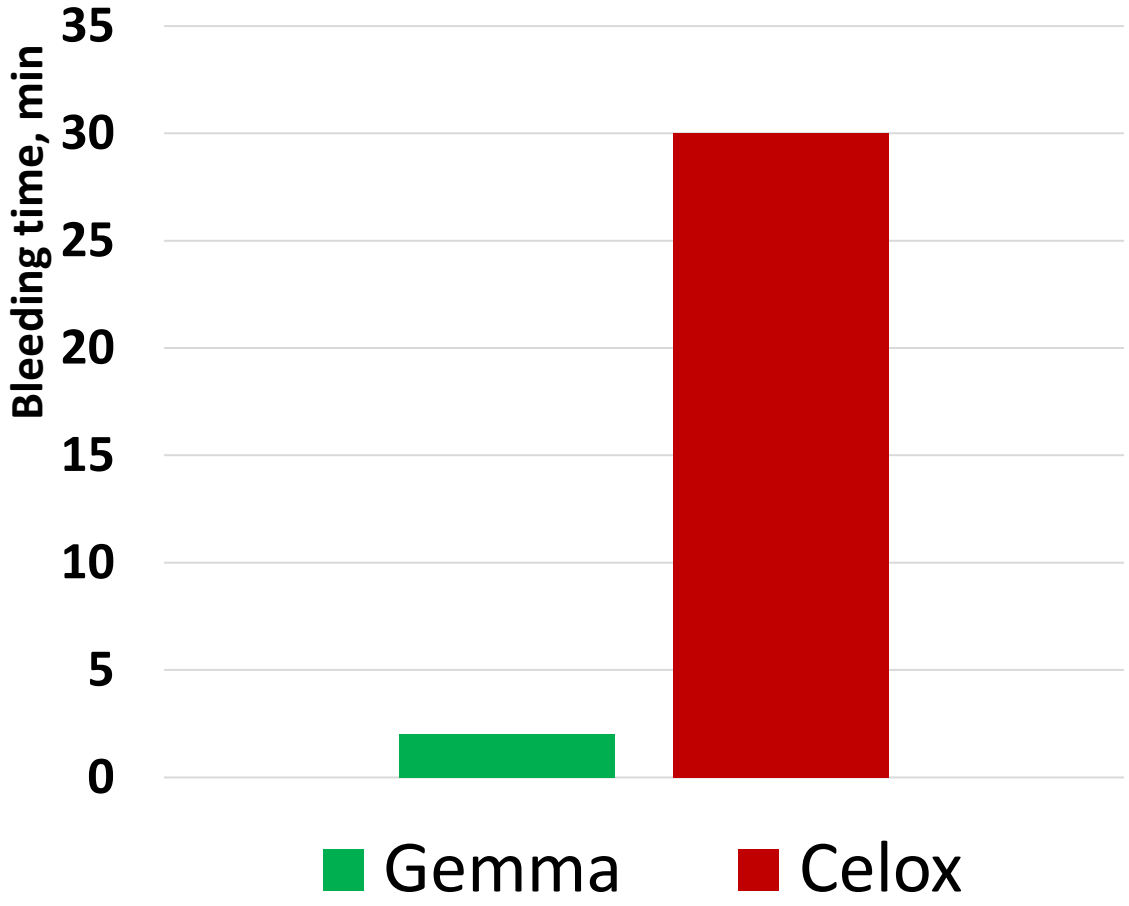


Current hemostatics

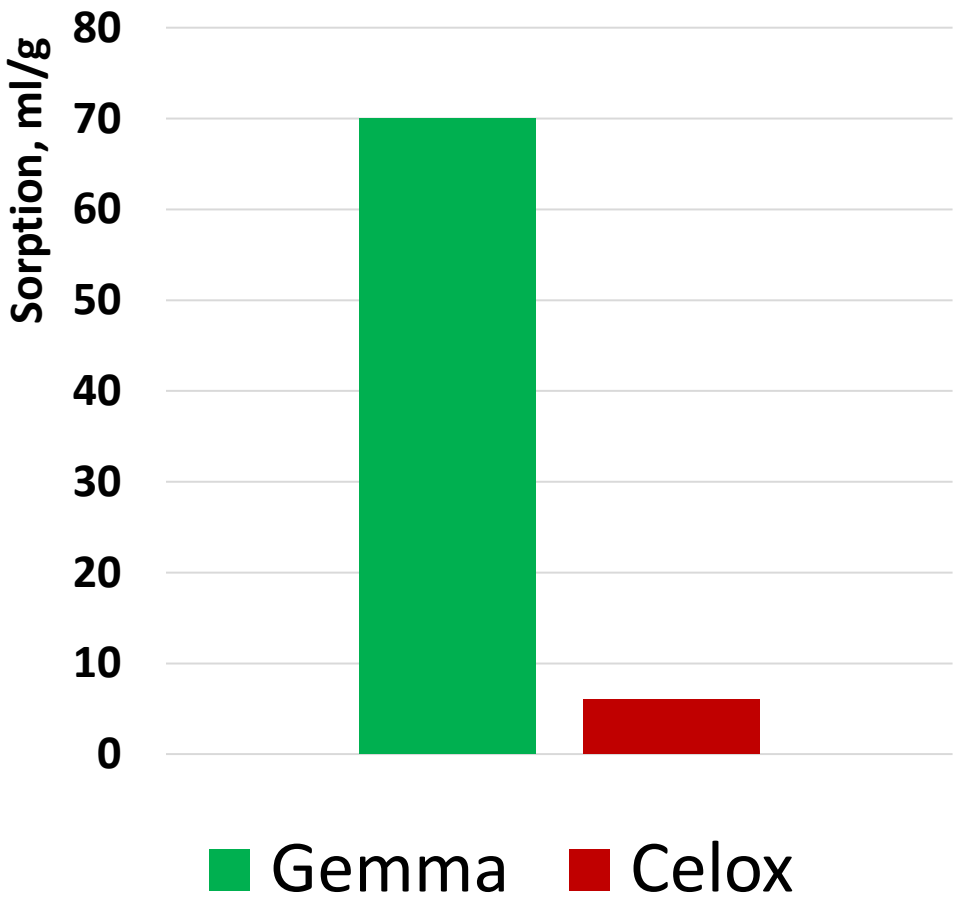
Celox and QuikClot are the most commonly used hemostatic agents by the military, emergency and hospital trauma centers.

GEMMA combined table

Influence of “Gemma" on clotting, bleeding time



Study of sorption activity “Gemma“, ml/g

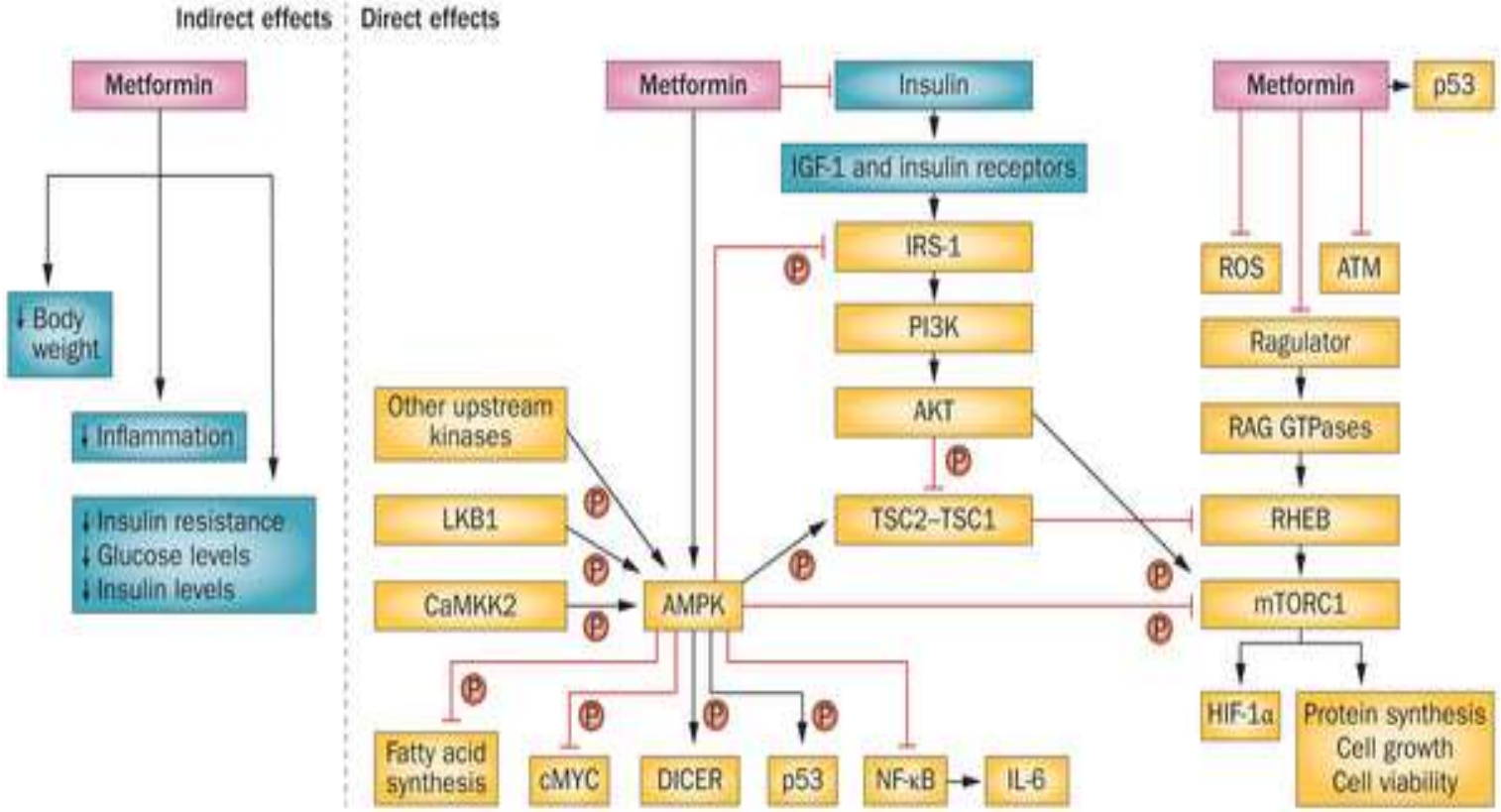


Advantages Binary hemostatic: Gemma

- Possesses biocompatibility with body tissues: no tissue necrosis and no local and systemic allergic reactions.
- No burn effect of the tissue during crystallization in the wound.
- Absorbs 70 times the amount of blood than existing products.
- Biodegradable, no wound debridement, no interference to wound healing.
- Gemma based on inexpensive materials, natural semisynthetic polymers.
- The manufacturing is simple and it is not affected by sterilization process.
- Gemma compound mixed to complete homogeneity and distributed in flexible packaging process and containers.

5- Metformin with reduced side effects

- Metformin does not directly affect the insulin production, but rather it successfully increases the tissues sensitivity to insulin. This leads to metformin's high efficiency for treatment of the insulin resistance with metabolic syndrome as prevention and therapy type 2 diabetes (T2D).
- Unfortunately, about 40% of patients are not able to use metformin due to side effect.



Disadvantages of Classic (static) drugs.

1) **Static** conservative chemical structures.

2) The presence of a “slippage effect” (change in the receptor sensitivity and response to the same medication over time) :

a) Diminished or loss of efficacy drugs over the time treating Hypertension, Diabetes etc.

b) The Multidrug resistant (MDR) infections due to antibiotics inability to adapt to new receptors and new microorganisms defense factors and mutations as result antibiotic function develop **“slippage effect”.** Similar development tumor resistance to therapy over time observed in oncology related to chemotherapeutic drugs **“slippage effect”.**

NOVEL Drugs with dynamic structures (Dynamic drugs) based on TRIZ

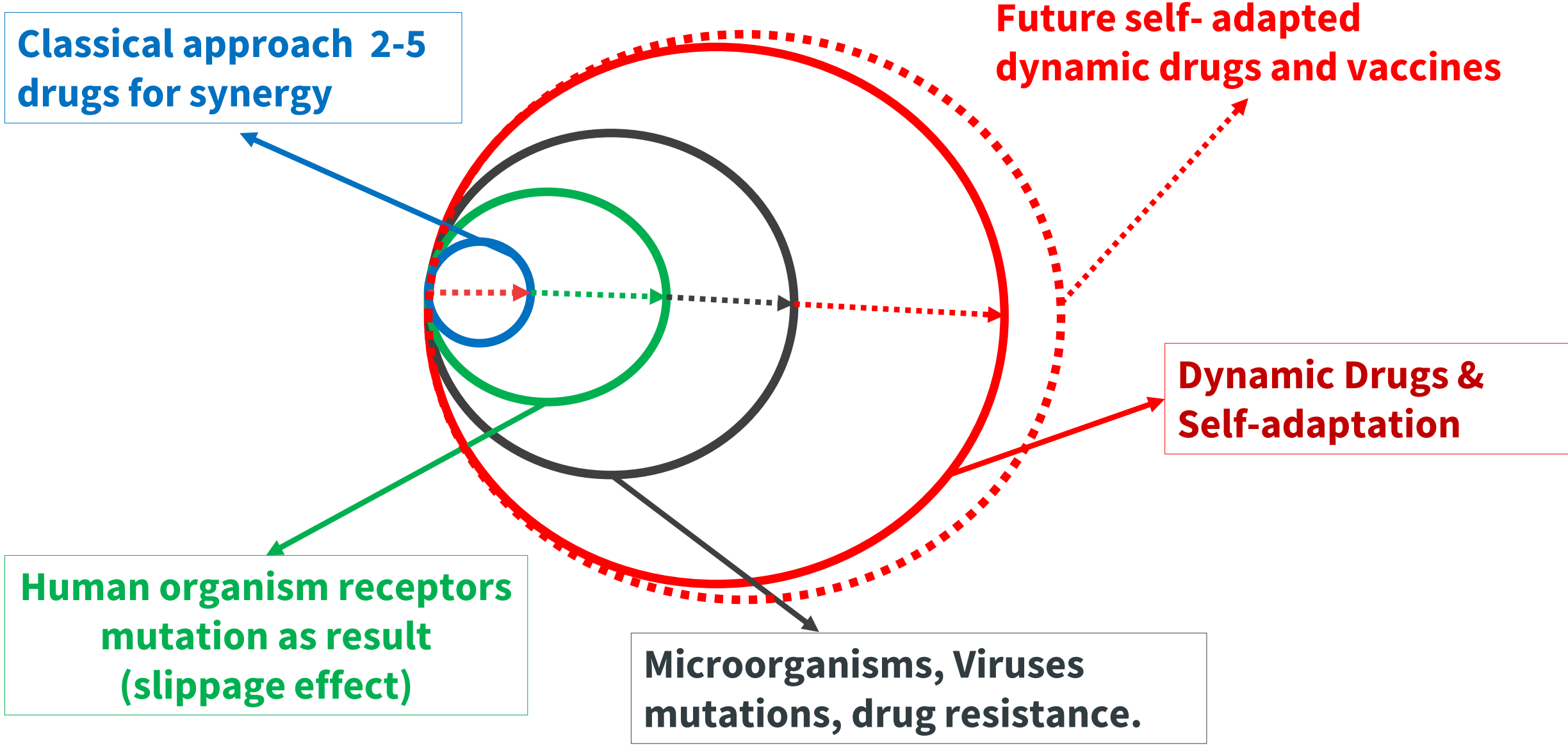
To survive, rate of Pathogen Microorganisms "innovations" faster than rate of new classical drugs development.
This is time to find another, Dynamic way to fight Patogen Microorganisms

Illustration

Instead of one "key" for one "lock" (the principle of a classic drug with a conservative structure), we propose a selection of "skeleton keys": a group of many similar molecules that "open" many "locks" and adapt to the target. This facilitates a practically 100% effectiveness rate and a maximally wide spectrum of drug activity

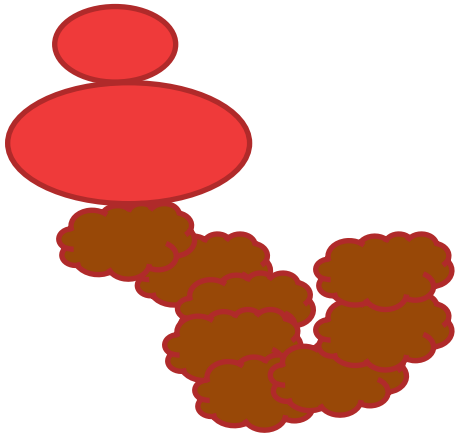
Вместо одного «ключа» на один «замок» (принцип классического препарата с консервативной структурой) мы предлагаем набор «скелетных ключей»: группу из множества одинаковых молекул, которые «открывают» множество «замков» и адаптируются к цели. Это обеспечивает практически 100% эффективность и максимально широкий спектр действия препарата.

Classic R & D vs. NOIGEL R&D approach



mRNA

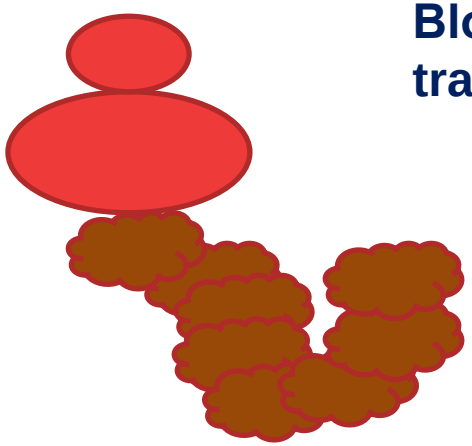
Polyribosome



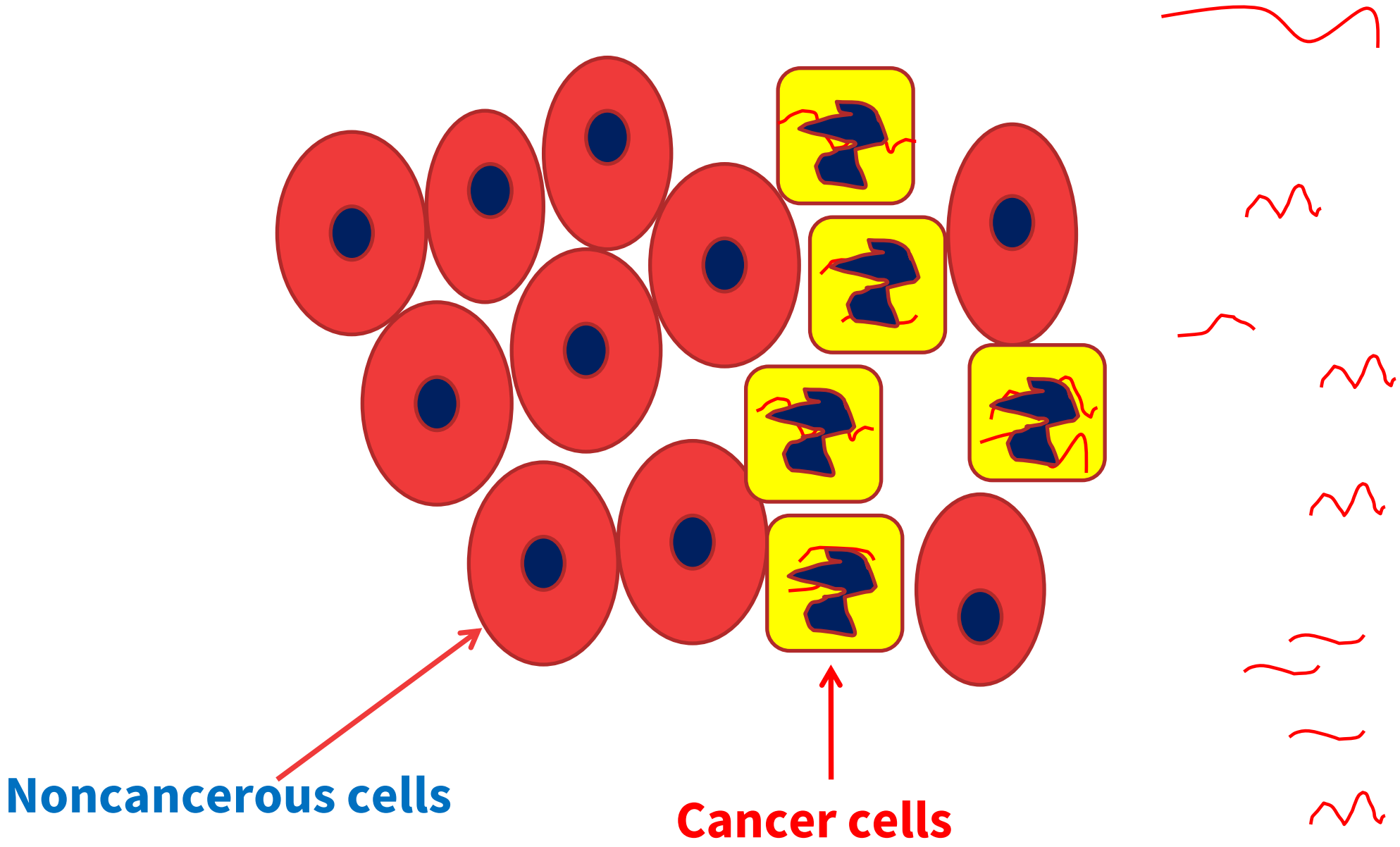
Translated protein

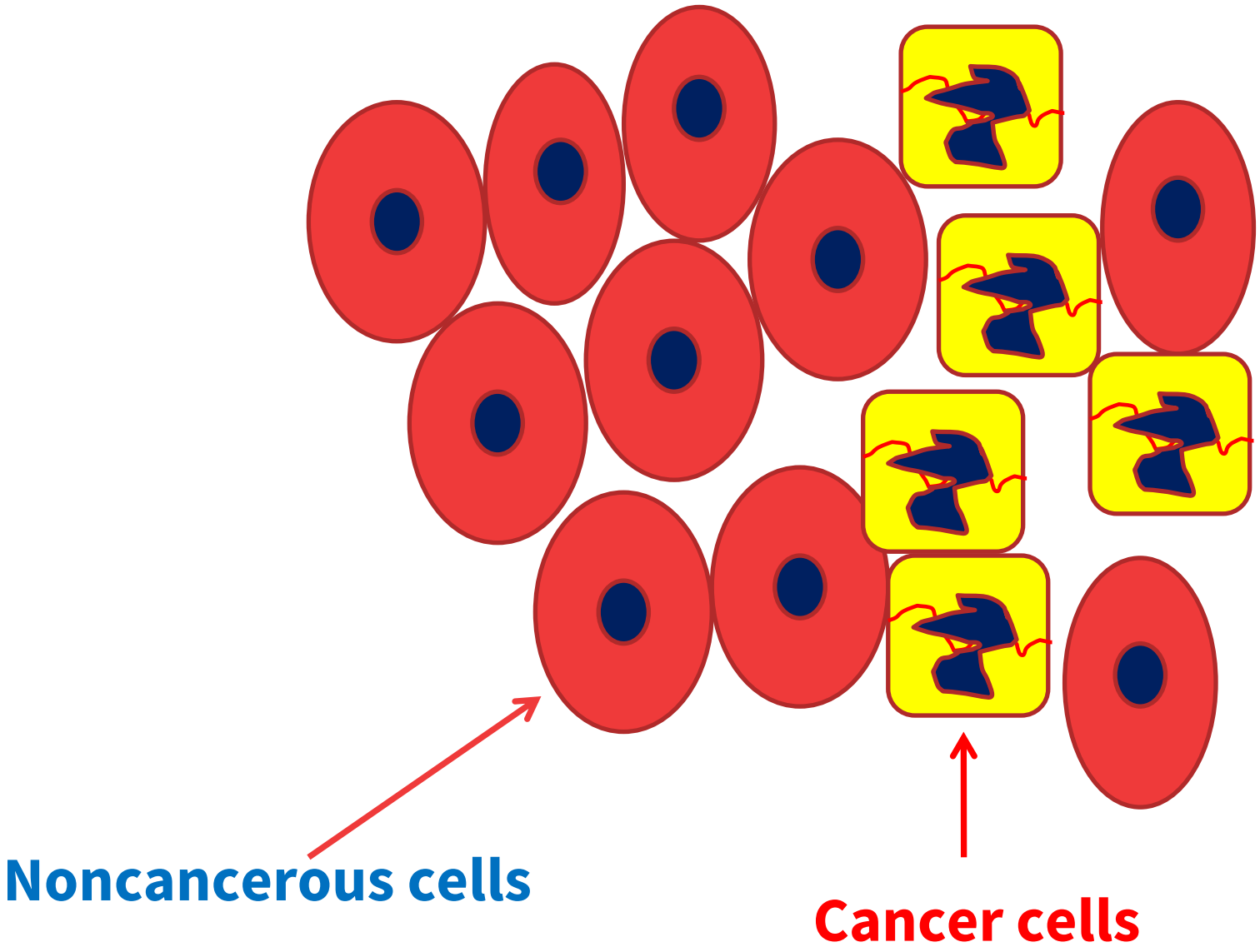
Fragment of m-RNA

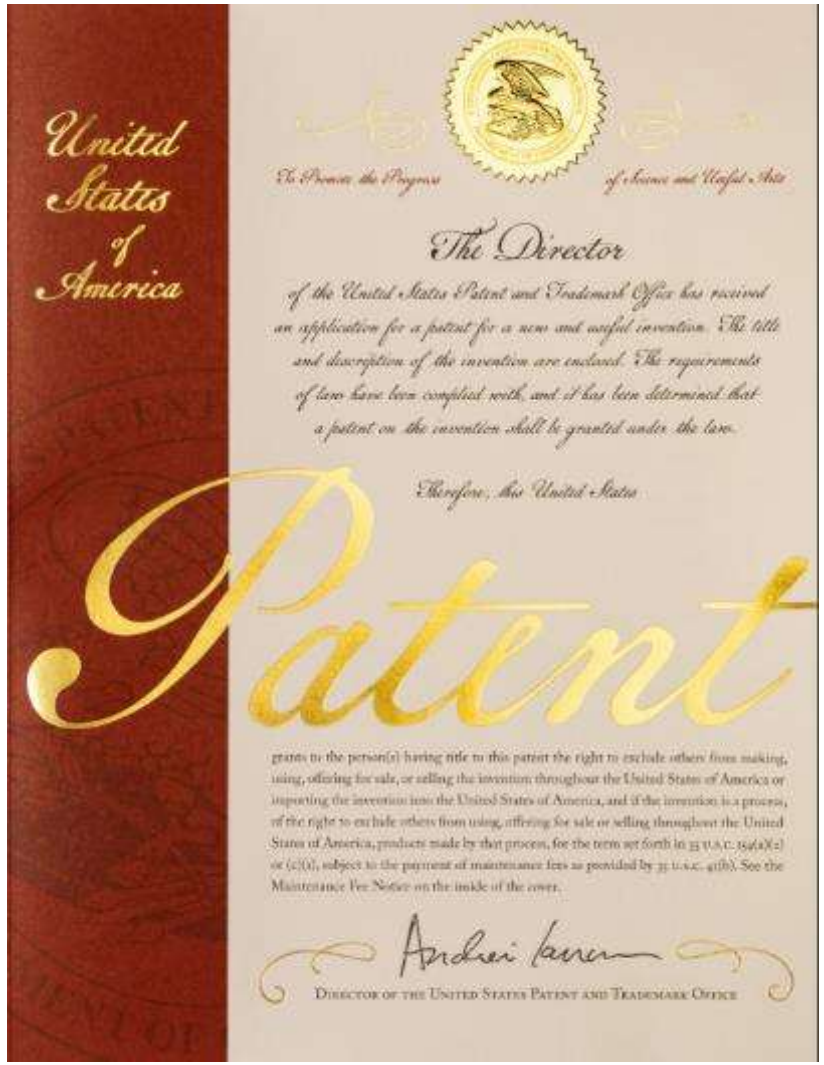
fRNA



Blockage of protein’s translation


Noncancerous cells
Cancer cells

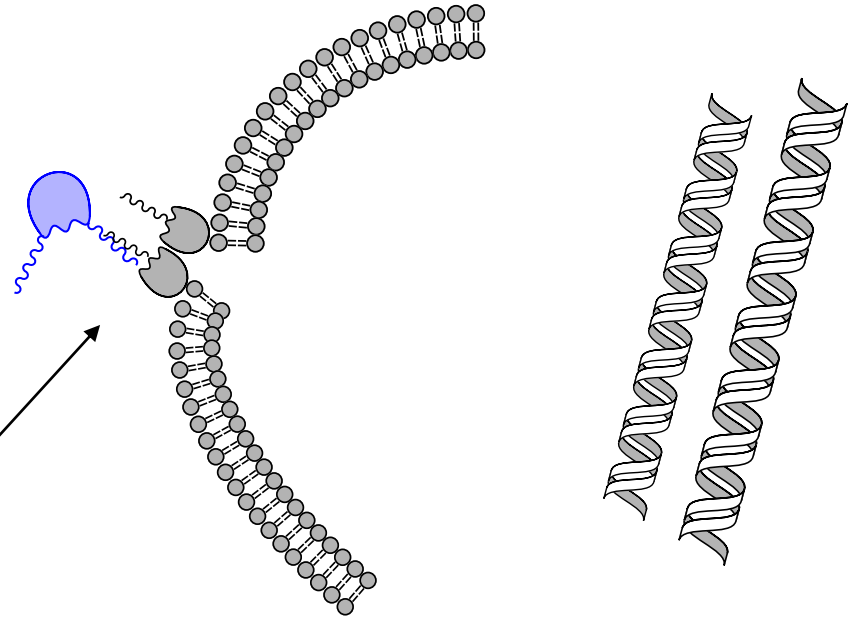

Noncancerous cells
Cancer cells


United States of America
To Promote the Progress of Science and Useful Arts
The Director
of the United States Patent and Trademark Office has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.
Therefore, this United States
Patent
grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America, and if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States of America, products made by that process, for the term set forth in 35 U.S.C. 154(a)(2) or (c)(1), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b). See the Maintenance Fee Notice on the inside of the cover.
Director of the United States Patent and Trademark Office

2. Antiviral, based on self-assembled modified peptides.

NGL030 contains mixture of acylated peptides. It effectively inhibits the process of nuclear importation of viral polynucleotides from those viruses that depend on the cell nucleus (FLU, Herpes Viruses, HIV/AIDS, etc)

The mechanism of the penetration of a viral genome without NGL030

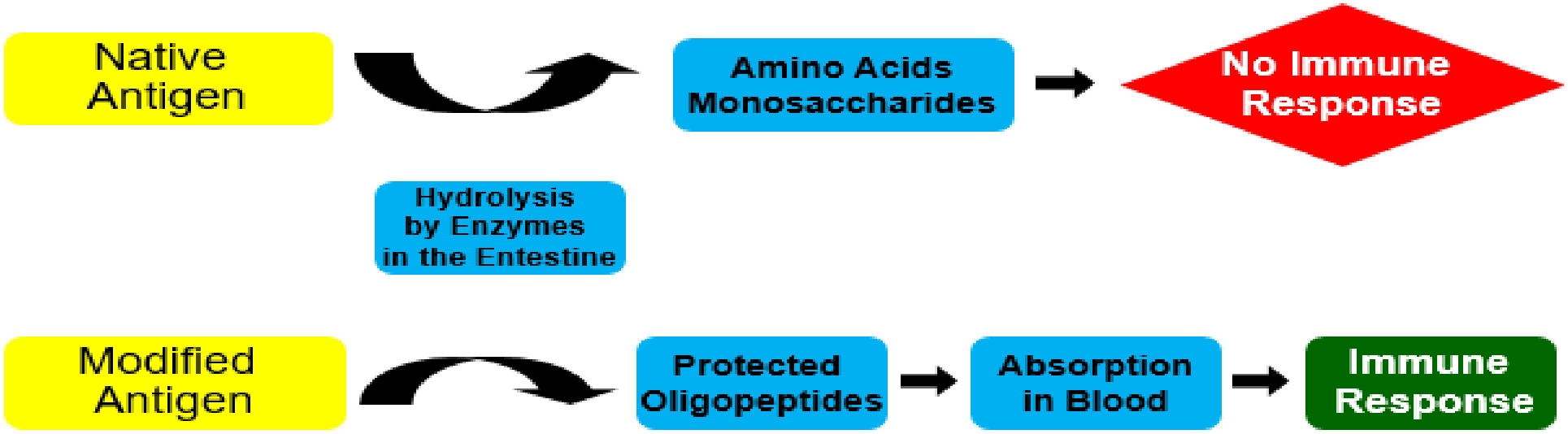


a-, b-importins
with Viral genome

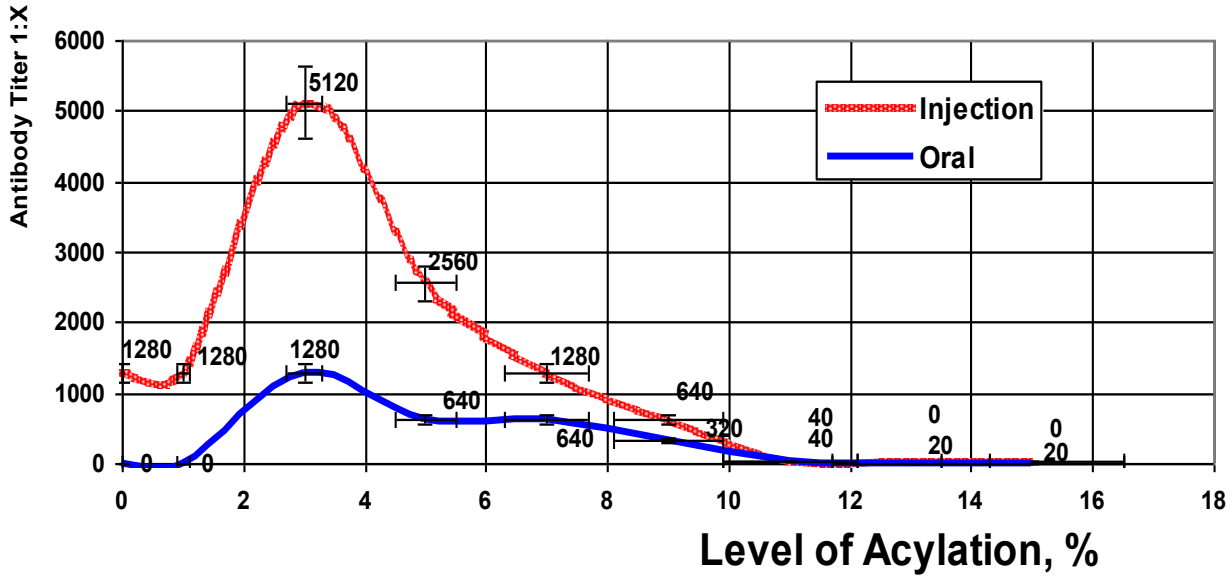
Nuclear
Membrane

Genomic Nuclear DNA

Dynamic vaccines based on self-assembled modified peptides



The mechanism of action of oral vaccines with partially modified antigens

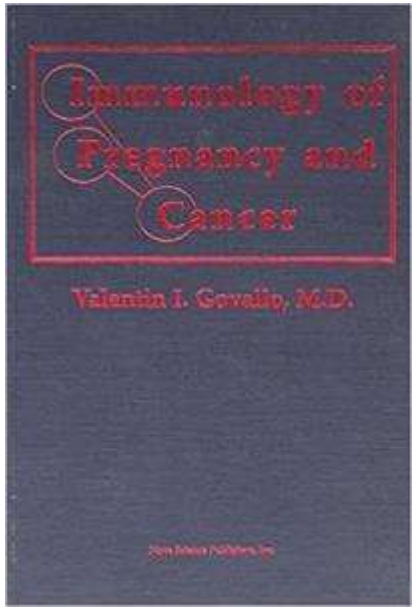


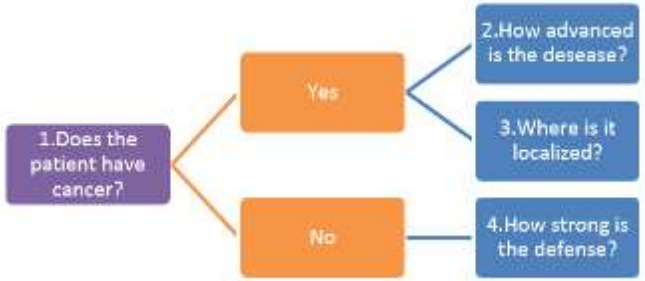
Line 3.
New diagnostic approaches

Early cancer detection
&
Early vascular atherosclerosis prediction.

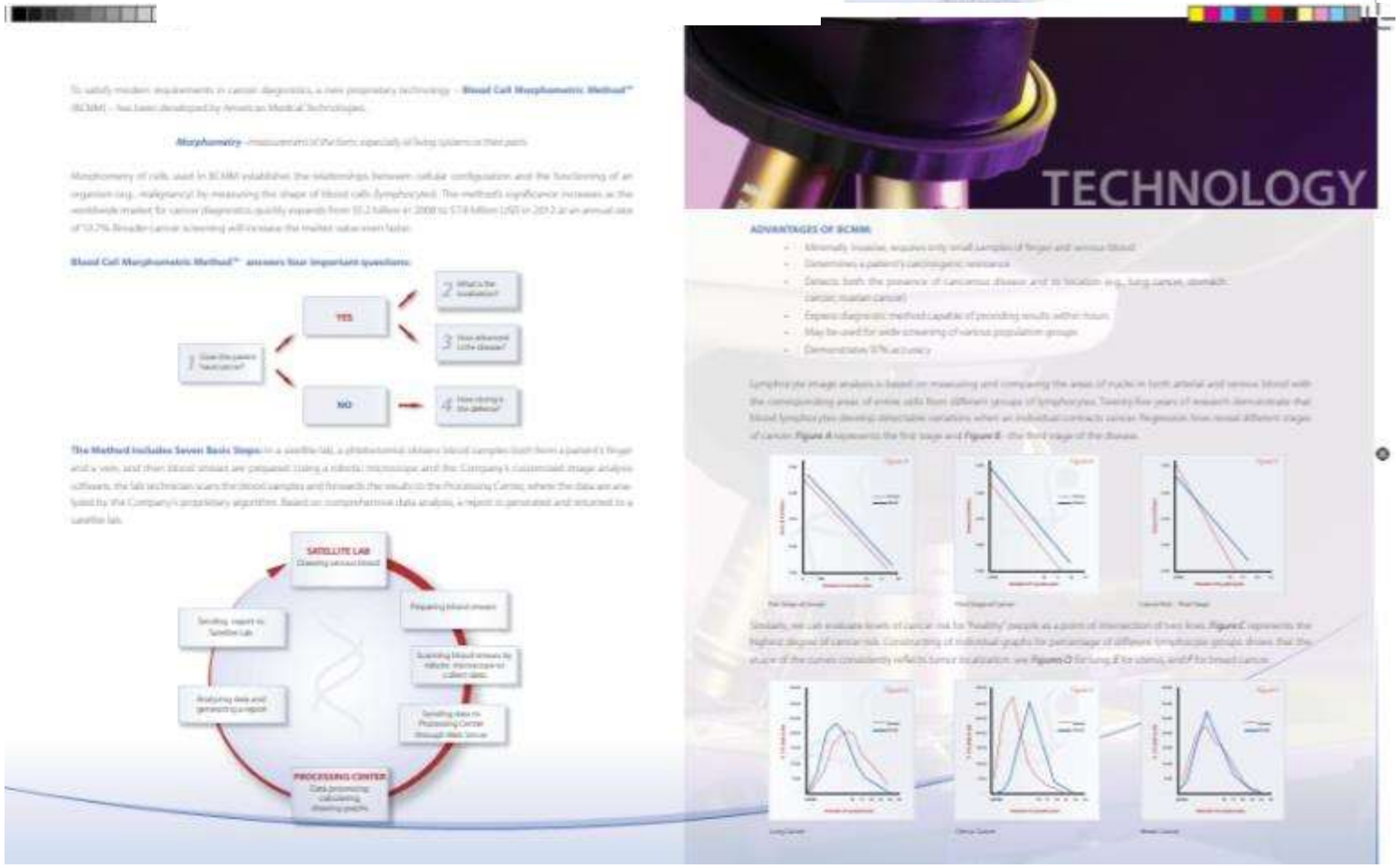
Blood Cell Morphometric Method (BCMM)

Professor Valentin I. Govallo, M.D. Ph.D., D.SCI. Member of the Russian Academy of Medicine





Dr. Evgenia S. Skobeltzin



СПОСОБ ДИАГНОСТИКИ ОПУХОЛЕВЫХ ЗАБОЛЕВАНИЙ ЧЕЛОВЕКА 2005 PCT
WO 2007/021211 Blood Cell Morphometric Method (BCMM)

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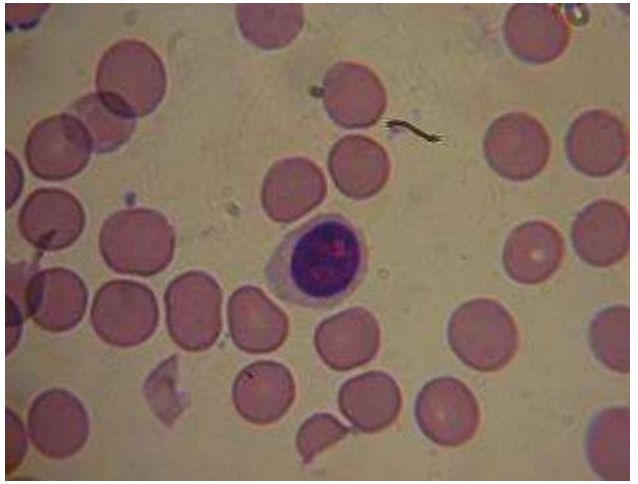
Декларация в соответствии с правилом 4.17:
— *об авторстве изобретения (правило 4.17 (iv))*

Опубликована:
— *с отчётом о международном поиске*

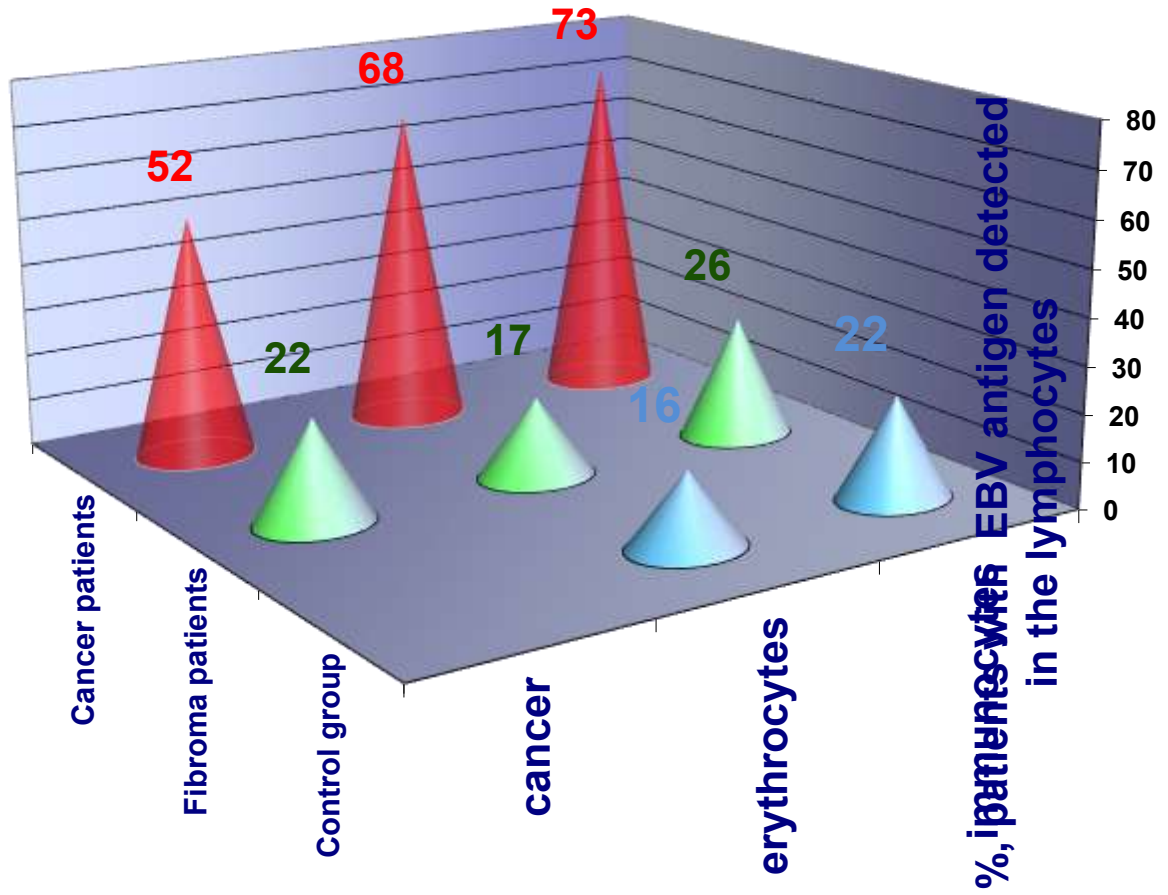
В отношении двухбуквенных кодов, кодов языков и других сокращений см. "Пояснения к кодам и сокращениям", публикуемые в начале каждого очередного выпуска Бюллетеня PCT.



Herpes virus Statistics

- More than 80% of the adult population has oral herpes and a recent study suggests this number could be 98% exposure among adults.
- One in five Americans have genital herpes (yet at least **80 percent** of those with herpes are **unaware they have it).**
- There are approximately one million new cases of herpes each year.
- 25 percent of American adults have symptomatic genital herpes.

Amount in % Epstein-Barr virus (EBV) infected population

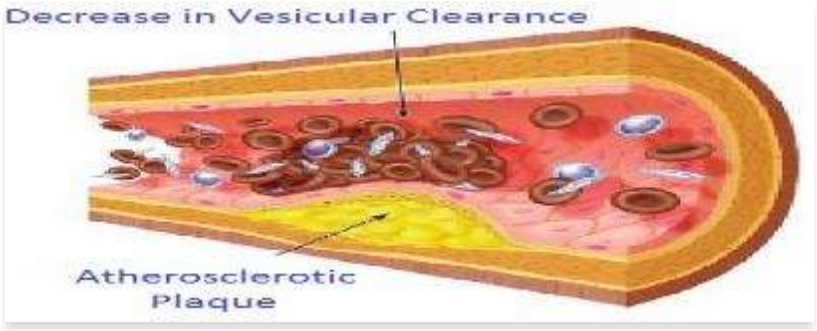


Cancer patients – patients with cancer of uterus, **Control group**- patients with acute Epstein-Barr virus, EBV-infection without cancer (mononucleosis, lymphadenitis etc.)

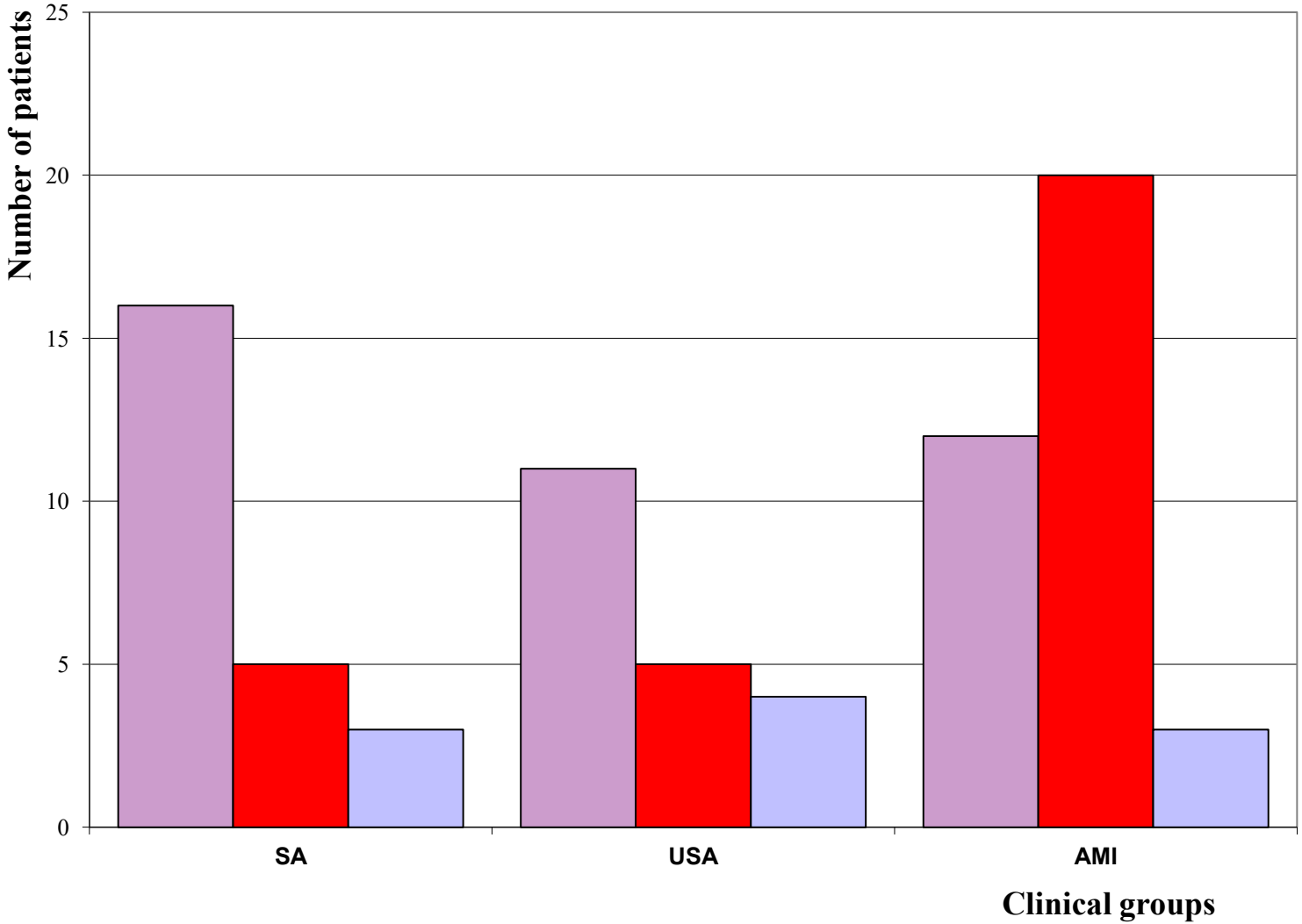
Criteria is infection by 50% or more by EBV

Herpes virus infection and CHD (> 50% EBV) (our data, 1998 - 2008)

Correlation of patients with Herpes virus infection and **Coronary Heart Disease (CHD)** in a different clinical groups (> 50% EBV) (our data, 1998 - 2008)



CHD- coronary heart disease
CMV- cytomegalovirus
HSV- herpes simplex virus
SA- stable angina
USA- unstable angina
AMI- acute myocardial infarction



Observing World Through “prism of Davinci Window” of house where he was born has been extremely productive

Acknowledgements 2

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NOIGEL, LLC

- Поздравляю всех с нашим замечательным праздником 95-летием со дня рождения Генриха Сауловича Альтшуллера и Международным Днем ТРИЗ!
- Сегодня мы поздравляем не только человека — сегодня мы разговариваем с эпохой-эпохой ТРИЗ.
- Генриху Сауловичу исполнилось сегодня 95 лет. Он навсегда останется в нашей памяти молодым и энергичным, и будет вдохновлять нас на новые идеи, свершения, задумки: **Мысли, Свершения, Мечты**. Уверен, что Генрих Саулович поддержал бы и одобрил нас, как продолжателей развития своего детища. С Международным Днем ТРИЗ, с юбилеем! Пусть рядом будут ученики, последователи, верные друзья! Побольше позитива, улыбок и прекрасного настроения!

TRIZ IN MEDICINE
(Optimistic Vision of Future)

"I have only made this letter longer because I have not had the time to make it shorter."
Blaise Pascal

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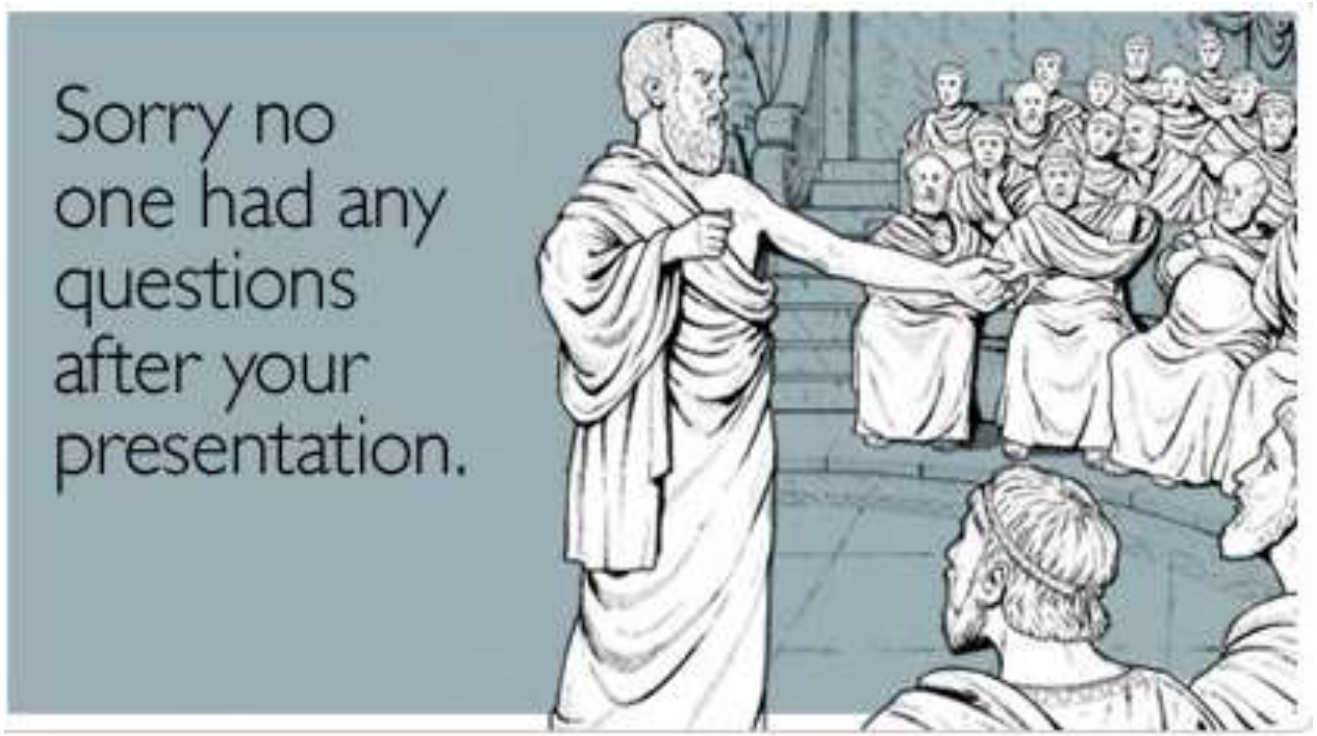
Q&A


Sorry no one had any questions after your presentation.