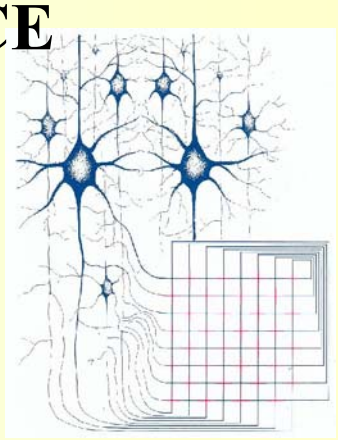
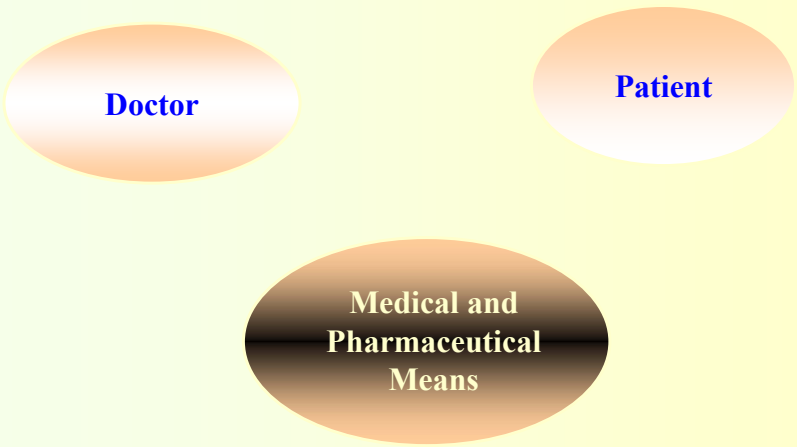
COMPUTATIONAL INTELLIGENCE

Medical Diagnostic Systems

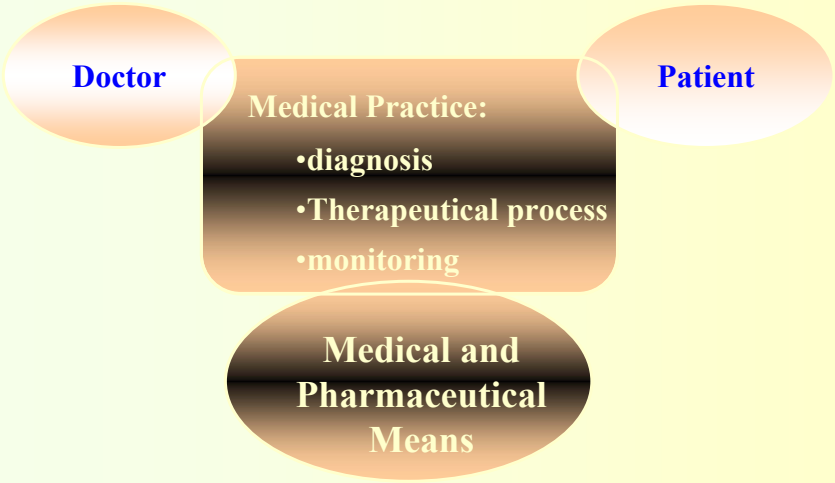


Christos N. Schizas, Professor of Artificial Intelligence

SYSTEM: Doctor-Patient-Means



Medical Practice



Main Target

- Improvement of citizen quality of life

RESULT

- Without any technical or geographical constrain

TOPICS

- Artificial Intelligence (Computational Intelligence)
- Biological Neuron
- Biological Neural Network
- Artificial Neuron
- Artificial Neural Networks
- Learning
- Applications

What is Intelligence

Difficult to Define.
It is roughly:

Η γενική ικανότητα που εκφράζεται μέσα από τις διαδικασίες υπολογισμών, λογικής, διακρίβωσης, μάθησης, γλώσσας, και εξοικείωσης σε νέο περιβάλλον.

Intelligence is the general mental ability involved in processes such as calculating, reasoning, classifying, learning, the use of language, and adjusting to new situations.

Computational Intelligence

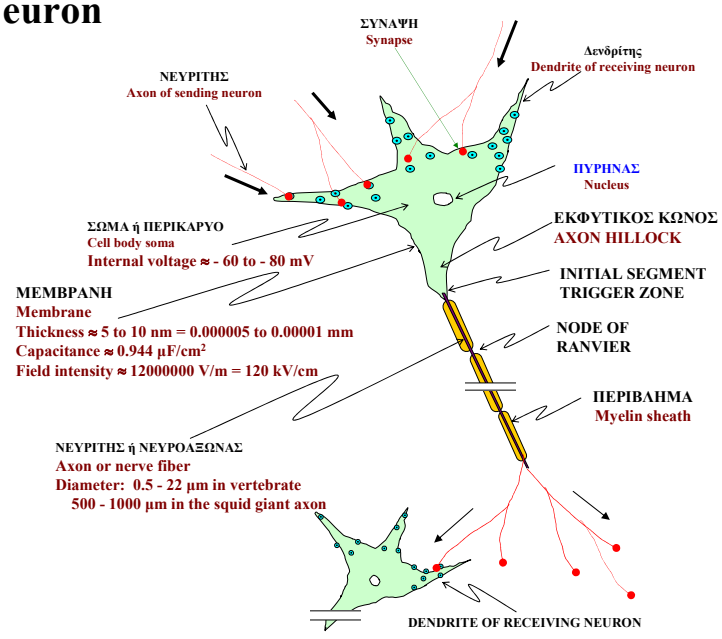
Tools and Means

- Artificial Neural Networks
- Artificial Life
- Genetic Algorithms
- Fuzzy Logic

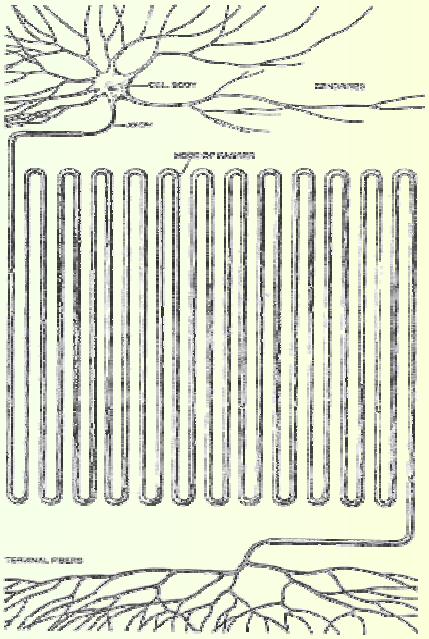
Biological Neuron

General Description

Biological Neuron

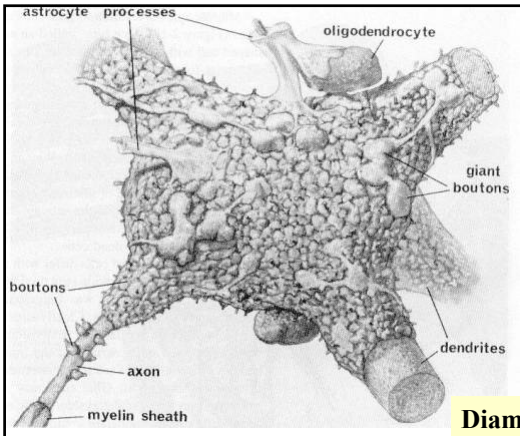


NEURON



The typical neuron of a vertebrate animal can carry time impulses for a considerable distance. The neuron depicted here, with its various parts drawn to scale, is enlarged 250 times. The nerve impulses originate in the cell body, and are propagated along the axon, which may have one or more branches. This axon, which is folded for diagrammatic purposes, would be a centimeter long at actual size. Some axons are more than a meter long. The axon's terminal branches form synapses with as many as 1,000 other neurons. Most synapses join the axon terminals of one neuron with the dendrites forming a "tree' around the cell body of another neuron. Thus the dendrites surrounding the neuron in the diagram might receive incoming signals from tens, hundreds, or even thousands of other neurons. Many axons, such as this one are insulated by a myelin sheath interrupted at intervals by the regions known as nodes of Ranvier.

[Caption and figure from C. F. Stevens 1979, "The neuron,- The Brain", Scientific American]

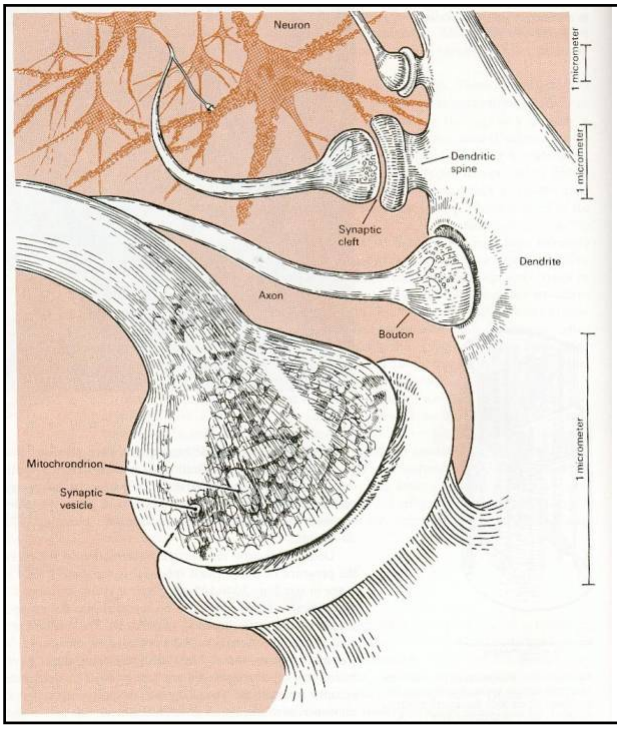


Synapse

Diameter ≈ 1 µm = 0.001mm
Gap ≈20 to 40 nm = 0.00002 to 0.00004 mm
Diameter/Gap ratio ≈ 100

Delay in the transmission of the pre-synaptic potential to a post-synaptic potential ≈ 0.3 to 1.0 ms

Velocity ≈ 0.2 cm/minute

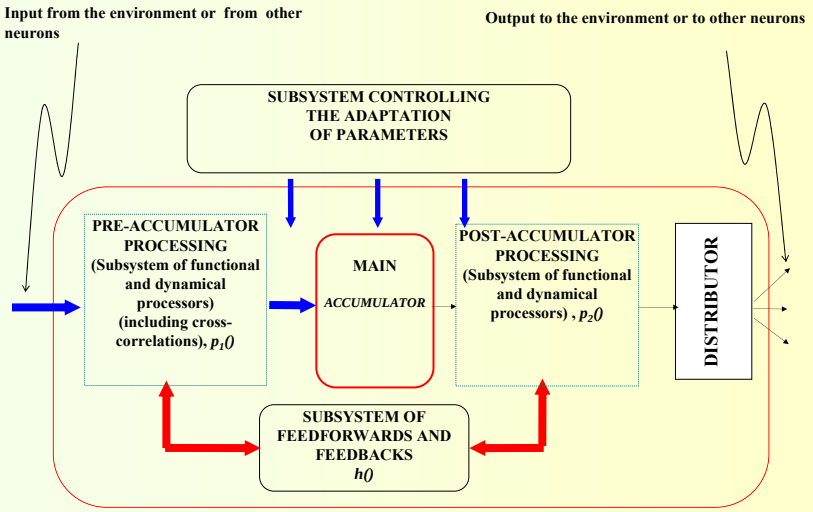


Synapse

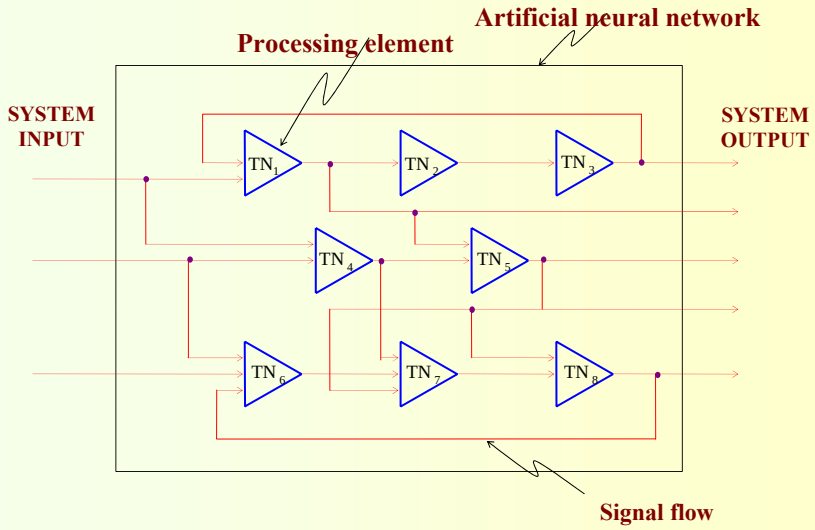
Artificial Neuron

- Software simulation
- Electronic or Biological construction

General form of a single-neuron model



Artificial neural network



Which are the main topics

- To understand how humans conceive, think and decide
- To build machine that simulate this human functioning and especially decision making under uncertainty and missing data

Artificial Neural Nets in Computer-Aided Macro Motor Unit Potential Classification

Christos N. Schizas*, Constantinos S. Pattichis+, Ian S. Schofield+, Peter R. Fawcett+, and Lefkos T. Middleton*
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+Department of Clinical Neurophysiology
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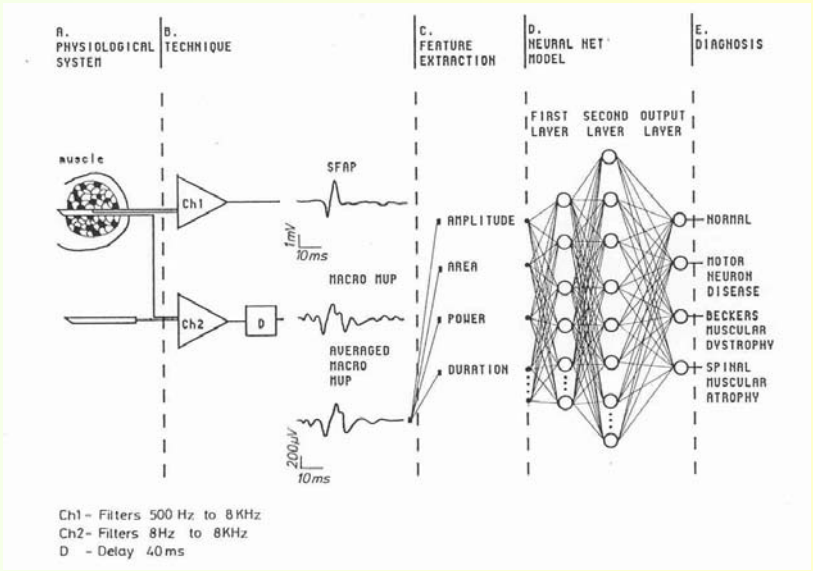
Newcastle Upon Tyne, U.K.

The electrical activity of muscle has been extensively studied since the beginning of the century. The rapid technological developments of succeeding years have permitted precise measurement of the properties of individual muscle fibers and the functional groups that constitute the motor unit.

A motor unit consists of 2 to 1000 fibers innervated by one motor nerve axon and hence the fibers discharge synchronously at rates typically between 2 and 30 Hz. A variety of techniques have been used to measure the motor unit potential (MUP), such as macro electromyography (EMG) introduced by Stalberg [1] in 1980. The macro EMG method uses a special needle electrode with a 15mm long by 0.8mm diameter cannula, with a 25μm diameter side port electrode 7.5mm from the tip. The side port electrode records the activity of one or more single muscle fibers from an individual motor unit recruited by gentle voluntary contraction of the muscle. The single fiber action potentials (SFAP) are used to trigger a signal averager into which the cannula signal is fed (Fig. 1). In general, about 200 discharges of the unit are averaged over an 80 ms sweep time to obtain a macro motor unit potential (MMUP). At least 20 potentials are measured from a single muscle to obtain a reasonable estimate of the parameters of an average motor unit potential.

The MMUP data is analyzed by means of the peak-to-peak amplitude and the integral of the central 50 milliseconds of the signal. An additional parameter to estimate the duration of the potential has been introduced [2], which is the 90 percent power duration. This is the width of the region of the potential that contains 90% of the power. Normal ranges for the amplitude and area by age decade have been obtained by Stalberg and Fawcett [3]. Following extensive simulation



Neural Network Models in EMG Diagnosis

Constantinos S. Pattichis, *Member IEEE*, Christos N. Schizas, *Senior Member, IEEE*, and Lefkos T. Middleton

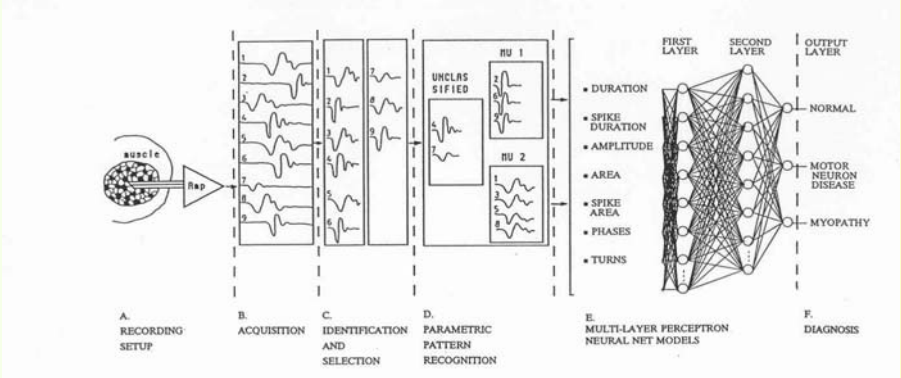


Fig. 1. An integrated system for computer-aided EMG using multilayer neural networks.

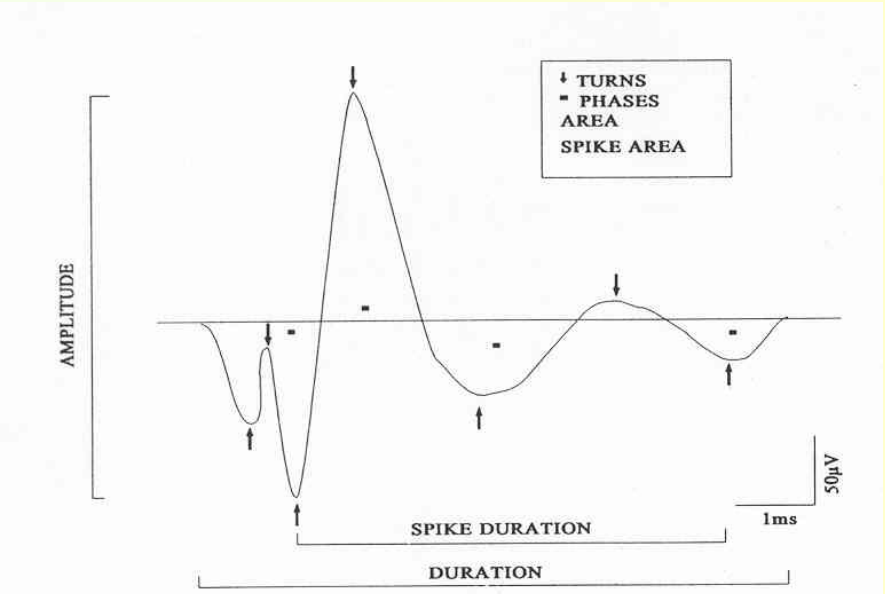


Fig. 2. MUAP parameters.

TABLE V
NEURAL NETWORK BACK PROPAGATION EMG MODELS

Model	Architecture	Weights	Gain (η)	Momentum (α)	Epochs	TSS	Training Time* (seconds)		Training	Evaluation						
							One epoch	Total	%CCs	%CCs	%FPs	%FNs	SE	SP	RE	PR
1	14-10-5-3	205	0.01	0.01	17316	0.89	0.124	2147	100	85	0	21	79	100	79	100
2	14-10-5-3	205	0.01	0.1	15745	0.89	0.124	1952	100	85	0	21	79	100	79	100
3	14-10-5-3	205	0.05	0.5	1867	0.89	0.124	231	100	85	0	21	79	100	79	100
4	14-10-5-3	205	0.1	0.5	1333	0.66	0.124	165	100	80	17	21	79	83	79	91
5	14-40-10-3	990	0.01	0.01	3745	0.89	0.529	1981	100	90	0	14	86	100	86	100
6	14-40-10-3	990	0.1	0.1	392	0.86	0.529	207	100	90	0	14	86	100	86	100
7	14-40-10-3	990	0.5	0.5	136	0.89	0.529	72	100	85	0	21	79	100	79	100
8	14-100-10-3	2430	0.01	0.01	2940	0.89	1.3	3822	100	90	0	14	86	100	86	100
9	14-100-10-3	2430	0.1	0.1	279	0.89	1.3	363	100	90	0	14	86	100	86	100
10	14-100-10-3	2430	0.5	0.5	81	0.89	1.3	105	100	90	0	14	86	100	86	100

*Measured on an NCR 3445 PC486 machine running at 33 MHz.

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Medical diagnostic systems: a case for neural networks

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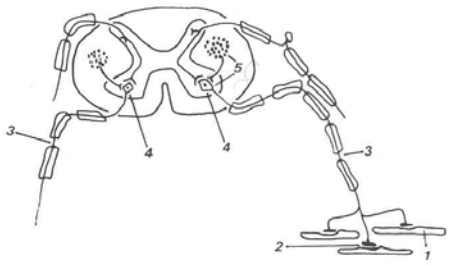
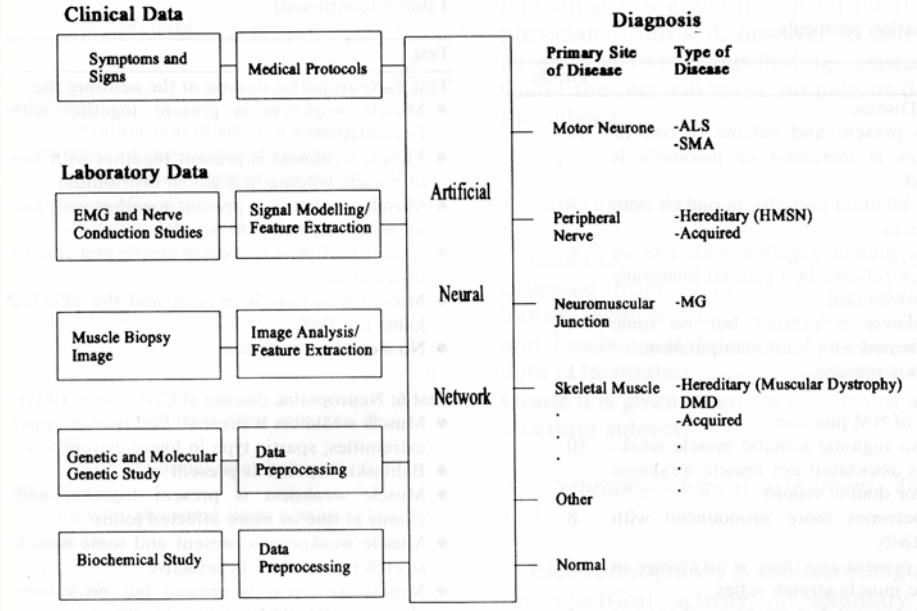


Fig. 1. Schematic diagram of the spinal cord, motor neuron, its axon (peripheral nerve), and muscle showing the sites of dysfunction of various neuromuscular disorders. Disease may affect function at: 1. Skeletal muscle (e.g. muscular dystrophy) 2. Neuromuscular junction (e.g. myasthenia gravis) 3. Peripheral nerve (e.g. chronic lead poisoning) 4. Motor neuron (e.g. spinal muscular atrophy) 5. Motor neuron plus one or more central pathways (e.g. amyotrophic lateral sclerosis).

Table 1
Selected material that was used during the training and evaluation phases

Type	Training	Evaluation	Age Range
DMD	10	7	1–18
MG	12	6	31–78
SMA	4	3	1–30
ALS	3	2	43–71
NOR	12	12	10–60
Total	41	30	



Analysis describing the factors that were taken into consideration for developing the clinical examination protocols

Anatomically in terms of	Pathologically in terms of	Muscle weakness in association with
Skeletal muscle	Congenital	Distribution
Motor endplate	Traumatic	Muscle volume
Peripheral nerve	Inflammatory	Muscle stretch reflex
• axon	Toxic	Altered muscle tone
• nerve root	Metabolic	Spontaneous muscle activity
• cell body	Neoplastic	Diagnostic phenomenon if any
Central nervous system	Vascular or degenerative etiologies	

Table 3
Clinical examination protocols

Test	Grade
Test 1: Muscle Disease	
• Weakness is present and volume of one or more muscles is increased or myotonia is demonstrated	10
• Weakness is bilateral and affects one or both girdles primarily.	8
• Weakness is present together with loss of muscle stretch reflexes in a general bilaterally symmetric distribution	6
• Muscle weakness is present but no tonic change is detected with joint manipulation.	4
• No weakness is present	1

Test 2: Disease of NM junction

● In addition to regional somatic muscle weakness, there is associated eye muscle weakness (ptosis and/or double vision)	10
● Weakness becomes more pronounced with sustained activity	8
● Weakness is present and there is no change in quality of the muscle stretch reflex	6
● Weakness is present but no tonic change is detected with joint manipulation	4
● Weakness is present but no change in volume of any muscle is noted	3
● No weakness is present	1

Test 3: Neuropathic disease affecting the axon

● Weakness is present together with loss of muscle volume limited to distribution of given nerve(s)	10
● Weakness is present with reflex diminution or loss limited to the distribution of given nerve(s)	8
● Muscle weakness is present clearly limited to the distribution of given nerve(s)	6
● Muscle weakness is present and the affected joint(s) is/are flail	4
● No weakness is present	1

Test 4: Neuropathic disease at the nerve root

- Muscle weakness is present together with loss of muscle volume limited to distribution of given nerve root(s) — 10
- Muscle weakness is present together with diminution or loss of muscle stretch reflex limited to the distribution of given nerve root(s) — 8
- Muscle weakness is present clearly limited to the distribution of given nerve root(s) — 6
- Muscle weakness is present and the affected joints are flail — 4
- No weakness is present — 1

Test	Grade
Test 5: Neuropathic disease at the neurone site	
• Muscle weakness is present together with fasciculations	10
• Muscle weakness is present together with loss of muscle volume in a global distribution	9
• Muscle weakness is present together with loss of muscle stretch reflexes globally	8
• Muscle weakness is present clearly global in its distribution	6
• Muscle weakness is present and the affected joints are flail	4
• No weakness is present	1

Test 6: Neuropathic disease at CNS [a] level (ALS)	
• Muscle weakness is present: flail type in upper extremities; spastic type in lower extremities	10
• Babinski response is present	9
• Muscle weakness is present together with clonus at one or more affected joints	8
• Muscle weakness is present and some muscle stretch reflexes are hyperactive	6
• Muscle weakness is present but no volume change is detected	4
• No weakness is present	1

[a] CNS: Central Nervous System

Table 4
Laboratory examination protocols

Test	Grade
Test 1: Needle EMG	
• Presence of denervation potentials (fasciculations or fibrillations) at rest, reduced recruitment pattern with increased duration, amplitude, and polyphasic MUAPs	3
• Spontaneous discharge of short duration MUAPs at rest, early recruitment pattern of low amplitude, short duration, and polyphasic MUAPs	2
• No activity at rest, normal recruitment pattern at voluntary activity	1

Test 2: Single fibre EMG

• Number of pairs with abnormal jitter greater than 10 out of 20	3
• Number of pairs with abnormal jitter between 3 to 9 out of 20	2
• Number of pairs with abnormal jitter less or equal to 2 out of 20	1

Test 3: Repetitive study

• Decrementing response (a reproducible decline in the amplitude of the M wave of successive responses to repetitive nerve stimulation) > 30%	3
• Decrementing response in the range of 11–30%	2
• Decrementing response < 10%	1

Test 4: Muscle biopsy

• Angular fibres, obvious grouping, large group atrophy	5
• Rare angular fibres, small group atrophy, tendency of grouping	4
• Round hypertrophic fibres, necrotic and regenerating fibres, splitting fibres	3
• Rare round fibres, splitting fibres, rare central nuclei, with increased connective tissue	2
• Polygonal fibres, normal presence of connective tissue, normal fibre distribution, absence of inflammation	1

Test 5: Genetic and molecular genetic assessment (specific for Duchenne Muscular Dystrophy (DMD))

• Deletion	3
• Duplication	2
• No deletion or duplication	1

Test 6: Serum creatine kinase (CK) level

• $CK \geq 1000$ IU/L	3
• 130 IU/L $\leq CK < 1000$ IU/L	2
• 10 IU/L $\leq CK < 130$ IU/L	1

Test	Grade
Test 7: Tensilon test	
• Obvious improvement of weakness	3
• Mild improvement of weakness	2
• No improvement of weakness	1
Test 8: Anti Acetylcholine antibodies	
• Present at high level	3
• Rare antibodies	2
• Absence of antibodies	1

Table 5
Feature vectors from selected subjects

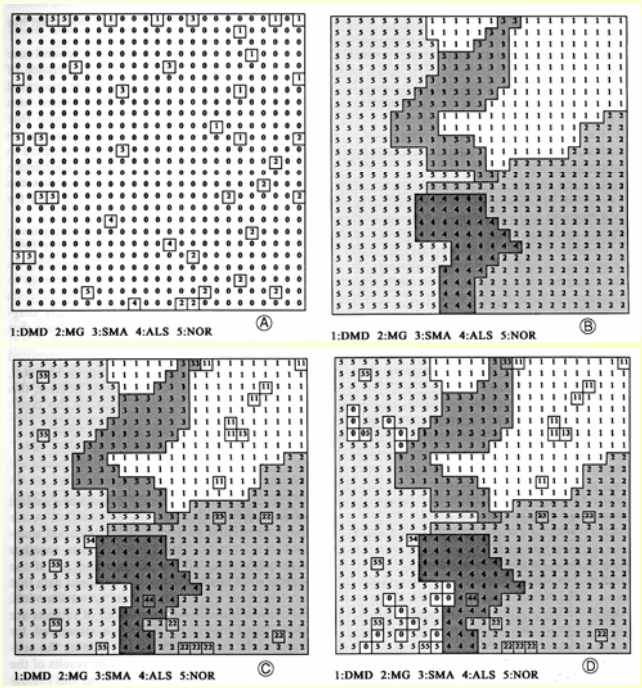
Subject	DMD2	MG8	SMA4	ALS2	NOR6
Sex (Male = 0, Female = 1)	0	0	1	0	0
Age	7	46	28	53	30
Clinical Data					
Protocols:					
• Test 1	8	6	6	0	1
• Test 2	4	8	0	3	1
• Test 3	0	0	0	0	1
• Test 4	0	0	0	0	1
• Test 5	6	6	9	6	1
• Test 6	0	4	0	10	1
Laboratory Data					
EMG and NCS:					
• Test 1	2	1	3	3	1
• Test 2	0	3	0	0	1
• Test 3	0	2	0	0	1
Muscle biopsy:					
• Test 4	2	0	4	5	1
Molecular Genetic Assessment:					
• Test 5	3	0	0	0	0
Biochemical:					
• Test 6	3	0	0	0	0
• Test 7	0	3	0	0	0
• Test 8	0	2	0	0	0

Table 6
Selected models trained with clinical data

Model	Grid size	Diagnostic yield					
		Epochs (1550)			Epochs (3150)		
		TR%	EV%		TR%	EV%	
			CM = 0	CM = 90		CM = 0	CM = 90
1	8× 8	92	86	73	92	86	86
2	10×10	97	93	73	97	93	80
3	15×15	100	93	80	100	93	86
4	20×20	100	90	76	100	90	76
5	25×25	100	93	86	100	93	86

Table 7
Models trained with combined clinical and laboratory data

Model	Grid size	Diagnostic yield					
		Epochs (1550)			Epochs (3150)		
		TR%	EV%		TR%	EV%	
			CM = 0	CM = 90		CM = 0	CM = 90
1	10×10	97	93	73	97	93	80
2	15×15	97	93	80	97	93	73
3	25×25	97	90	83	97	90	83
4	40×40	97	96	90	97	96	90
5	60×60	100	100	90	100	100	90



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- C.S. Pattichis, and C.N. Schizas, *Genetics-Based Machine Learning Models for the Diagnosis of Certain Neuromuscular Disorders*, **IEEE Transactions on Neural Networks,** Vol. 7, No. 2, pp. 427-439, 1996.

The Terms

Hybrid System and

Integrated System

Like it is in a medical environment

Hybrid System:

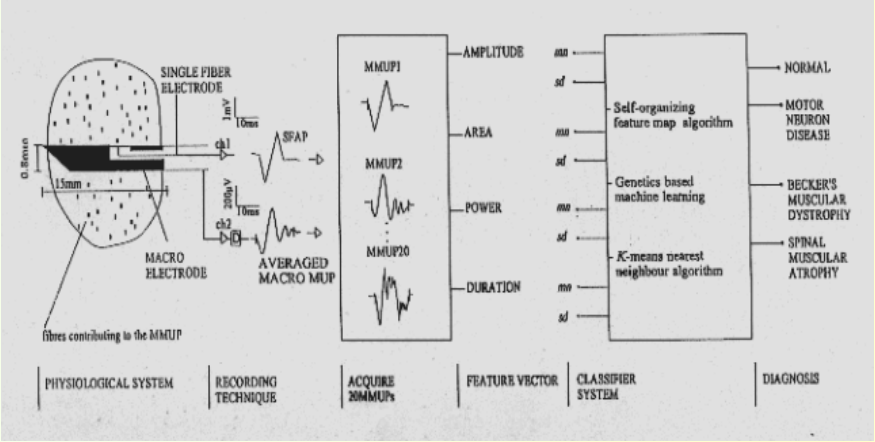
- A case is examined by many specialists of the same specialization
- A Medical Council is called for reaching final conclusion

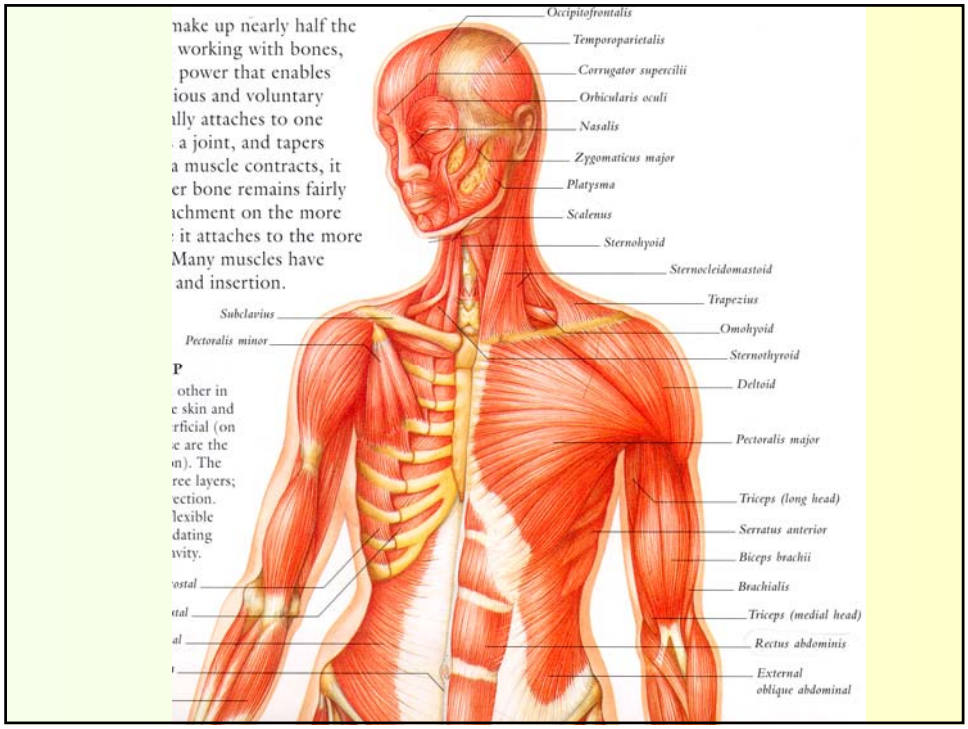
Integrated System:

- A case is examined by many specialists of different, but relevant specializations.
  (e.g. a subject that is suspected of a neuromuscular disorder is examined separately by a clinical neurologist, a histopathologist, and a geneticist)

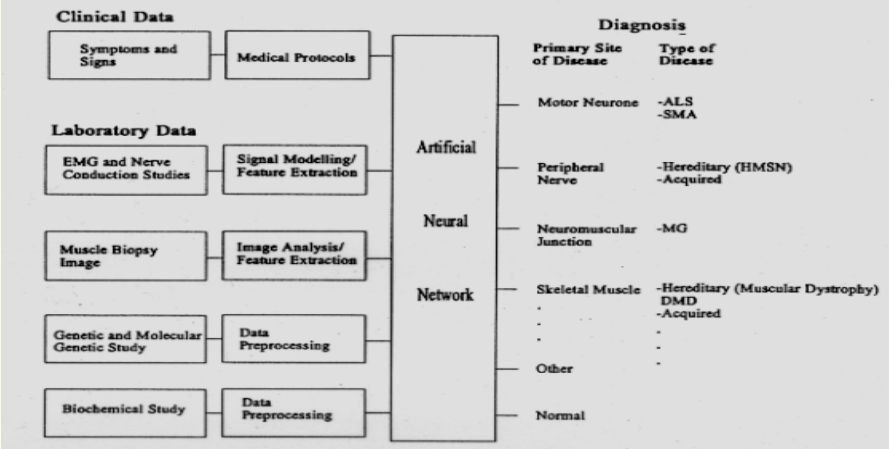
- A Medical Council is called for reaching final conclusion.

Hybrid System, for the diagnosis of neuromuscular disorders





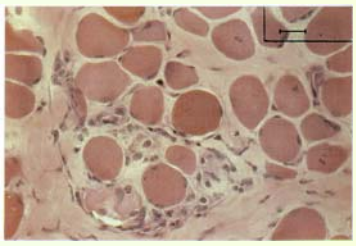
Integrated System, ***for the diagnosis of neuromuscular disorders***



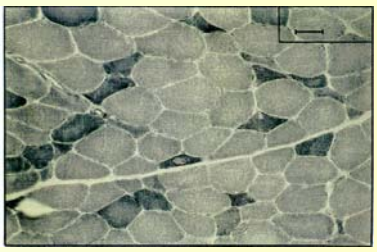
Test 1: Muscle Disease

Test	*Grade*
• Weakness is present and volume of one or more muscles is increased or myotonia is demonstrated.	10
• Weakness is bilateral and affects one or both girdles primarily.	8
• Weakness is present together with loss of muscle stretch reflexes in a general bilaterally symmetric distribution.	6
• Muscle weakness is present but no tonic change is detected with joint manipulation.	4
• No weakness is present.	1

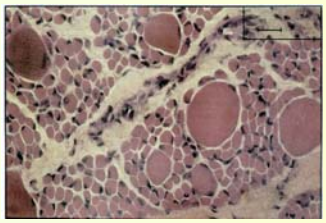
Clinical Examination Protocol



Muscle biopsy of a DMD subject. Staining with H&E, showing variation in fibre size, increase in connective tissue.



Muscle biopsy of a MND subject. Staining for NADH, showing dark colored angular fibres among light colored normal polygonal fibres.

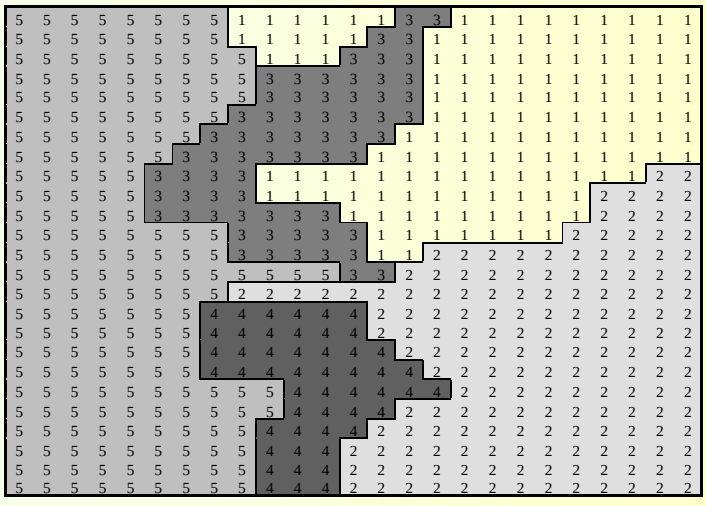


Muscle biopsy of a SMA subject. Staining with Gomoris Trichrome, showing hypertrophic fibers surrounded by a large group of atrophic fibres.

Test 4: Muscle Biopsy

Test	*Grade*
• Angular fibres, obvious grouping, large group atrophy.	5
• Rare angular fibres, small group atrophy, tenedency of grouping.	4
• Round hypertrophic fibres, necrotic and regenerating fibres, splitting fibres.	3
• Rare round fibres, splitting fibres, rare central nuclei, with increased connective tissue.	2
• Polygonal fibres, normal presence of connective tissue, normal fibre distribution, absence of inflammation.	1

Laboratory Examination Protocol

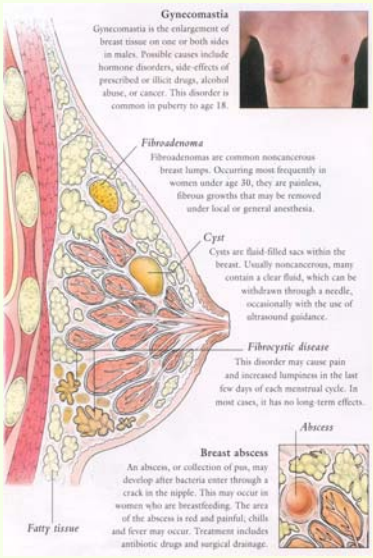


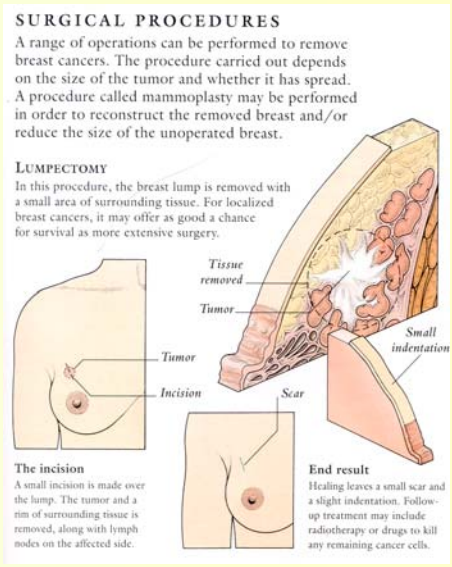
1:DMD 2:MG 3:SMA 4:ALS 5:NOR

Self Organizing Feature Map

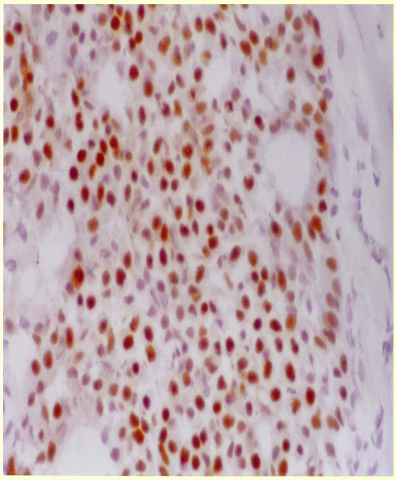
T. Kohonen

Breast Cancer





Ποσοτική αξιολόγηση των προγνωστικών παραγόντων του καρκίνου του μαστού



Manual, semi-quantitative, immunohistochemical score

% of Cells Positive	Score	Staining Intensity	Score	Total Score	Diagnostic Index
0	0	Negative	0	0	0
0–25%	1	Weak	1	1–4	1+
26–50%	2	Moderate	2	5–8	2+
51–75%	3	Strong	3	9–12	3+
≥76%	4	Very Strong	4	>13	4+

EPILOGE

- **Historical challenge**

  - Constructive use of technology

"To make predictions is difficult, especially for the future"

Niels Bohr

Thank you for your attention