

Salve Omnes

NEUROPLASTICITA' DEL BAMBINO

tra videogames e smartphone

ovvero...

Gravitazione

versus

Smartphone

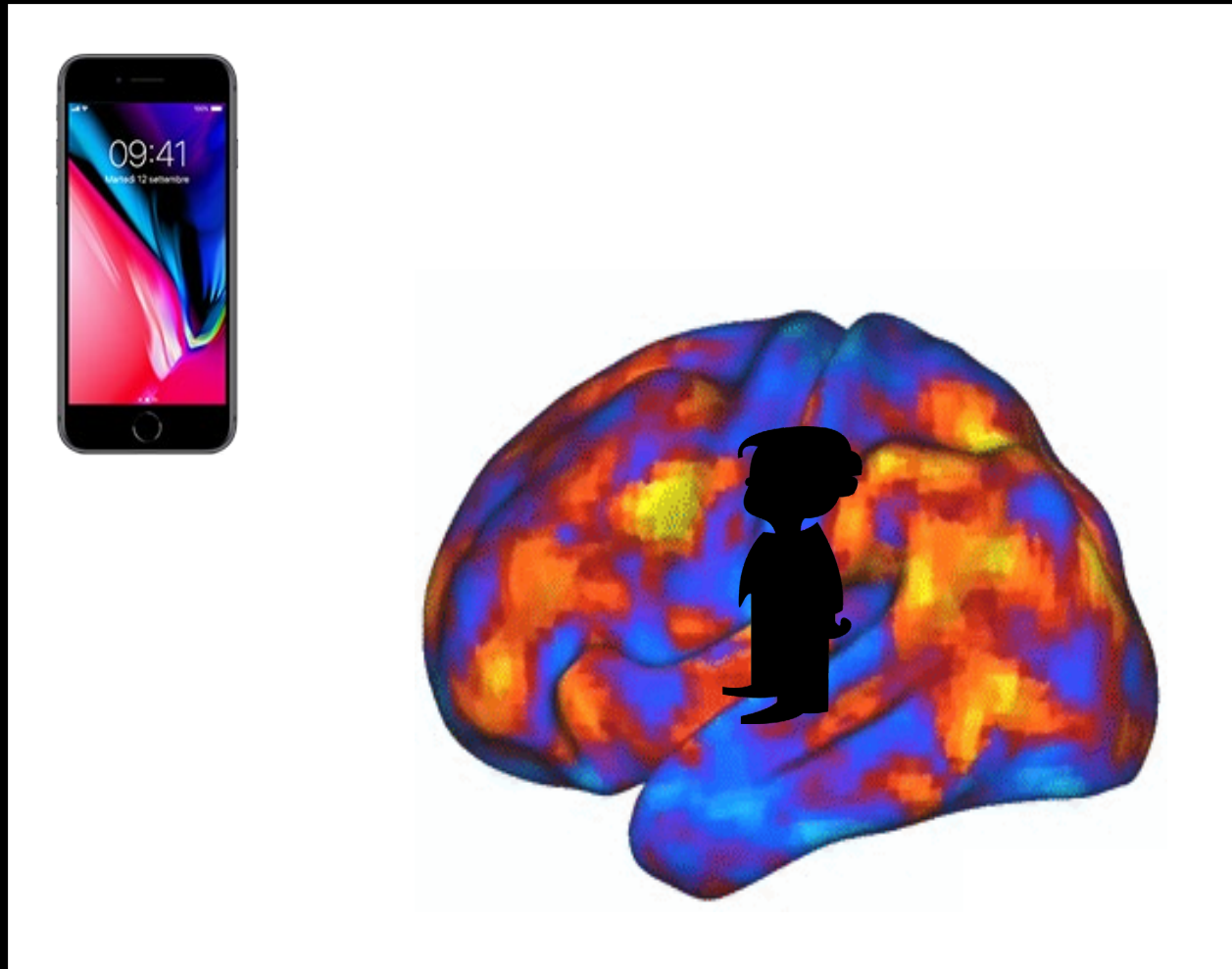
NEUROPLASTICITA' DEL BAMBINO

tra videogames e smartphone

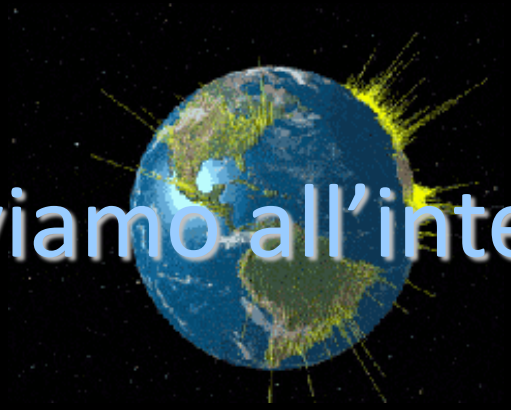


NEUROPLASTICITA' DEL BAMBINO

tra videogames e smartphone



Noi viviamo all'interno di un



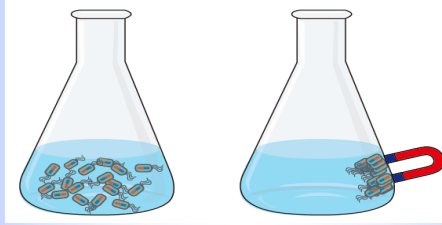
A diagram illustrating the Earth's magnetic field. The Earth is shown as a small globe in the center, with a vertical line representing the magnetic axis. Multiple concentric, glowing blue loops represent the magnetic field lines, which are denser near the poles and spread out at the equator. The background is a dark, starry space.

CAMPO MAGNETICO

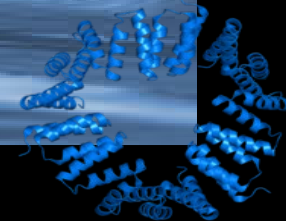
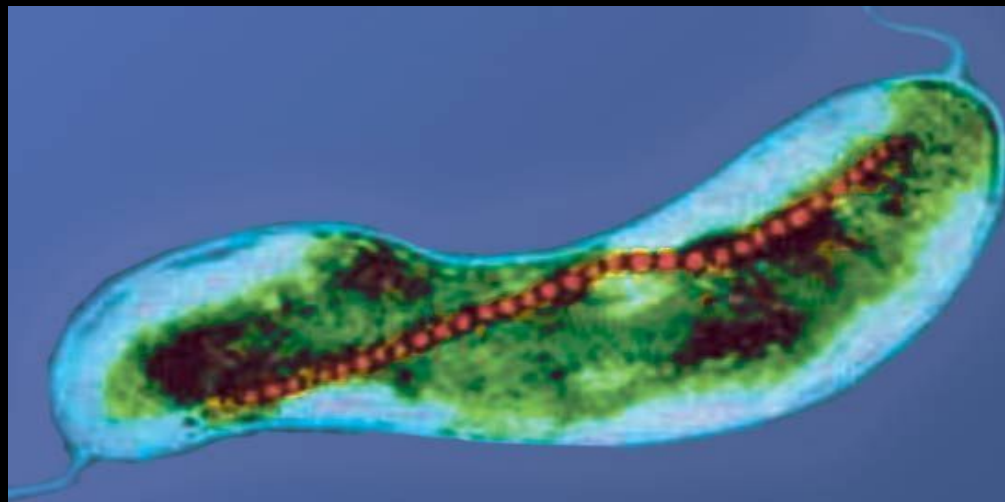
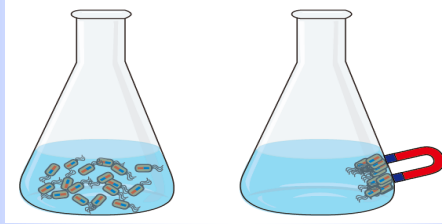
Viviamo come onde di energia
nel vasto oceano dell'energia.

Deepak Chopra





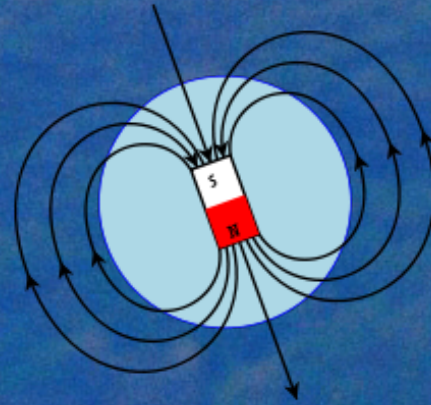
Batteri Magnetotattici



Uccelli migratori



Possiedono una mappa magnetica per riconoscere ed orientarsi lungo i campi geomagnetici di migrazione



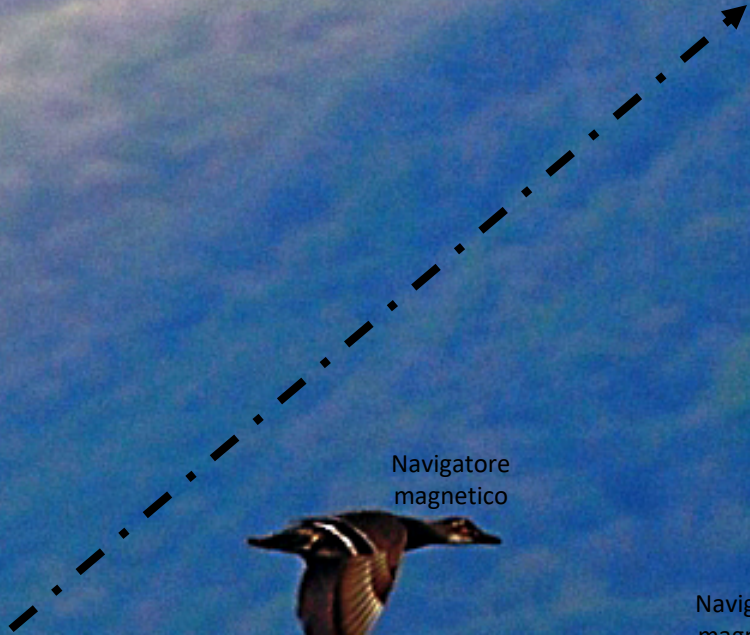
Navigatore
magnetico



Navigatore
magnetico



Pista Magnetica



Possediamo
MAGNETOSOMI ?



il nostro corpo è un
SISTEMA ELETTROMAGNETICO ?



Arch Pathol Lab Med. 1986 Jul;110(7):618-21.

Identification and significance of magnetite in human tissues.

Moatamed F & Johnson FB.

Identification of **magnetite in** human tissue has been mainly based on **magnetometry**. The iron-containing particles from the digestion procedure were aligned in a parallel manner along the north-south poles of the magnet and were confirmed to be magnetite by **x-ray diffraction**.

Nature. 1983 Jan 6;301(5895):79-80.

Magnetic bones in human sinuses.

Baker RR,

We report here that bones from the region of the **sphenoid/ethmoid sinus** complex of humans are magnetic and contain deposits of ferric iron.

Nihon Eiseigaku Zasshi. 2001 Jul;56(2):523-7.

Study of remanent magnetization of the human body: lung and liver tissues

Sakai H

This finding indicates that both **lung and liver** tissues contain magnetic materials.

Bioelectromagnetics. 1992;Suppl 1:101-13.

Magnetite in human tissues: a mechanism for the biological effects of weak ELF magnetic fields.

Kirschvink JL et al.

Including humans, biochemically precipitate the **ferrimagnetic mineral magnetite (Fe₃O₄)**. A simple calculation shows that magnetosomes moving in response to **earth-strength ELF** fields are capable of opening **trans-membrane ion channels**, in a fashion similar to those predicted by ionic resonance models.

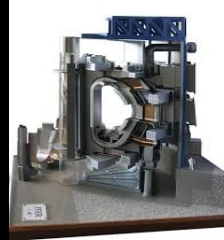
Proc Natl Acad Sci U S A. 1992 Aug 15;89(16):7683-7.

Magnetite biomineralization in the human brain.

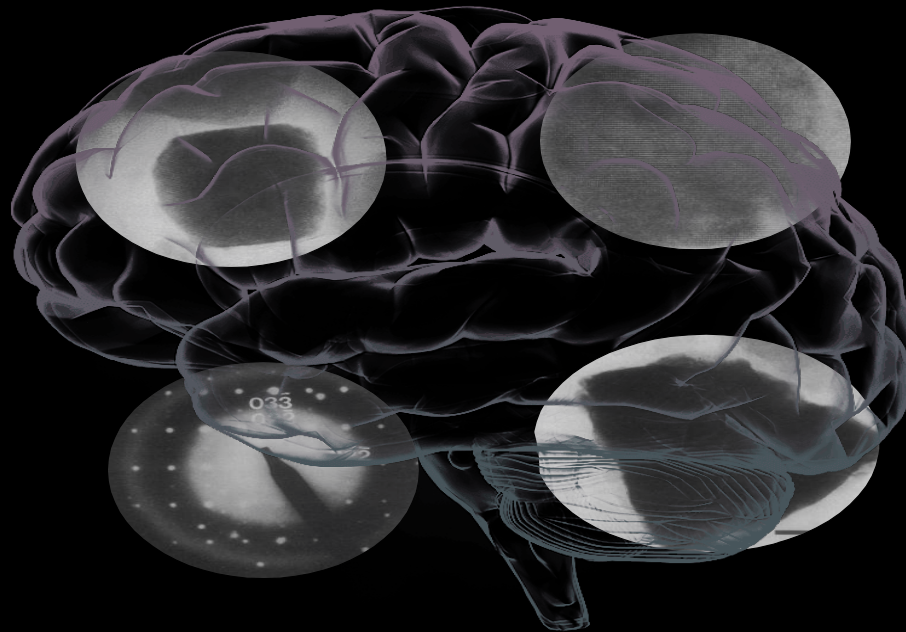
Kirschvink JL et al.

SQUID

Superconducting Quantum
Interference Devices

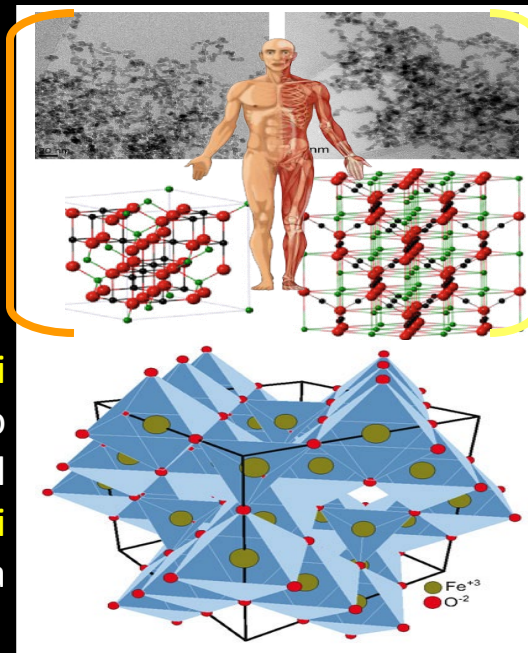


Microscopia elettronica trasmissione HR
Diffrazione elettronica
Analisi elementi costitutivi



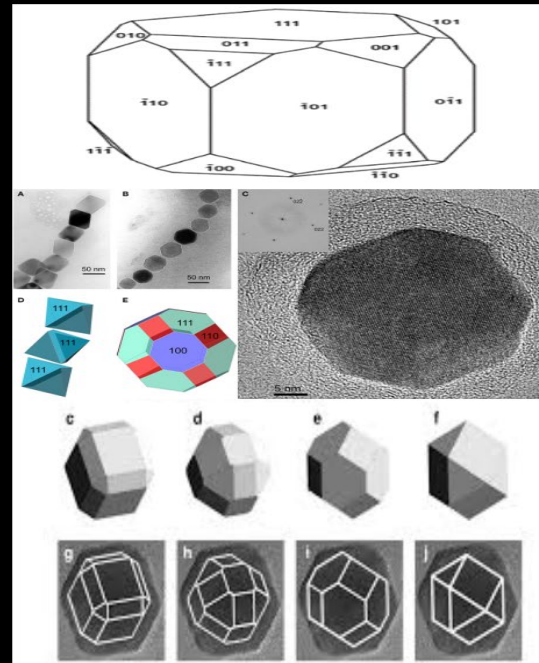
Magnetite

Presenza di un minimo di **5 milioni di cristalli a dominio singolo** per grammo per la maggior parte dei tessuti nel cervello e oltre **100 milioni di cristalli** per grammo per pia e dura

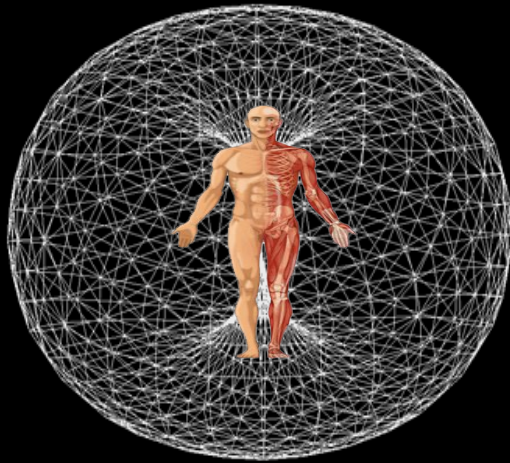


Maghemite

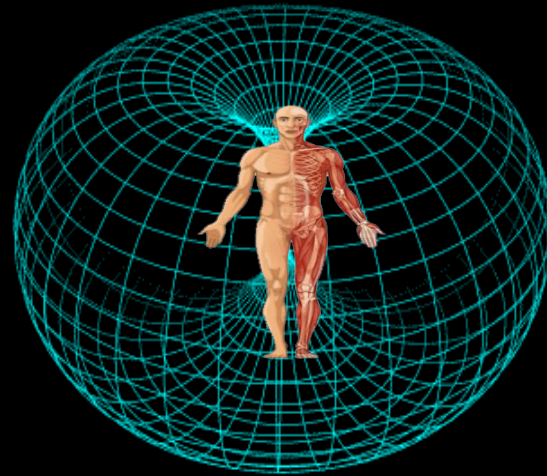
La **magnetite biogenica** nel cervello umano può spiegare gli effetti di saturazione ad alto campo osservati nei valori $T1$ e $T2$ della risonanza magnetica e, **forse, per una varietà di effetti biologici dei campi magnetici a bassa frequenza**



ELETTROMAGNETISMO



Campi elettrici



Campi magnetici



ISTANBUL

Giugno 2004

INVISIBLE KILLER



The International EMF Project

investigates health effects of electromagnetic fields

advises national authorities on EMF radiation protection

THE SPECTRUM
People all over the world are exposed to electromagnetic fields (EMF) to varying degrees, and the levels of exposure will increase as technology advances further. These EMF are found in the non-ionizing part of the electromagnetic spectrum (between 0 and 300 GHz) and are emitted from common sources such as power lines and cellular phones. They are different to ionizing radiations, such as X-rays and gamma rays, which have enough energy to break molecular bonds.

STATIC **INTERMEDIATE FREQUENCIES**

EXTREMELY LOW FREQUENCIES **RADIO FREQUENCIES**

www.who.int/emf/

A composite image for the International EMF Project. It includes a spectrum diagram with frequency markers (0Hz, 50Hz, 100Hz, 500Hz, 1000Hz, 100MHz, 100GHz) and labels for 'STATIC', 'INTERMEDIATE FREQUENCIES', 'EXTREMELY LOW FREQUENCIES', and 'RADIO FREQUENCIES'. The diagram is color-coded from blue (low frequency) to red (high frequency). Other elements include a red train, a person in a green protective suit, a power line tower, and a woman on a mobile phone.

Killer invisibili

Il tempo, la forza di gravità e l'amore

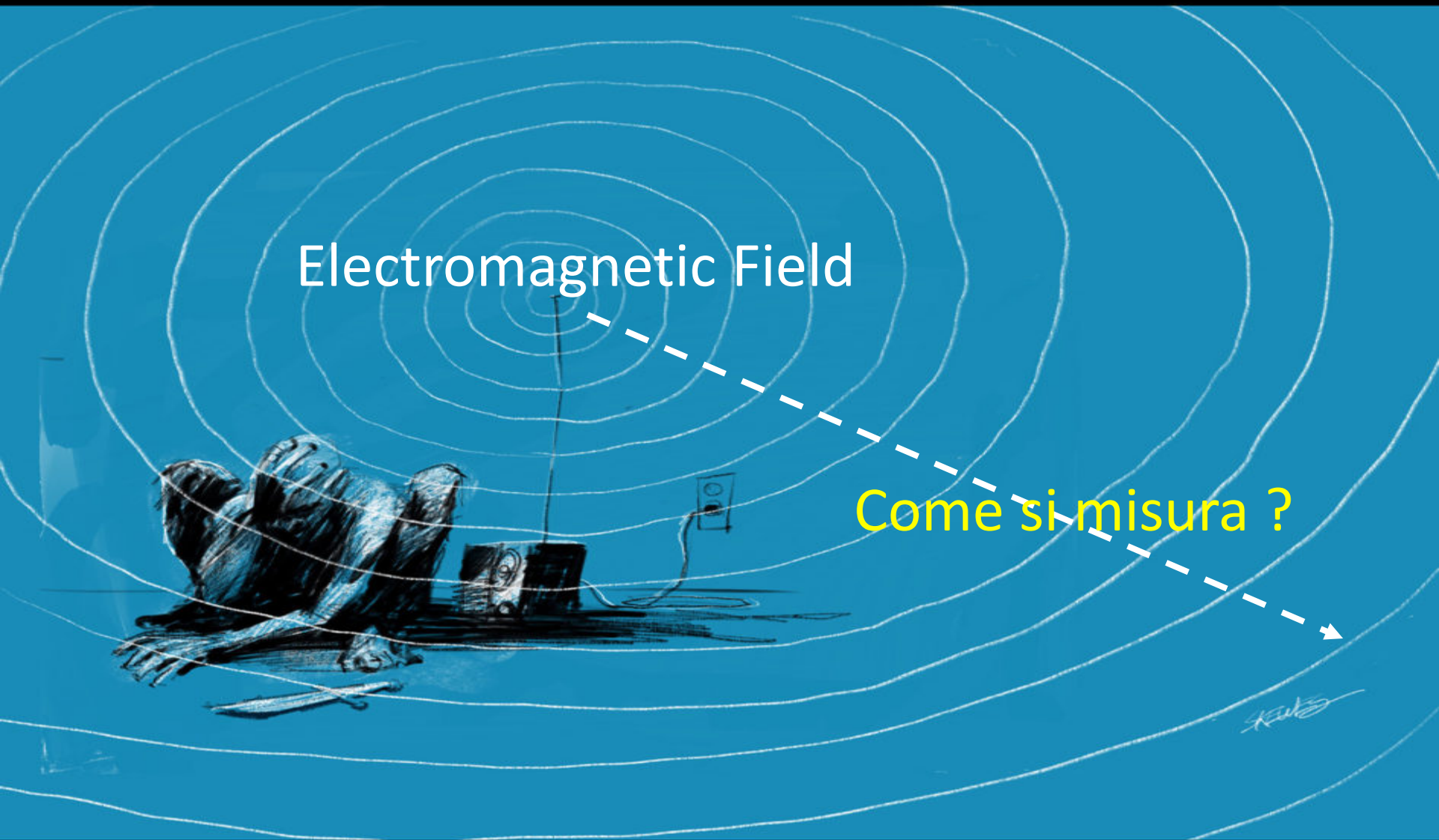
Tutte le forze che fanno girare il mondo sono invisibili.

David Mitchell

Il Killer invisibile

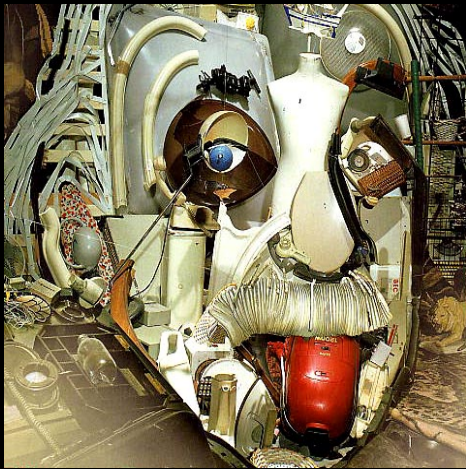
Electromagnetic Field

Come si misura ?





Misura ciò che è misurabile
e rendi misurabile ciò che non lo è
Galileo Galilei



Non tutto quello che è importante
si può misurare
Non tutto quello che si può misurare
è importante
Albert Einstein

L'induzione magnetica si misura in

tesla

e sottomultipli

millitesla	mT	un millesimo di tesla
microtesla	μ T	un milionesimo di tesla
nanotesla	nT	un miliardesimo di tesla

se ha un andamento oscillante nel tempo si misura in

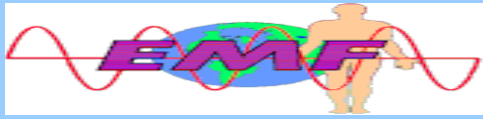
hertz

Indica il numero delle oscillazioni in un secondo.



ATTENZIONE

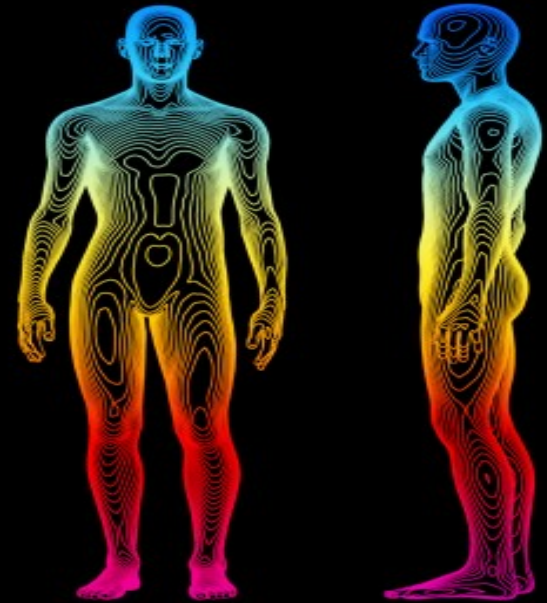
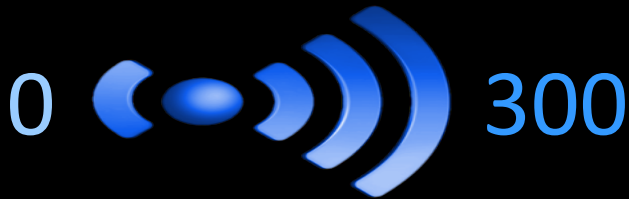
La frequenza **NON** È una indicazione di intensità!



Obiettivo:

Definire l'effetto di un campo elettromagnetico debole

GigaHertz



1 Gigahertz equivale a 1 miliardo di hertz
 $1 \text{ GHz} = 10^9 \text{ Hz}$.



Gli effetti interessano:

NEUROGENESI

NEUROLOGIA

COMPORAMENTO

EMATOLOGIA

IMMUNO

GENETICA

TERATOGENESI

CARDIOVASCOLARE

ATTEGIAMENTO

MISCELLANEA

NEUROGENESI

Interferiscono con i meccanismi dello sviluppo

Sharma A

The influence of prenatal 10 GHz microwave radiation exposure on a developing mice brain.

Gen Physiol Biophys. 2017 Jan;36(1):41-51

Hernández-Rabaza V et al

Inhibition of adult hippocampal neurogenesis disrupts contextual learning but spares spatial working memory, long-term conditional rule retention and spatial reversal.

Neuroscience. 2009 Mar 3;159(1):59-68.

Mitchell CL

Results of a United States and Soviet Union joint project on nervous system effects of microwave radiation.

Environ Health Perspect. 1989 May;81:201-9.

Lagroye I

Measurement of DNA damage after acute exposure to pulsed-wave 2450 MHz microwaves in rat brain cells by two alkaline comet assay methods.

Int J Radiat Biol. 2004 Jan;80(1):11-20.

Hodges H

Late behavioural and neuropathological effects of local brain irradiation in the rat.

Behav Brain Res. 1998 Mar;91(1-2):99-114.

Kesari KK

Mutagenic response of 2.45 GHz radiation exposure on rat brain.

Int J Radiat Biol. 2010 Apr;86(4):334-43.

Kesari KK et al

Pathophysiology of microwave radiation: effect on rat brain.

Appl Biochem Biotechnol. 2012 Jan;166(2):379-88.

Paulraj R,

Protein kinase C activity in developing rat brain cells exposed to **2.45 GHz** radiation.

Electromagn Biol Med. 2006;25(1):61-70.

Paulraj R

Biochemical changes in rat brain exposed to low intensity **9.9 GHz** microwave radiation.

Cell Biochem Biophys. 2012 May;63(1):97-102.

Kesari KK

900-MHz microwave radiation **promotes oxidation** in rat brain.

Electromagn Biol Med. 2011 Dec;30(4):219-34. 0

Deshmukh PS

Effect of Low Level Subchronic Microwave Radiation on Rat Brain.

Biomed Environ Sci. 2016 Dec;29(12):858-867.

Bachmann M

Adaptation of human brain bioelectrical activity to low-level microwave.

Conf Proc IEEE Eng Med Biol Soc. 2007;2007:4747-50.

COMPORTAMENTO

Alterano la memoria e non solo...

Cosquer

Whole-body exposure to **2.45 GHz** electromagnetic fields does not alter anxiety responses in rats: a plus-maze study including test validation.

Behav Brain Res. 2005 Jan 6;156(1):65-74

Wang H,

Impairment of long-term potentiation induction is essential for the disruption of **spatial memory** after microwave exposure.

Radiat Biol. 2013 Dec;89(12):1100-7.

Narayanan SN

Spatial memory performance of Wistar rats exposed to **mobile phone**.

Clinics (Sao Paulo). 2009;64(3):231-4.

Ntzouni MP

Short-term memory in mice is affected by mobile phone radiation.

Pathophysiology. 2011 Jun;18(3):193

D'Andrea JA

Intermittent exposure of rats to **2450 MHz** microwaves at **2.5 mW cm²**: **behavioral and physiological effects.**

Bioelectromagnetics. 1986;7(3):315-28.

Lai H

Low-level microwave irradiation and central **cholinergic systems.**

Pharmacol Biochem Behav. 1989 May;33(1):131-8.

Ntzouni MP

Short-term memory in mice is affected by mobile phone radiation.

Pathophysiology. 2011 Jun;18(3):193-9.

Lass J

Effects of **7 Hz-modulated 450 MHz** electromagnetic radiation on human performance **in visual memory tasks.**

Int J Radiat Biol. 2002 Oct;78(10):937-44.



EMATOLOGIA

Deprimono l'eritropoiesi

Sisodia R

Effects of **10-GHz** microwaves on **hematological parameters** in Swiss albino mice and their modulation by Prunus avium.

J Environ Pathol Toxicol Oncol. 2013;32(3):205-17.

Ragan HA

Hematologic and immunologic effects of pulsed microwaves in mice.

Bioelectromagnetics. 1983;4(4):383-96.

IMMUNO

Interferiscono con le reazioni immunitarie

Vijayalaxmi

Cytogenetic studies in human blood **lymphocytes** exposed in vitro to **2.45 GHz or 8.2 GHz** radiofrequency radiation.

Radiat Res. 2006 Sep;166(3):532-8.

Trosic

Blood-forming system in rats after whole-body microwave exposure; reference to the **lymphocytes**.

Toxicol Lett. 2004 Dec 1;154(1-2):125-32.

Liddle CG

Circulating antibody response of mice exposed to **9-GHz** pulsed microwave radiation.

Bioelectromagnetics. 1986;7(1):91-4

GENETICA

Svolgono una azione genotossica

Lee JY

Gene Expression in **Mice Testes** Exposed to 1.765 GHz Microwave in Utero.

J Reprod Med. 2017 May-Jun;62(5-6):324-8.

Beechey CV

Cytogenetic effects of microwave irradiation on male **germ cells** of the mouse.

Int J Radiat Biol Relat Stud Phys Chem Med. 1986 Nov;50(5):909-18.

TERATOGENESI

Inducono malformazioni

Nawrot PS
Teratogenic, biochemical, and histological studies with mice prenatally exposed to 2.45-GHz microwave radiation.
Radiat Res. 1985 Apr;102(1):35-45.

Nawrot PS
Effects of 2.45 GHz CW microwave radiation on embryofetal development in mice.
Teratology. 1981 Dec;24(3):303-14.

Zhang Y
Effects of fetal microwave radiation exposure on offspring behavior in mice
J Radiat Res. 2015 Mar;56(2):261-8.

Lagroye I
Measurement of DNA damage after acute exposure to pulsed-wave 2450 MHz microwaves in rat brain cells by two alkaline comet assay methods.
Int J Radiat Biol. 2004 Jan;80(1):11-20.

CARDIOVASCOLARE

Possono avere una azione aritmogena

Lauchem JP
Cardiovascular and thermal effects of microwave irradiation at 1 and/or 10 GHz in anesthetized rats.
Bioelectromagnetics. 2000 Apr;21(3):159-66.

MISCELLANEA

Intriganti effetti...

Chou CK
Long-term, low-level microwave irradiation of rats.
Bioelectromagnetics. 1992;13(6):469-96.

Palmisano WA
Some considerations of microwave hazards exposure criteria.
Mil Med. 1966 Jul;131(7):611-8.

ATTEGIAMENTO

Agiscono sulle funzioni cognitive

DeWitt JR,

Behavioral effects of chronic exposure to 0.5 mW/cm² of 2,450-MHz microwaves.

Bioelectromagnetics. 1987;8(2):149-57.

Li HJ

Alterations of cognitive function and 5-HT system in rats after long term microwave exposure.

Physiol Behav. 2015 Mar 1;140:236-46.

Ntzouni MP

Transient and cumulative **memory impairments** induced by GSM 1.8 GHz cell phone signal in a mouse model.

Electromagn Biol Med. 2013 Mar;32(1):95-120.

Nittby H

Cognitive impairment in rats after long-term exposure to GSM-900 mobile phone radiation.

Bioelectromagnetics. 2008 Apr;29(3):219-32.





Gli effetti interessano:

NEUROGENESI

NEUROATOLOGIA

COMPORAMENTO

EMATOLOGIA

IMMUNO

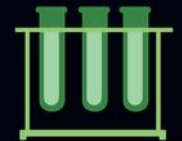
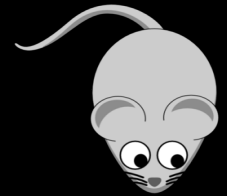
GENETICA

TERATOGENESI

CARDIOVASCOLARE

ATTEGIAMENTO

MISCELLANEA





Ipocrisia Scientifica



I NOSTRI PAZIENTI





I NOSTRI PAZIENTI

I NOSTRI PAZIENTI





EMF

World Health Organization

The International EMF Project

investigates health effects of electromagnetic fields

advises national authorities on EMF radiation protection

THE SPECTRUM
People all over the world are exposed to electromagnetic fields (EMF) to varying degrees, and the levels of exposure will increase as technology advances further. These EMF are found in the seen (visible) part of the electromagnetic spectrum (between 0 and 300 GHz) and are emitted from common sources such as power lines and cellular phones. They are different to ionizing radiations, such as X-rays and gamma rays, which have enough energy to break molecular bonds.

www.who.int/emf/

STATIC
EXTREMELY LOW FREQUENCIES
INTERMEDIATE FREQUENCIES
RADIO FREQUENCIES

NON-IONIZING
IONIZING



PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Pediatrics. 2005 Aug;116(2):e303-13.

The sensitivity of children to electromagnetic fields.

Kheifets L, Repacholi M,
Saunders R, van Deventer E.

Department of Epidemiology, University of
California School of Public Health, Los Angeles,

millitesla	mT	un millesimo di tesla
microtesla	μ T	un milionesimo di tesla
nanotesla	nT	un miliardesimo di tesla

 **Rischio: 0,4 μ T**

Leucemia infantile

Linfoblastica acuta (ALL)
Mieloblastica acuta (LMA)

Linnet MS et al.
Descriptive epidemiology of childhood leukemia.
*Br J Cancer.*1991;63 :424– 429

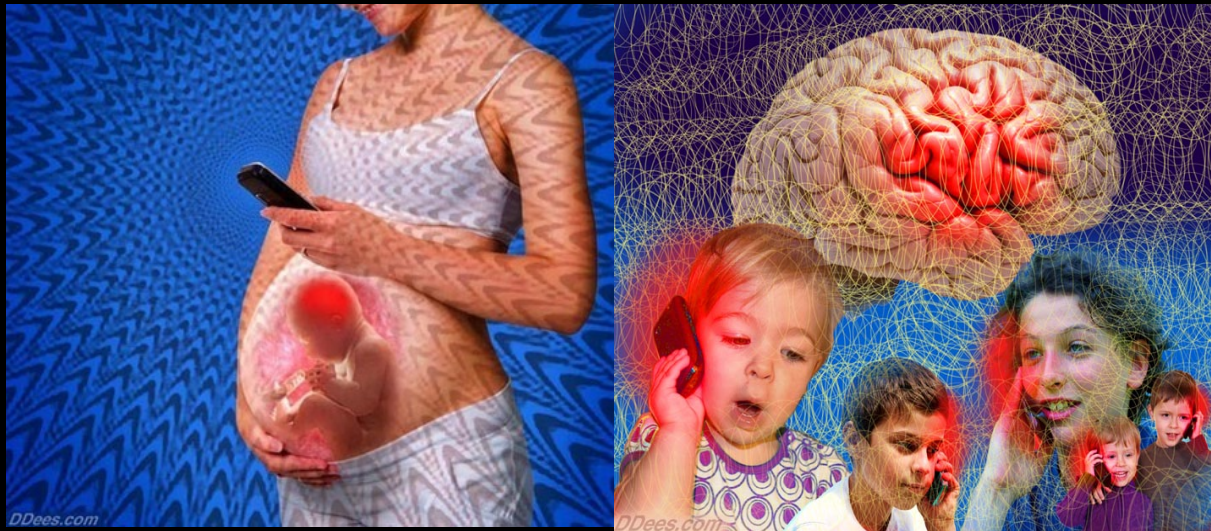


Neoplasie Cerebrali

Linnet MS et al.
Interpreting epidemiologic research: lessons from studies of childhood cancer.
*Pediatrics.*2003;112(1 pt 2) :218– 232

Pediatrics. 2005 Aug;116(2):e303-13.
The sensitivity of children to electromagnetic fields.
Kheifets et al.

CONTINUUM *senza interruzione...*



Pulli EP et al.

**Prenatal exposures and infant brain:
Review of magnetic resonance
imaging studies and a population
description analysis.**

*Hum Brain Mapp. 2019 Apr 15;40(6):
1987-2000.*

Friedman DR et al.

**Childhood exposure to magnetic fields:
residential area measurements compared
to personal dosimetry.**

Epidemiology.1996;7 :151– 155

Trasmettitori a bassissima frequenza

Centrali di produzione e stazioni di trasformazione dell'energia elettrica •Elettrodotti di trasmissione e di distribuzione, aerei ed interrati. •Cabine e quadri di distribuzione stradali. •Impianti di illuminazione pubblica.

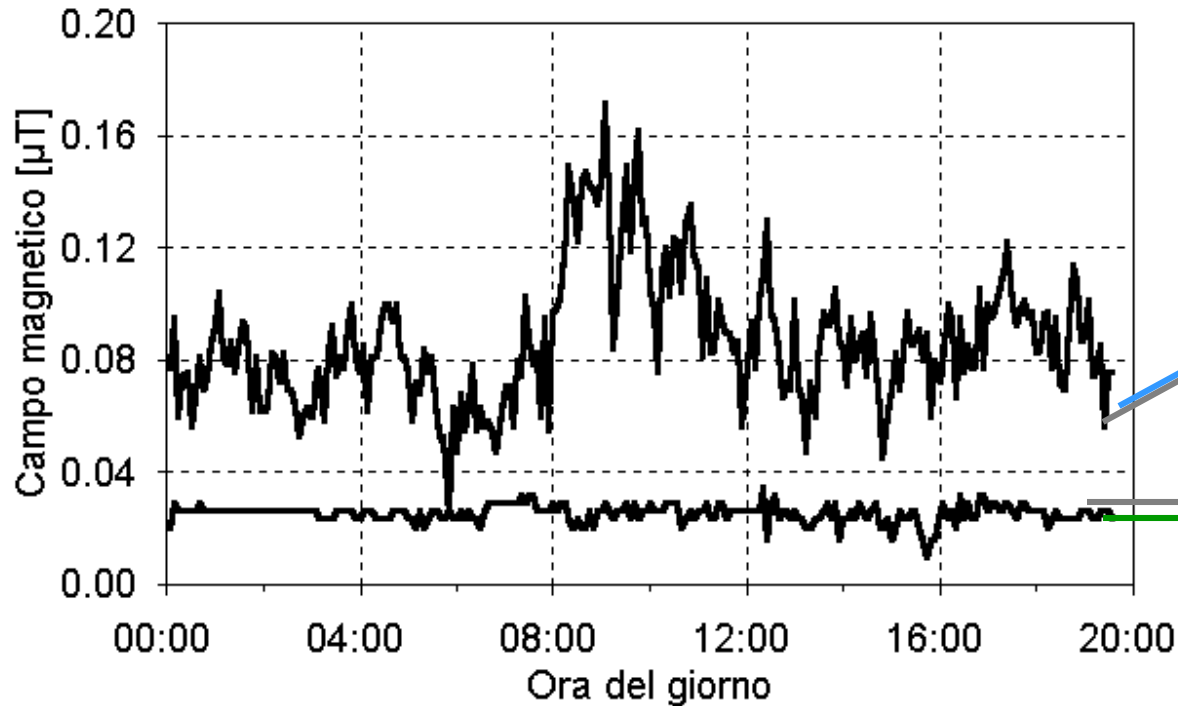


Generano campi
magnetici alternanti



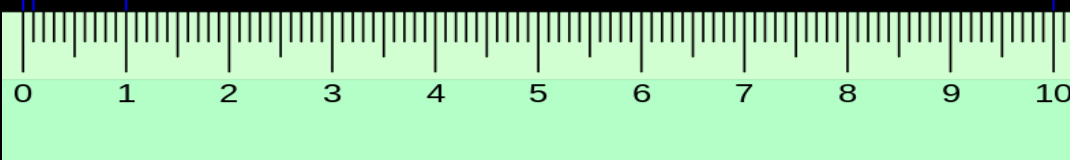
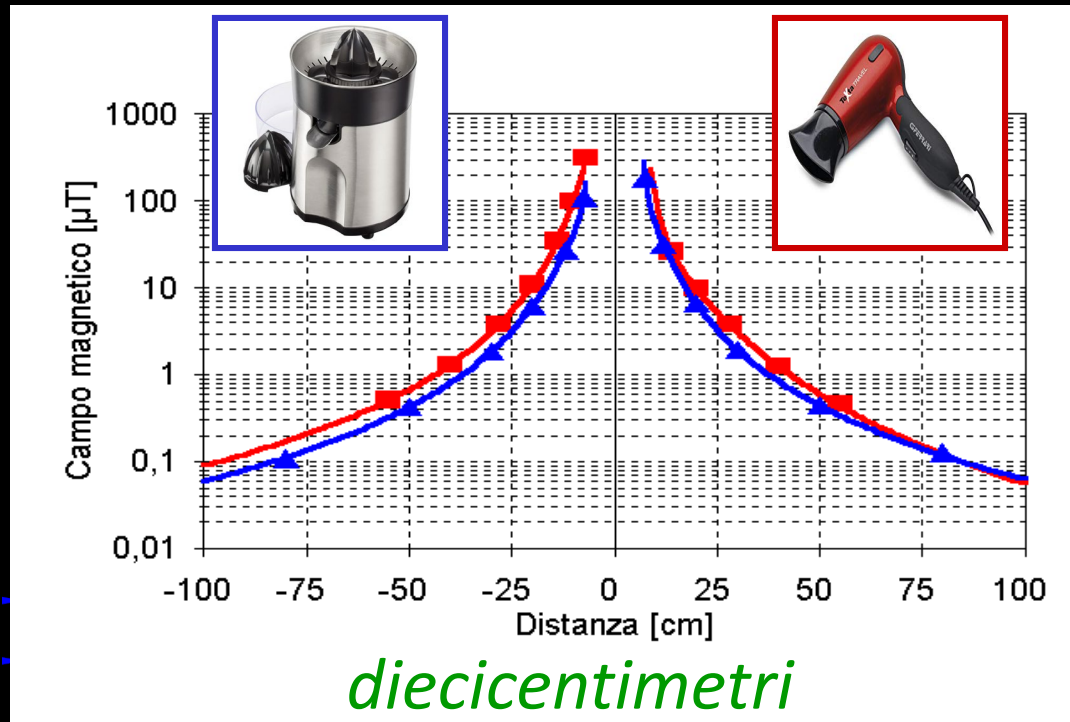


Misure di induzione magnetica eseguite su un arco di 20 ore



Ogni 5 minuti, in un punto di un tipico appartamento in **condominio urbano** e di una **abitazione singola** in quartiere periferico semirurale

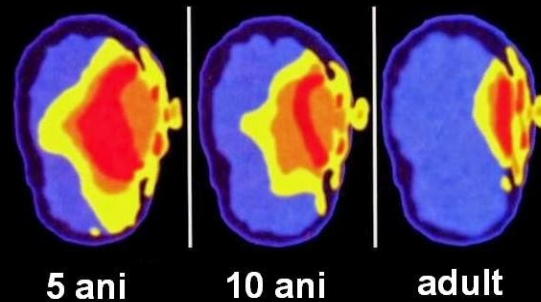
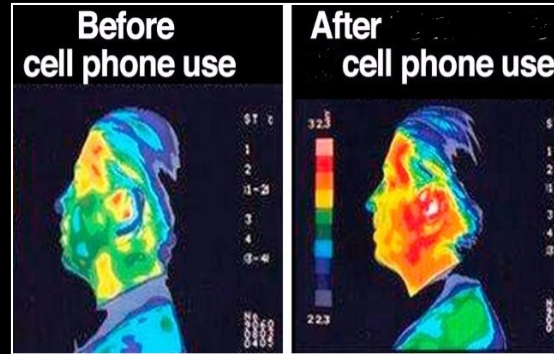
Soglia di Attenzione Epidemiologica



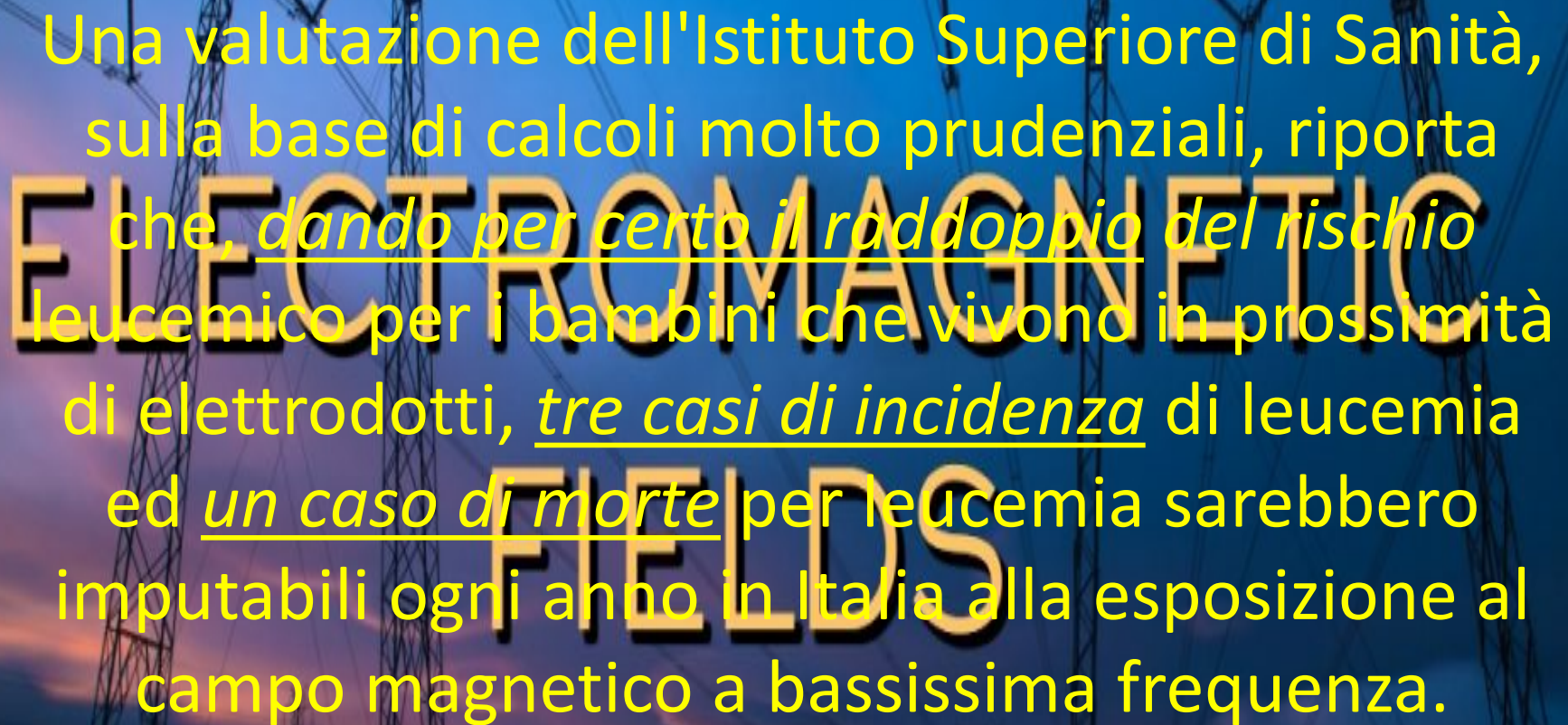
Distanza di sicurezza



Il “cellulare” genera un campo magnetico alternato capace di indurre correnti elettriche all'interno delle strutture conduttrici del corpo umano



Il campo magnetico si manifesta come forza che agisce su altre correnti elettriche.



Una valutazione dell'Istituto Superiore di Sanità, sulla base di calcoli molto prudentziali, riporta che, dando per certo il raddoppio del rischio leucemico per i bambini che vivono in prossimità di elettrodotti, tre casi di incidenza di leucemia ed un caso di morte per leucemia sarebbero imputabili ogni anno in Italia alla esposizione al campo magnetico a bassissima frequenza.

ELECTROMAGNETIC FIELDS



Independent Expert Group on
Mobile Phones

International Agency for Research on Cancer



Health Council of the Netherlands



Il tessuto cerebrale del bambino è più conduttivo di quello degli adulti perché ha un più elevato contenuto di acqua e **una elevata concentrazione ionica**.
Ha un maggiore assorbimento di energia prodotta dalle radiofrequenze dei telefoni cellulare.

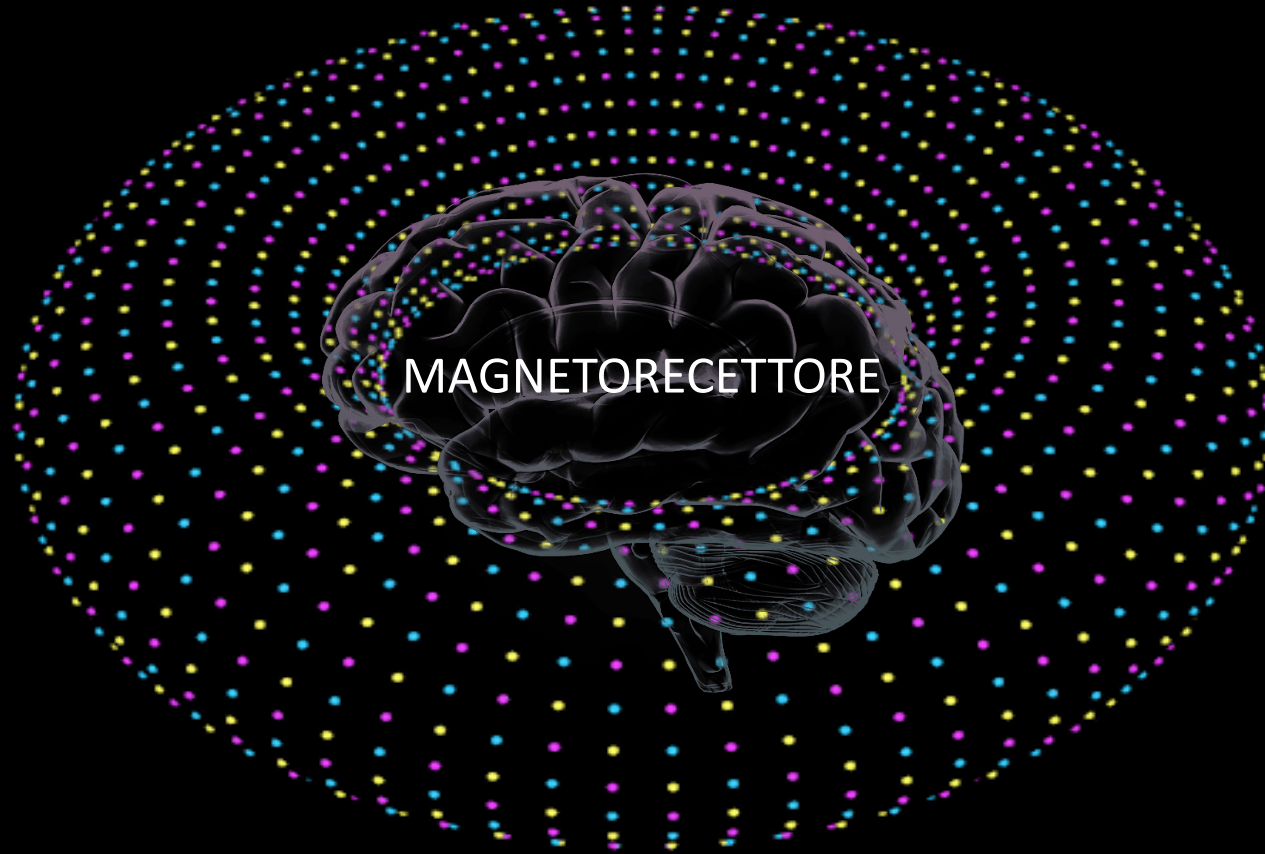


PLoS Biol. 2017 Oct 23;15(10):e2003234.

Magnetoreception: a sense without a receptor

Nordmann GC1

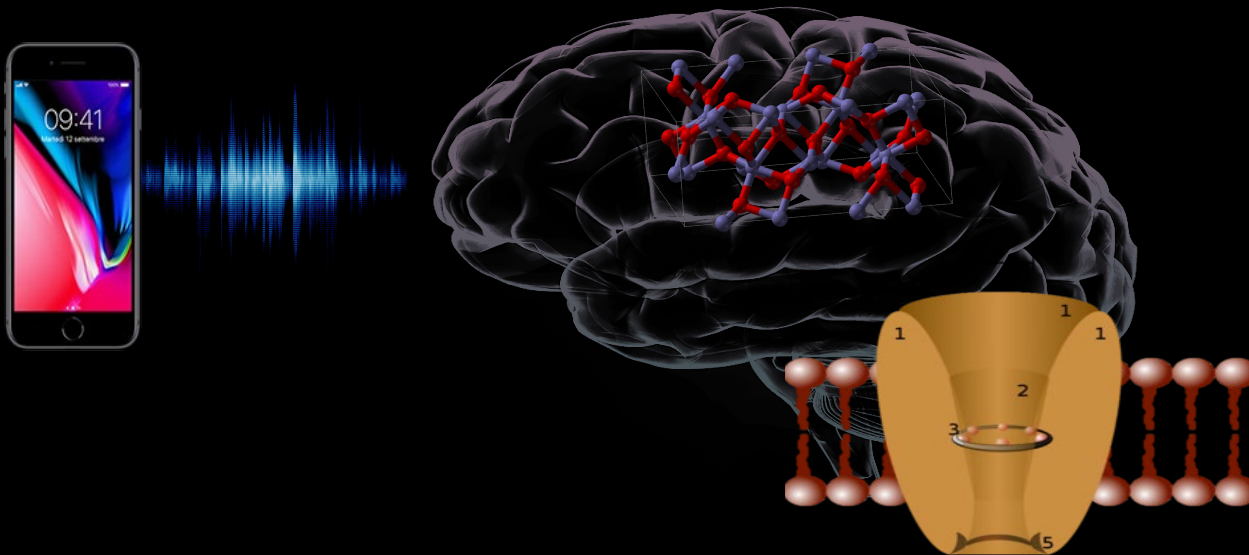
Research Institute of Molecular Pathology, Vienna, Austria



Preliminary evaluation of nanoscale biogenic magnetite-based ferromagnetic transduction mechanisms for mobile phone bioeffects.

Cranfield Cet al.

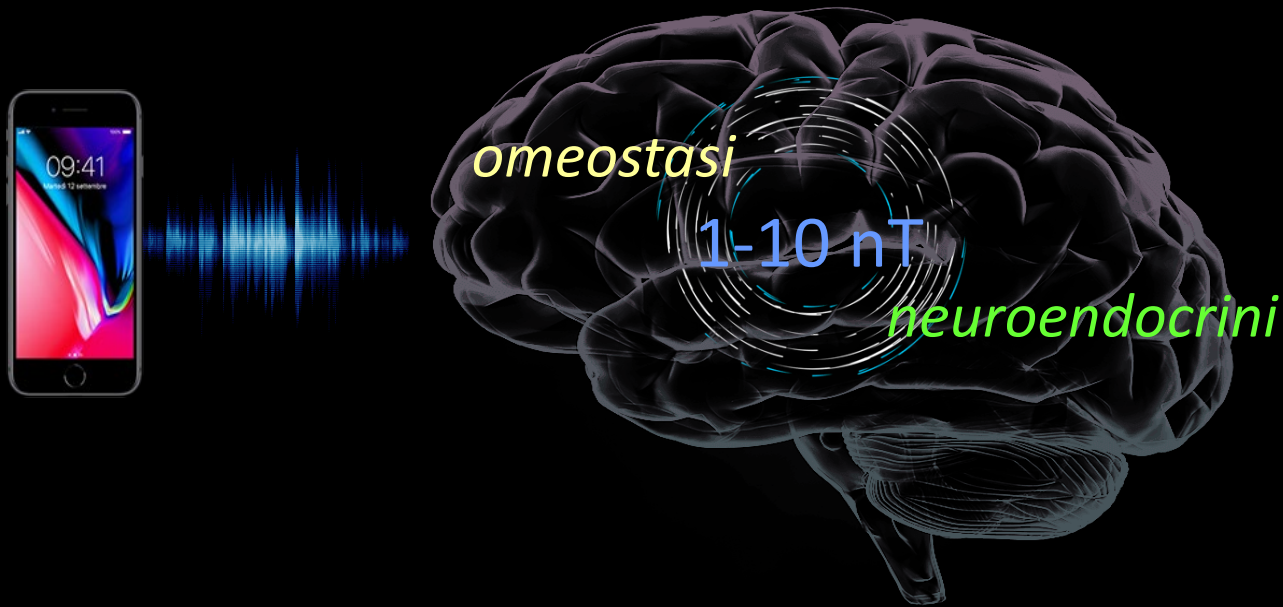
Le **emissioni elettromagnetiche pulsanti** interagiscono con la magnetite biogenica (Fe_3O_4) presente nel cervello umano tramite risonanza ferromagnetica con attivazione meccanica di **canali ionici cellulari**



Il test: utilizzato un analogo batterico (*Magnetospirillum magnetotacticum*) che produce magnetite biogenica intracellulare simile a quella presente nel cervello umano

A human source for ELF magnetic perturbations.

Liboff AR



Il cervello rappresenta una fonte aggiuntiva di campi magnetici ELF ambientali deboli (1-10 nT).

Touchscreen generation

I bambini sono come il cemento umido
tutto quello che li colpisce lascia un'impronta.

Haim G. Ginott

PERICOLI



*S*onno

*S*olitudine

*S*ocial

Sonno



Addormentamento



CONTINUUM

Need.
More.
Sleep.



EFFECTS OF SLEEP DEPRIVATION

Sleep deprivation may have a more profound impact on children than adults.



Sleep-deprived kids may seem grouchy, but something deeper is going on in their brains.

SPECTRUM
TALK



Touchscreen generation



Sleep deprivation

Touchscreen generation



Assathiany R et al.

Children and screens: A survey by French pediatricians.

Arch Pediatr. 2018 Feb;25(2):84-88.



Anderson DR et al.

Cognitive Impacts of Digital Media Workgroup.

Digital Screen Media and Cognitive

Development. Pediatrics. 2017 Nov;140(Suppl 2):S57-S61.



Nathanson AI et al.

The role of sleep in the relation between young children's mobile media use and effortful control.

Br J Dev Psychol. 2018 Mar;36(1):1-21.



Kostyrka-Allchorne K et al.

Touchscreen generation: children's current media use, parental supervision methods and attitudes towards contemporary media.

Acta Paediatr. 2017 Apr;106(4):654-662.



Montes G et al

Children With **Autism Spectrum Disorder** and Screen Time: Results From a Large, Nationally Representative US Study.

Acad Pediatr. 2016 Mar;16(2):122-8.



Hysing M et al.

Sleep and use of electronic devices in adolescence: results from a large population-based study.

BMJ Open. 2015 Feb 2;5(1):e006748.



Sleep deprivation

etcetera

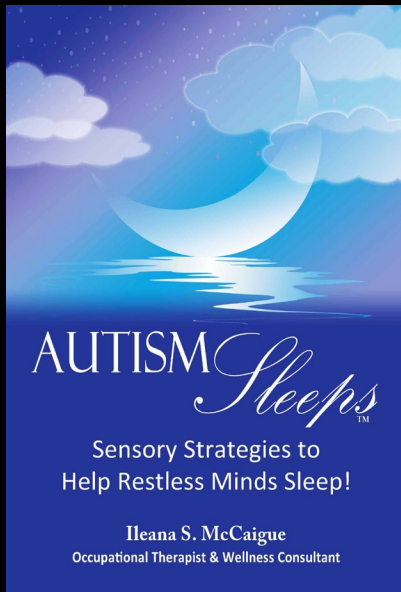
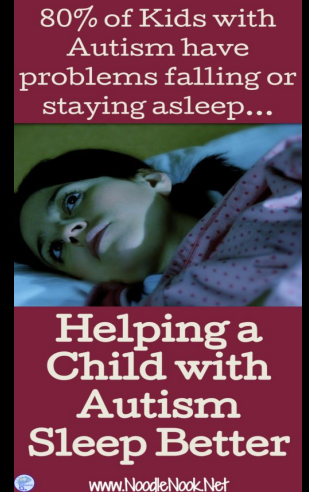
Insonnia

Autism Res. 2017 Jul;10(7):1221-1238.

Shorter sleep duration is associated with social impairment and comorbidities in ASD.

Veatch OJ et al.

In un campione di 2.714 bambini con ASD (Simons Simplex Collection) valutati secondo l'Autism Diagnostic Interview-Revised (ADI-R), l'Autism Diagnostic Observation Schedule (ADOS), si è dimostrata come una ridotta quantità di sonno sia correlata a sintomi gravi quali il fallimento nello sviluppo delle relazioni tra pari, disturbi da deficit di attenzione, depressivi, e disturbo ossessivo-compulsivo.



Indian J Pediatr. 2019 Jan;86(1):12-17.

Sleep Dysfunction and Behavioral Daytime Problems in Children with Autism Spectrum Disorders: A Comparative Study.

Malhi P et al.

I bambini con ASD sono ad alto rischio di disturbi del sonno e questo è associato a disturbi del comportamento diurno. I pediatri dovrebbero sottoporre a screening sistematico i bambini con ASD per problemi di sonno e avviare interventi tempestivi e appropriati

Sleep in Children with Autism Spectrum Disorder.

Souders MC



Sessanta bambini con ASD (85% ragazzi) (età media = 6,1 anni, DS = 2,4) ed un gruppo controllo di uno stato socio-economico corrispondente a un gruppo di bambini in via di sviluppo (N = 60).

Il questionario sulle abitudini di sonno dei bambini (CSHQ) è stato utilizzato per misurare i problemi del sonno.

I problemi di sonno erano quasi due volte più diffusi tra i bambini con ASD (88,3%) rispetto al gruppo TD (46,7%) ($\chi^2 = 23,74$, $P = 0,0001$).

I bambini con ASD hanno mostrato una resistenza a coricarsi significativamente maggiore rispetto ai controlli ($t = 3,95$, $P = 0,001$).

La sottoscala della durata del sonno ha mostrato che i bambini con ASD, rispetto al gruppo TD, dormivano troppo poco ($\chi^2 = 23,08$, $P = 0,0001$), non dormivano la giusta quantità di tempo ($\chi^2 = 11,86$, $P = 0,003$), e mostravano significativi variazioni della durata del tempo dormito ($\chi^2 = 11,96$, $P = 0,003$).

Inoltre, la disfunzione del sonno riferita dai genitori ha avuto una relazione significativa con le difficoltà di comportamento riportate durante il giorno ($r = 0,53$, $P = 0,01$) nei bambini con ASD.

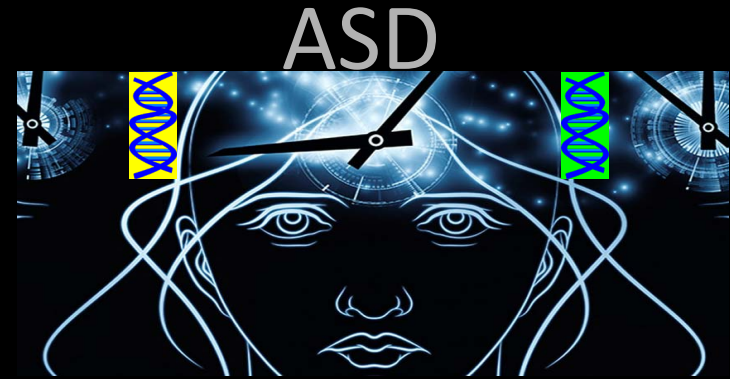
I bambini con ASD sono ad alto rischio di disturbi del sonno e questo è associato a disturbi del comportamento diurno.

Bioritmi

J Physiol Paris. 2016 Nov;110(4 Pt B):434-438.

Are circadian rhythms new pathways to understand Autism Spectrum Disorder?

Geoffray MM et al.



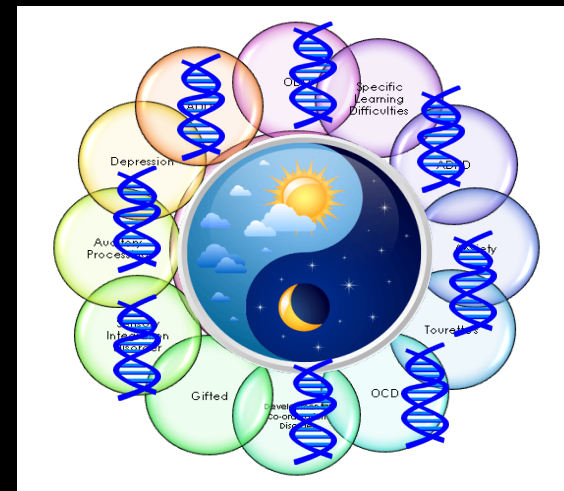
I ritmi circadiani sono generati da circuiti di feedback genetici auto-regolatori, guidati dai fattori di trascrizione **CLOCK** e **BMAL1**, che guidano i pattern di trascrizione giornaliera per molecole sinaptiche associate alla suscettibilità ASD.

Brain Dev. 2016 Jan;38(1):91-9.

Circadian-relevant genes are highly polymorphic in autism spectrum disorder patients.

Yang Z et al.

Nei pazienti con disturbo del sonno stati rilevati **36 variazioni di base con cambiamenti di aminoacidi in 11 geni.**



PER1

PER2

NPAS2

MTNR1A

MTNR1B.

I campioni di **28 pazienti con ASD** (14 con disturbi del sonno e 14 senza) e **23 soggetti di controllo** sono stati analizzati i geni principali del controllo circadiano

Melatonina

Curr Clin Pharmacol. **2014** ;9(4):326-34.

Melatonin in autism spectrum disorders.

Rossignol DA et al.

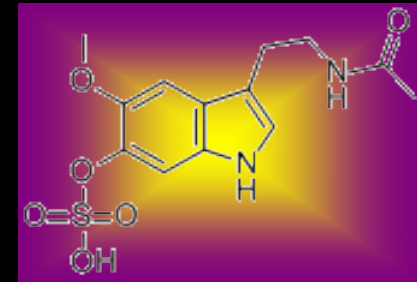
- 4** **Quattro studi** hanno osservato una correlazione tra anormali concentrazioni di melatonina e la gravità dei comportamenti autistici.
- 20** **Venti studi** hanno riportato **miglioramenti** nei parametri del sonno con integrazione esogena di melatonina nell'ASD, tra cui una maggiore durata del sonno, meno risvegli notturni e un sonno più rapido.
- 5** **Cinque studi** crossover randomizzati, in doppio cieco, controllati con placebo dimostrano che la supplementazione di melatonina esogena nell'ASD induce **miglioramenti significativi** con dimensioni di grande effetto nella durata totale del sonno e latenza nell'insorgenza del sonno rispetto al basale e al placebo.
- 6** **Sei studi** hanno riportato che la somministrazione notturna della melatonina esogena era associata a **migliori comportamenti** durante il giorno.
- 4** **Quattro studi** hanno riportato **miglioramenti con** la supplementazione di melatonina esogena quando altri farmaci per il sonno avevano precedentemente fallito.



Zhonghua Er Ke Za Zhi. **2017 Dec** 2;55(12):911-915.

Sleep problems and the association with the levels of 6-sulfatoxy melatonin in children with autism spectrum disorder.

Han PP et al.



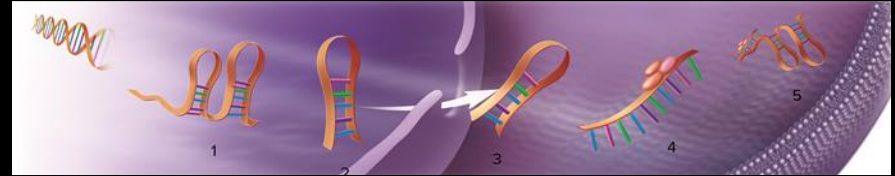
Il principale metabolita della melatonina, 6-sulfatoxymelatonin (6-SM) è aumentato in un campione di 212 bambini ASD (età media 6 anni) rispetto al controllo (312) e correla con la gravità e con problemi del sonno

Epigenetica

BMC Pediatr. **2016 Apr 22**;16:52.

Salivary miRNA profiles identify children with autism spectrum disorder, correlate with adaptive behavior, and implicate ASD candidate genes involved in neurodevelopment.

Hicks SD et al.



La misurazione del *miRNA salivare* in questo studio pilota su soggetti con ASD lieve ha dimostrato l'espressione differenziale di **14 miRNA** che sono espressi nel cervello in via di sviluppo, influisce sugli mRNA correlati allo sviluppo del cervello e si *correlano con le misure dello sviluppo neurologico del comportamento adattivo*. Questi miRNA hanno un'elevata specificità e un'utilità cross-validata come potenziale strumento di screening per l'ASD.

Mol Autism. **2018 Jun 28**;9:40.

Case-control meta-analysis of blood DNA methylation and autism spectrum disorder.

Andrews SV et al.



Nessun singolo sito **CpG ha** mostrato una differenza di DNAm abbastanza ampia tra i casi e i controlli per raggiungere un significato a livello di epigenoma in questa dimensione del campione. L'EWAS orientato alla scoperta per l'ASD che utilizza campioni di sangue probabilmente richiederà campioni ancora più grandi e dati genetici unificati per comprendere ulteriormente le differenze di DNAm nell'ASD.

Genetic variation in the oxytocin receptor gene is associated with a social phenotype in autism spectrum disorders.

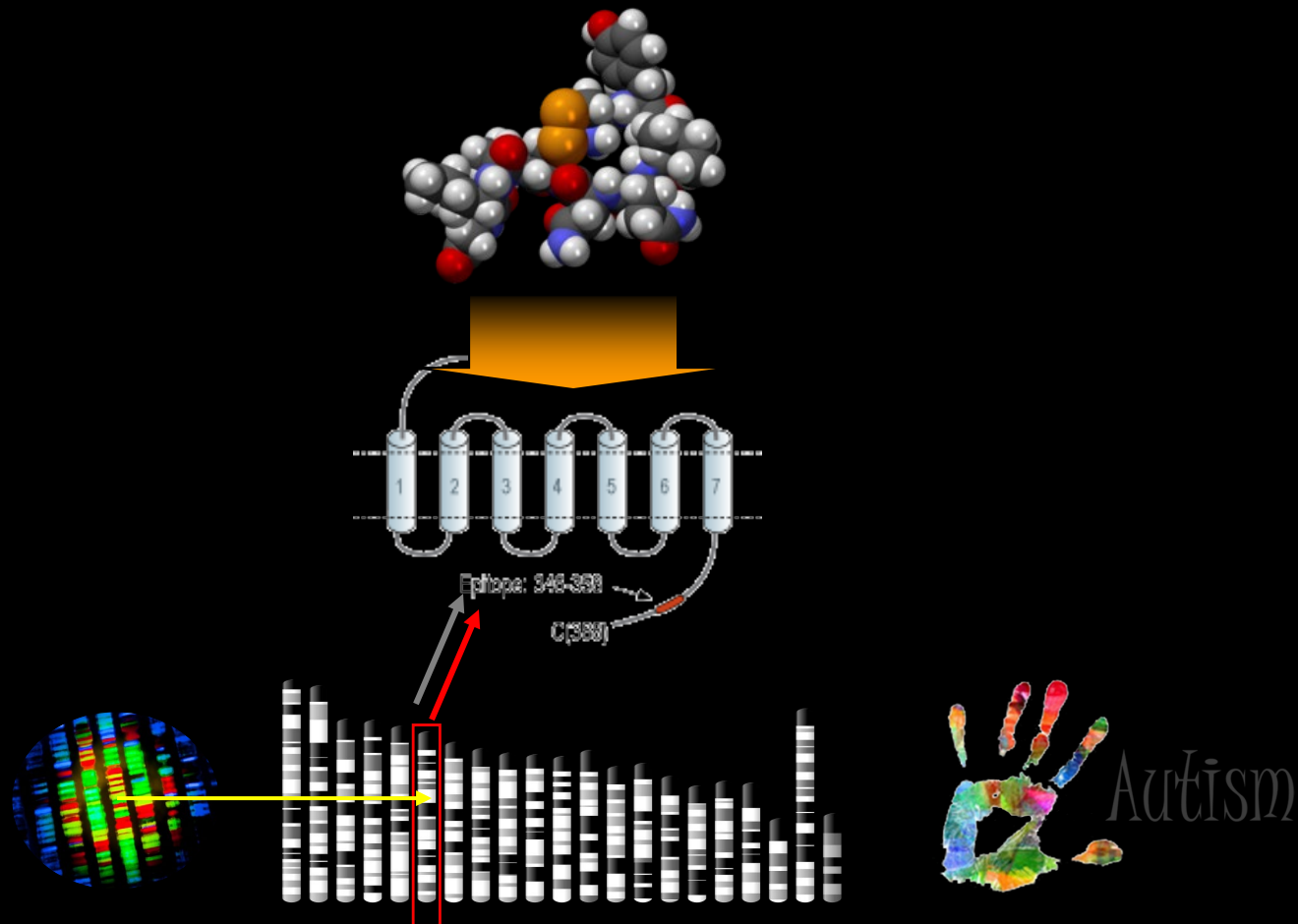
Harrison AJ, Gamsiz ED, Berkowitz IC, Nagpal S, Jerskey BA.

Department of Educational Psychology, College of Education, University of Georgia, Athens, Georgia.

Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University, Providence, Rhode Island.

Developmental Disorders Genetics Research Program, Emma Pendleton Bradley Hospital, Riverside, Rhode Island.

Department of Molecular Biology, Cell Biology and Biochemistry and Institute for Brain Science, Brown University, Providence, Rhode Island.

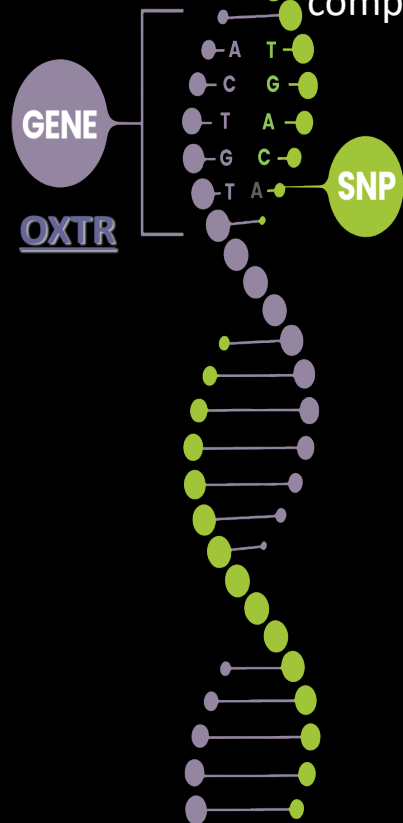


Sono stati analizzati **10 SNPS (polimorfismo a nucleotide singolo)** nel gene OXTR precedentemente dimostrati associati all'ASD.

E la loro associazione a fenotipi sociali e del comportamento ripetitivo secondo Simplex di Simons (SSC).

La mappatura del linkage disequilibrium (LD) suggerisce che **due SNP** sono sovrapposti alla regione 3' non tradotta (3'-UTR) del gene OXTR.

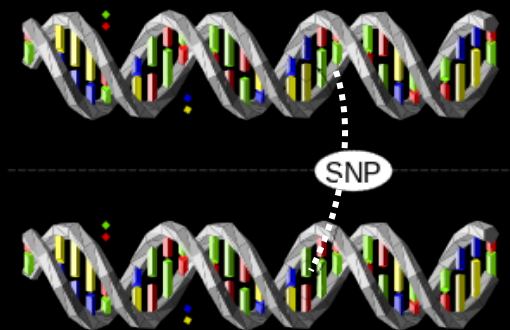
Questi **due SNP** erano anche associati a una maggiore compromissione della scala del comportamento ripetitivo.



I risultati indicano che la disabilit  sociale e i comportamenti ripetitivi nell'ASD sono associati alla variazione genomica nel **3'UTR del gene OXTR**

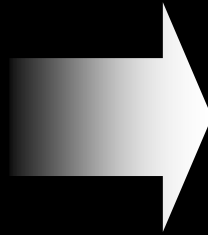


Queste varianti potrebbero essere collegate a un allele che altera la **stabilit  del mRNA**



Solitudine

Gli adolescenti
stanno lasciando

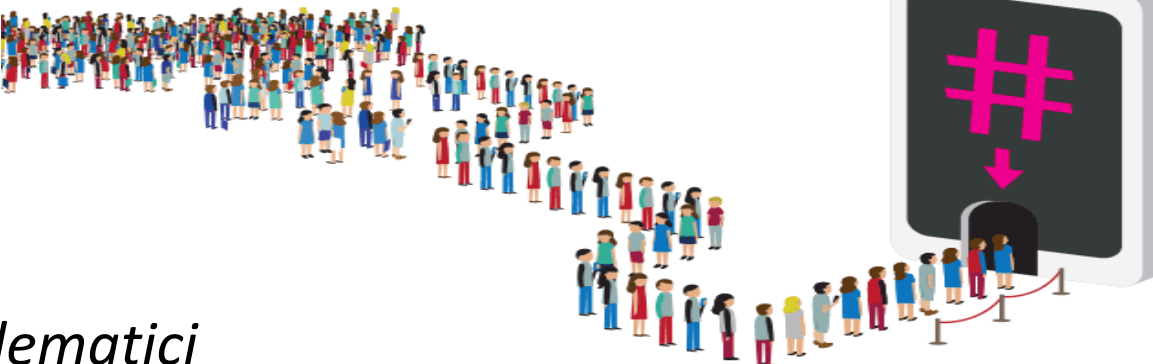


Per vivere all'interno di
un mondo "virtuale"



*Se non sapete con certezza
dove volete andare*

Dal mondo
REALE

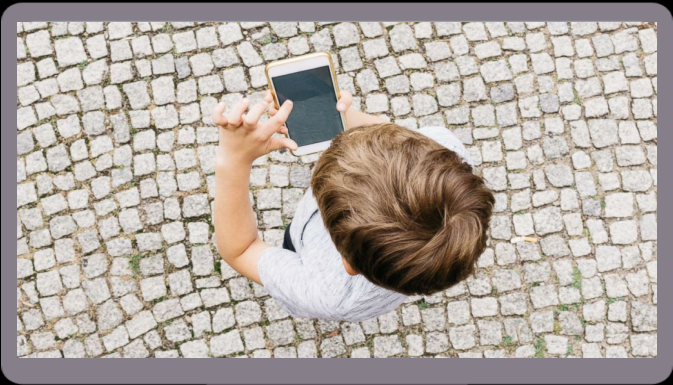


Migranti telematici

*Rischiate di trovarvi altrove
E di non accorgevene*

J.J. Guilbert





*La vita è per ogni uomo una cella solitaria
dove le pareti sono specchi.*

Eugene O'Neill

*Da solo con uno smartphone
non sei mai veramente solo*



*In compagnia con
uno smartphone
non sei mai veramente
in compagnia.*

*Secondo il galateo lo smartphone deve
andare alla destra o alla sinistra del piatto?*





86%

Non praticano
e non credono
nella politica



93%

Non reputano
importante la
religione



39%

Ammettono di
"sentirsi soli".



Anche se i social media ti permettono di restare sempre in contatto con milioni di amici, ma alla fine sei tu, davanti al tuo schermo da solo a comunicare. Da solo. con il tuo smartphone...

Social



Persone che hanno rinunciato
ad incontrarsi, guardarsi, toccarsi,
curarsi l'uno dell'altro

Avere una vita di relazione vera





*Esternazioni di
un "tecnoleso"*

C'era una volta il 68...

Era strategico avere questa chiave:



Tutte le conoscenze del pianeta



*Accesso alla CONOSCENZA
Semplicemente schiacciando un bottone...*

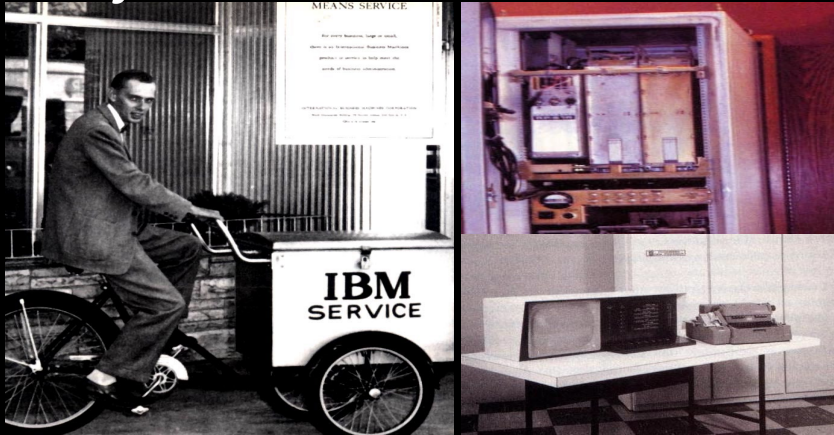
Non solo "rivoluzionari"...



**Siate realisti: chiedete
l'impossibile**

...anche visionari...

L'informatica nel 68



Anche tanta demagogia



Leonard Kleinrock

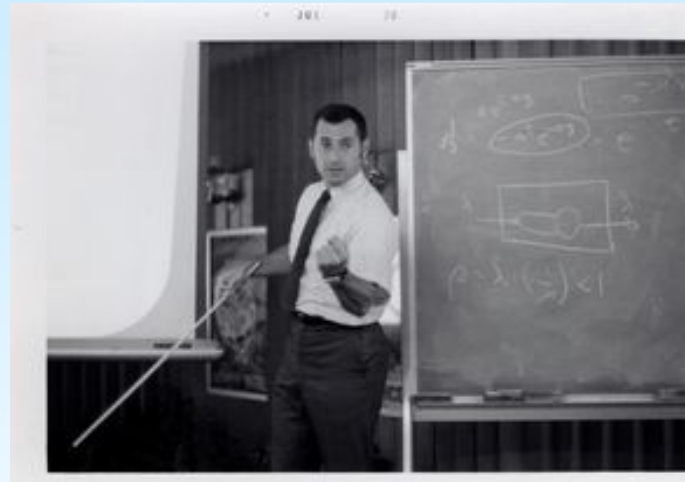


Ph.D. Thesis, Massachusetts Institute of Technology, July 1961

**Information Flow in Large
Communication Nets**



Leonard Kleinrock Group







ARPANET

T H E F I R S T I N T E R N E T



John Postel

Vinton Cerf

Steve Crocker

Arpanet



1969

ARPA

1971

Microprocessore INTEL

1976

Steve Wozniak e Steve Jobs lanciano l'Apple II

1978

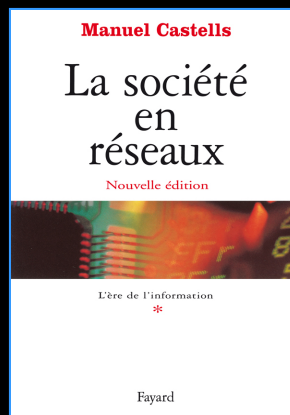
Due studenti dell'università di Chicago
inventano il MODEM

1979

Studenti della Duke University
modificano l'UNIX della Bell Labs

1980

Nasce INTERNET



*...è grazie all'informatica che gli
studenti allevati nella cultura
contestataria dei campus
americani degli anni 60
troveranno il modo di infrangere
la standardizzazione del mondo
creato dai loro genitori*

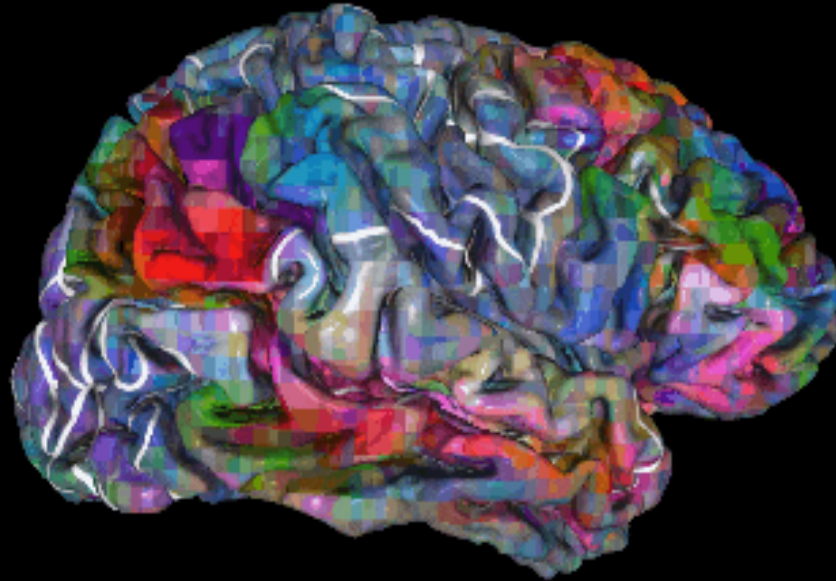


Il primo computer italiano a collegarsi con PUBMED ?



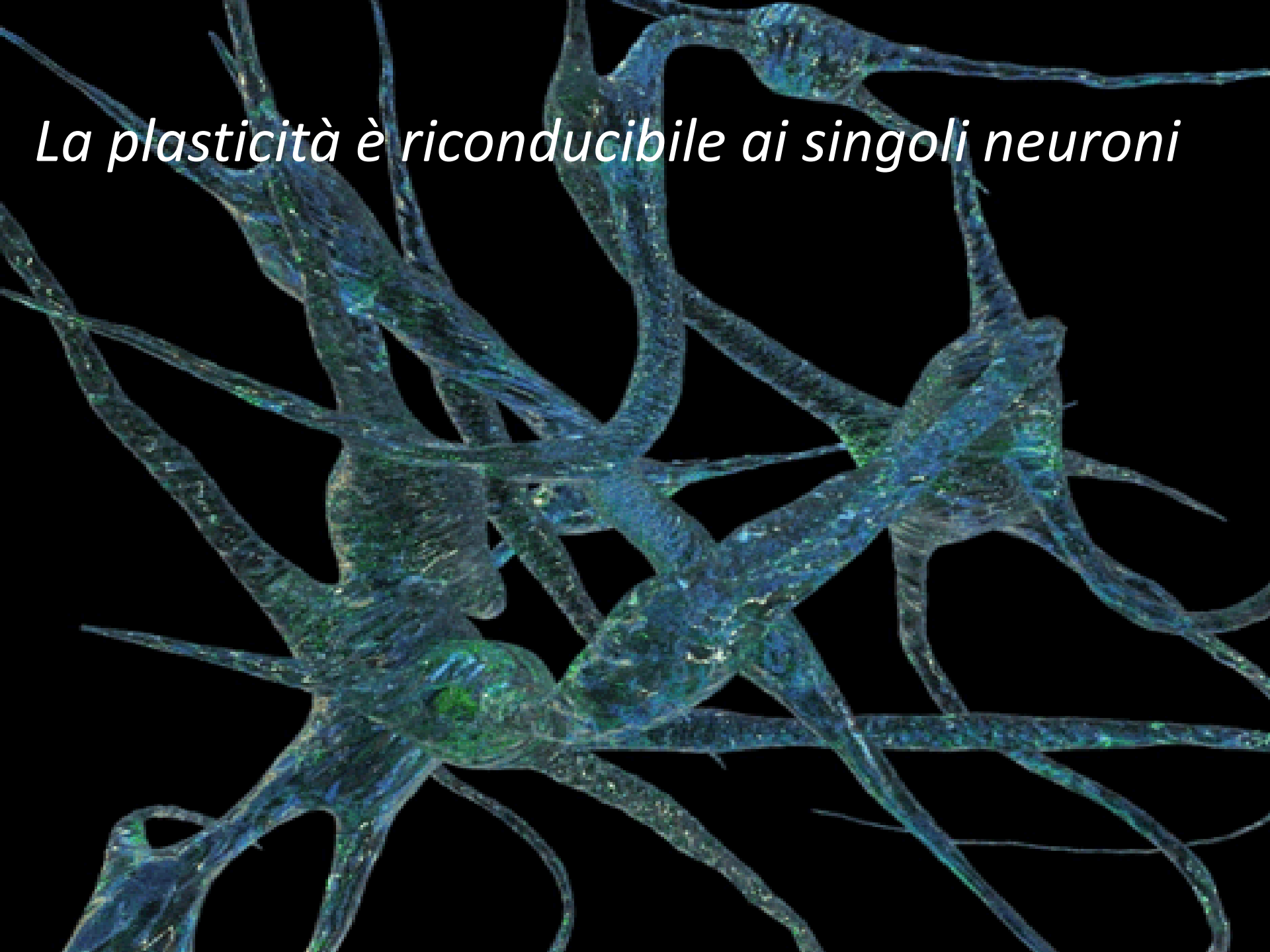
Il 20 novembre 1955

Laboratorio di
MEDICINA COMPUTAZIONALE
della settimana della formazione

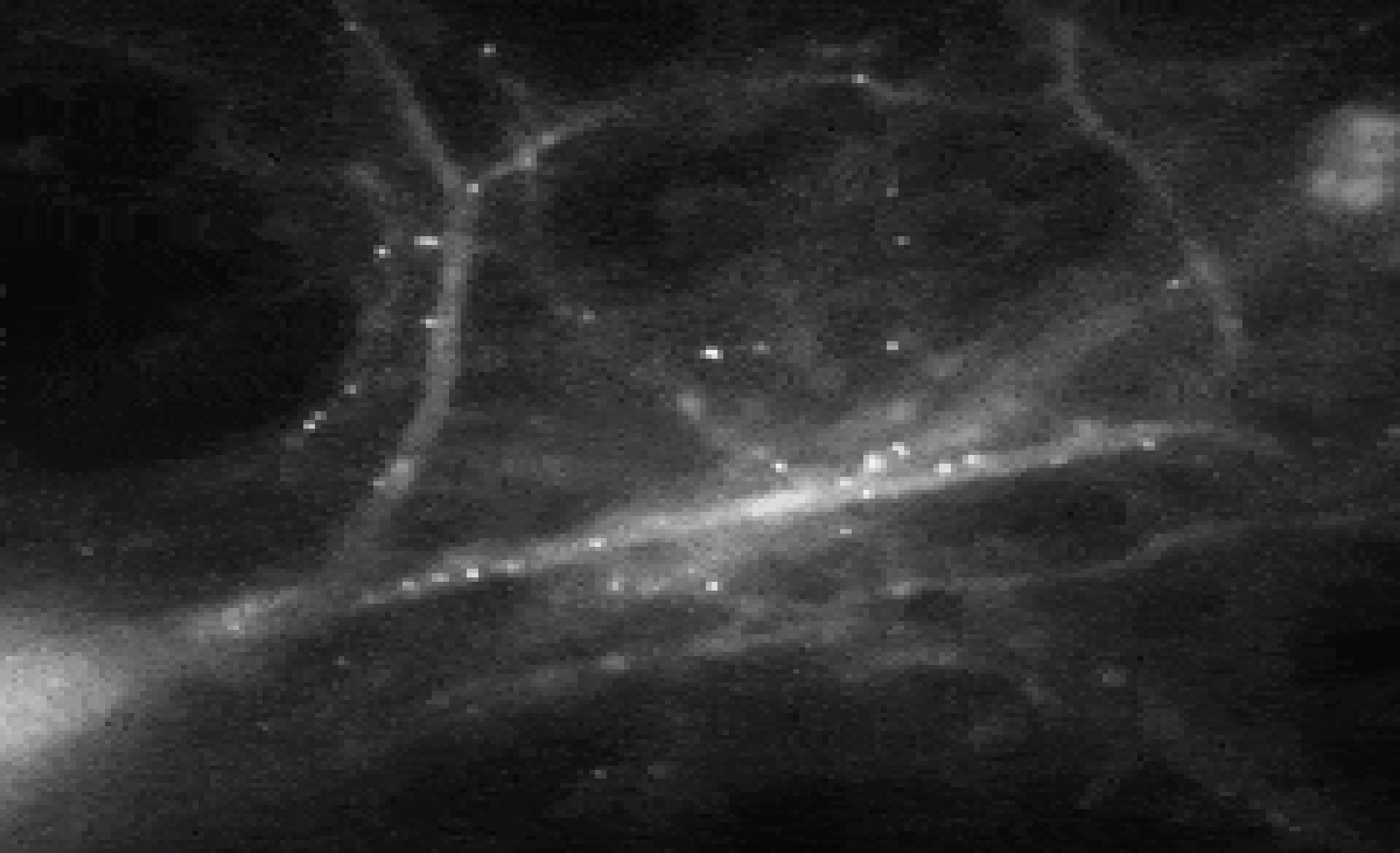


Neuroplasticità

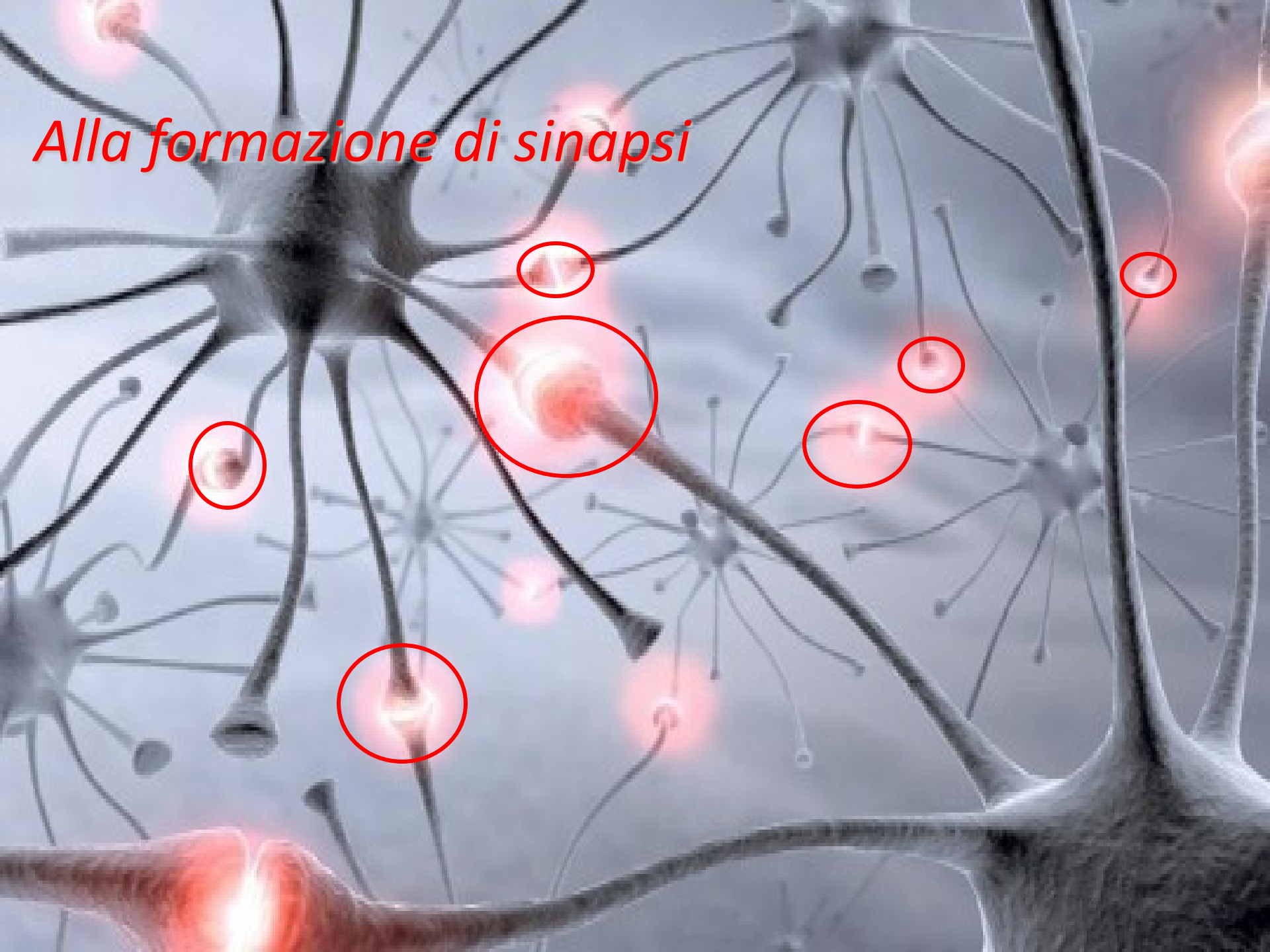
La plasticità è riconducibile ai singoli neuroni



Ai meccanismi di flusso intraneuronici



Alla formazione di sinapsi



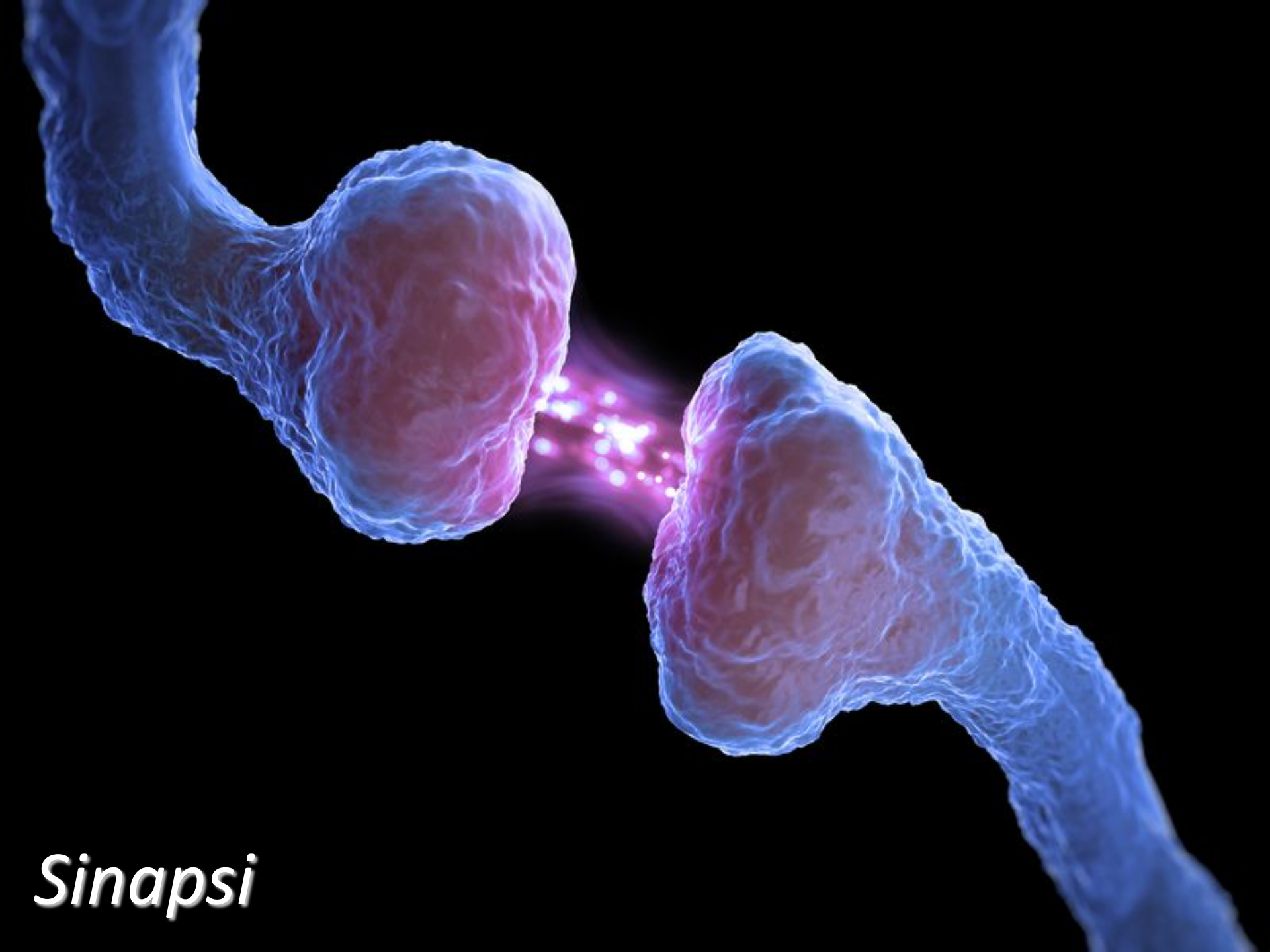
Alla loro convalida funzionale



A 3D reconstruction of a complex neural network, likely a hippocampal CA1 pyramidal neuron, showing a dense network of dendrites and spines. The dendrites are color-coded: a central yellowish-brown trunk, blue and purple branches, and a greyish-white network on the right. The spines are small protrusions along the dendrites. The background is black.

*Attraverso la formazione di "spine"
dendritiche*

La base morfologica della memoria



Sinapsi

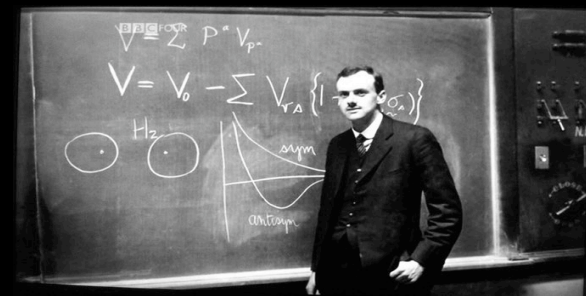
100
miliardi

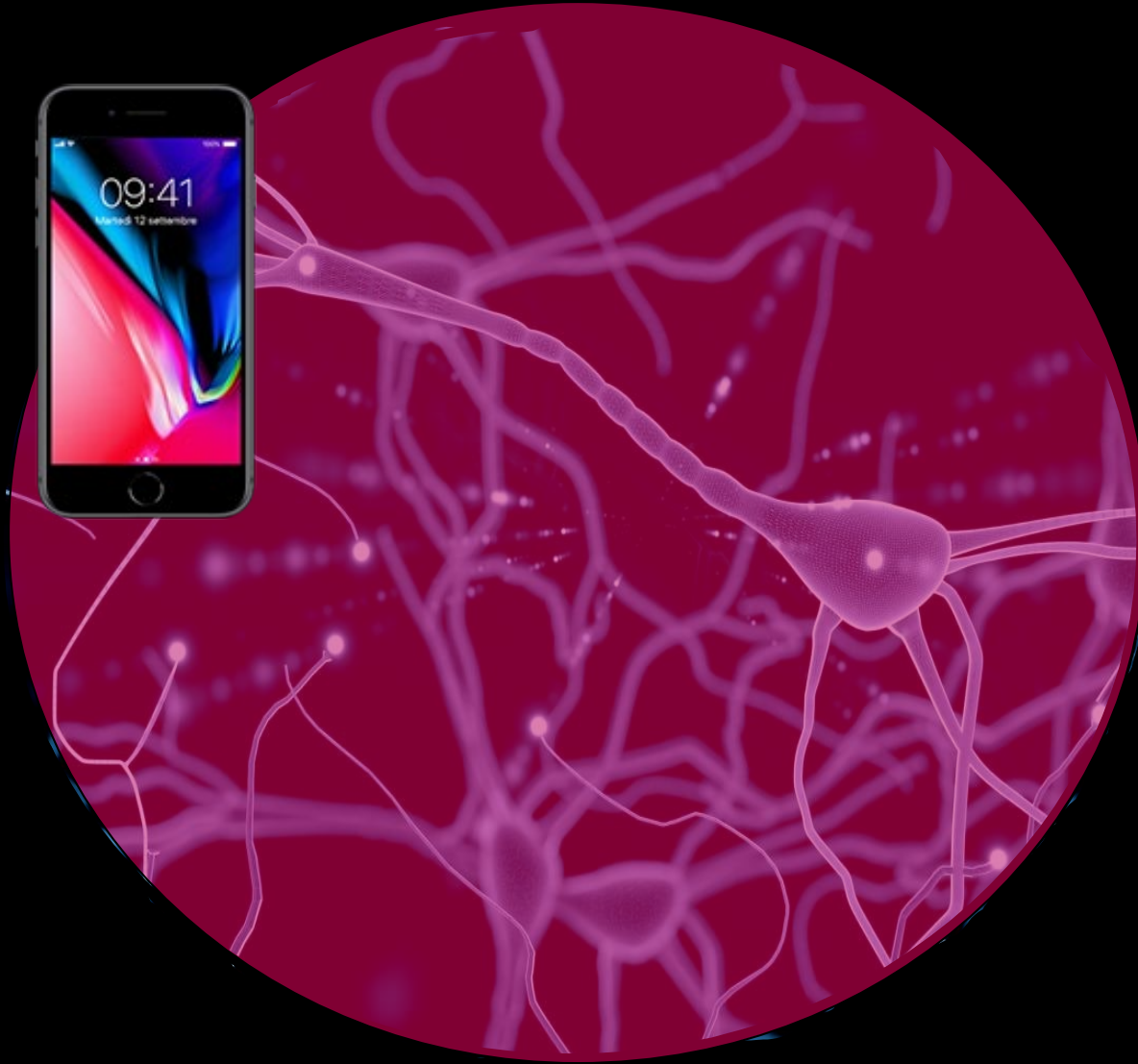
Numero sinapsi

2.783.000
10

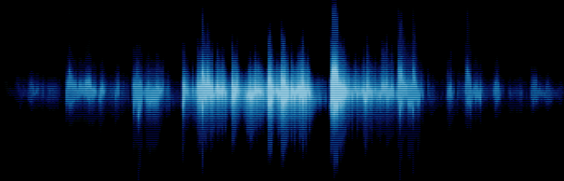
Raggio di curvatura Universo
Secondo l'equazione di Dirac
40
10 cm

$$\left[i\hbar A^\mu \gamma_{(a)}^\mu \partial_\mu - m_0 c \right] \psi = 0,$$





Neurogenesi



Motawi TK

Biochemical modifications and neuronal damage in brain of young and adult rats after long-term exposure to mobile phone radiations.

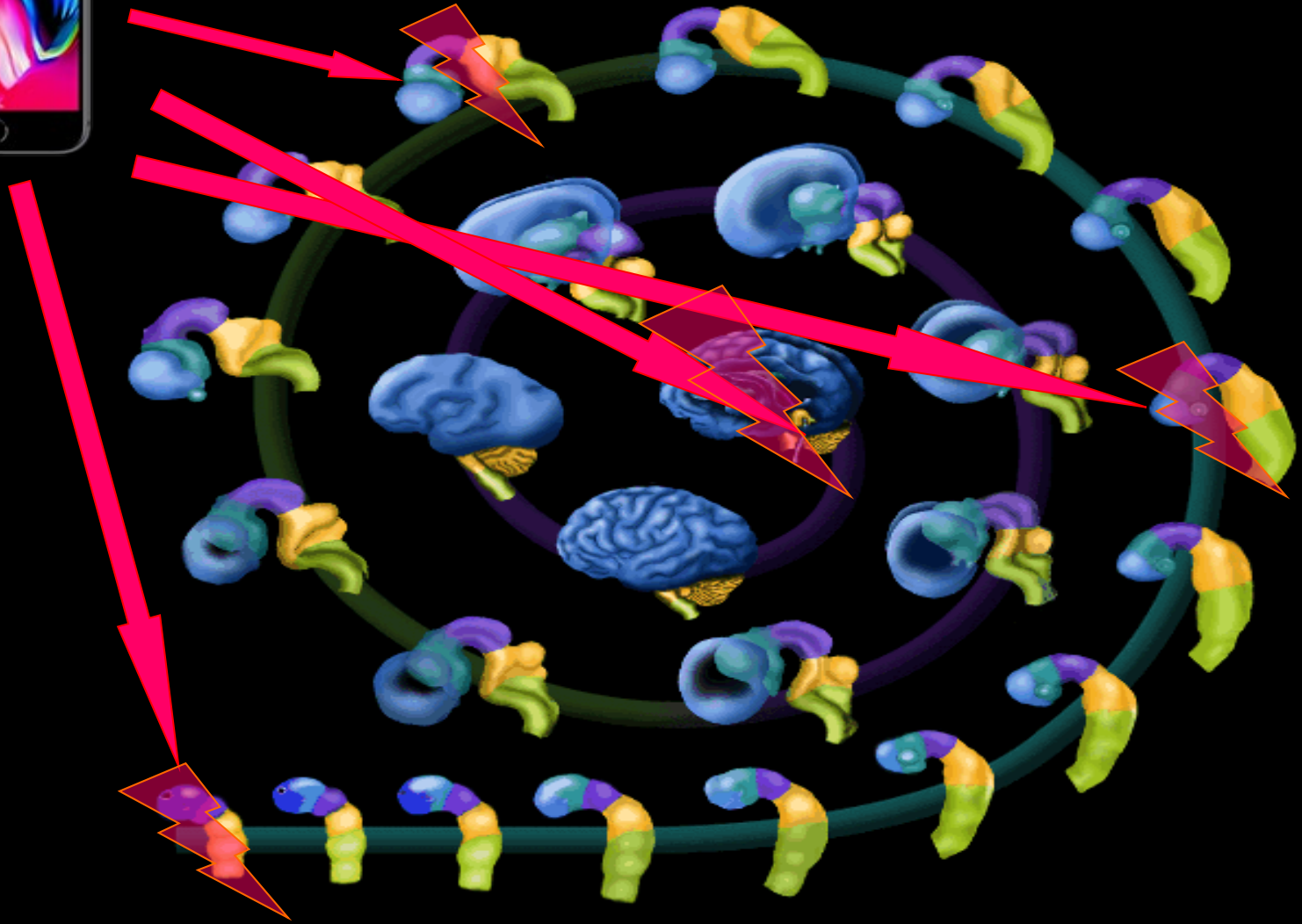
Cell Biochem Biophys. 2014 Nov;70(2):845-55.

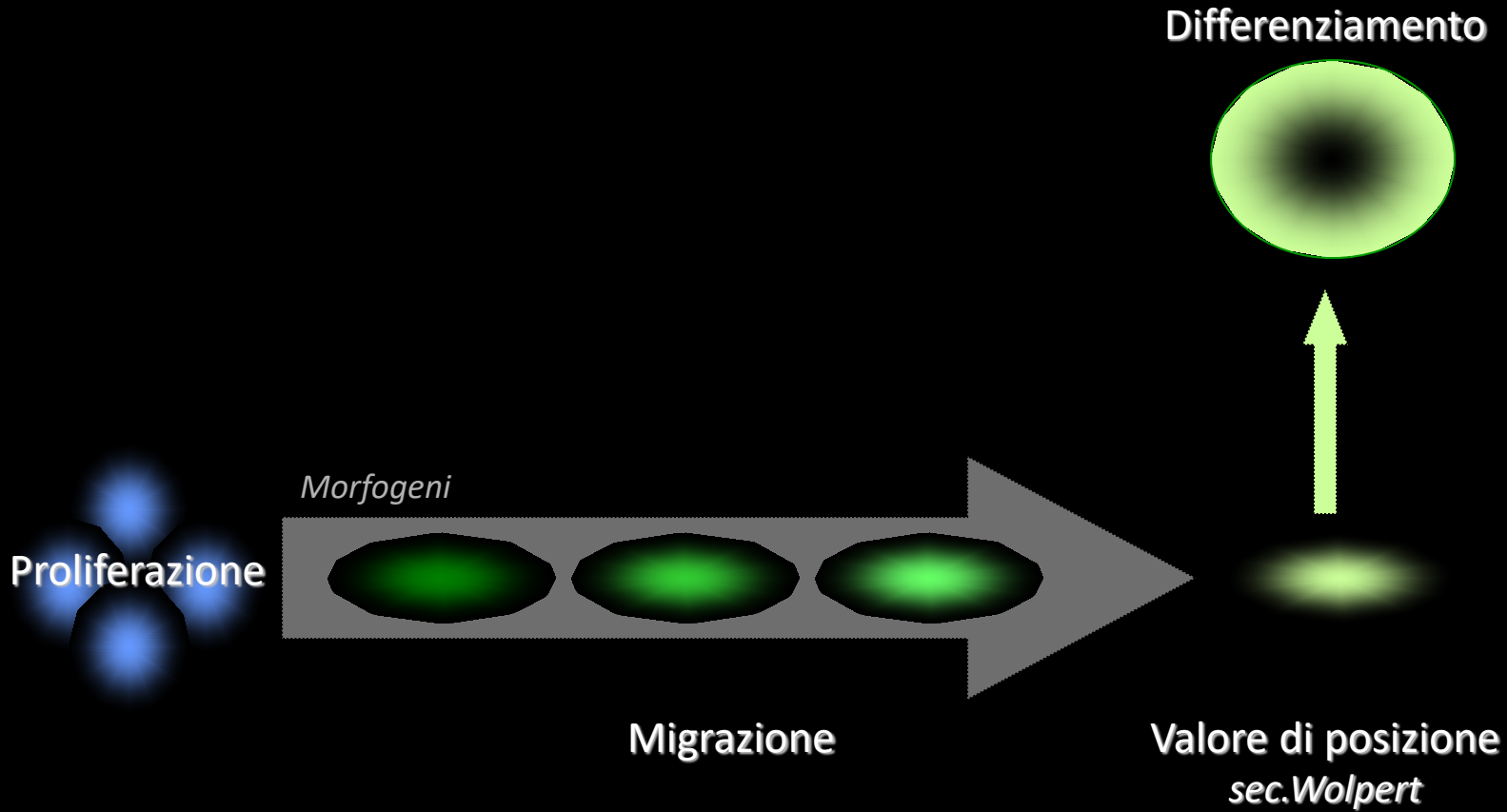


Kaplan S

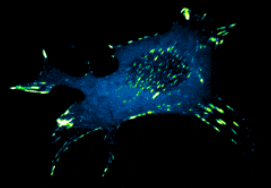
Electromagnetic field and brain development.

J Chem Neuroanat. 2016 Sep;75(Pt B):52-61.

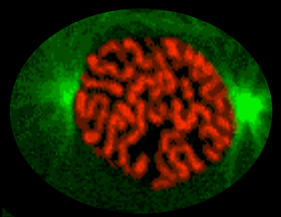




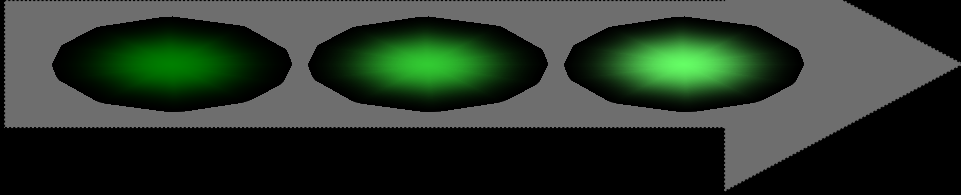
NEUROBLASTI



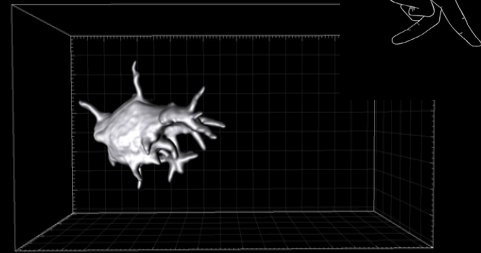
Proliferazione



Morfogeni



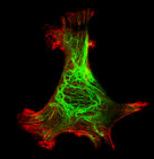
Migrazione



Differenziamento

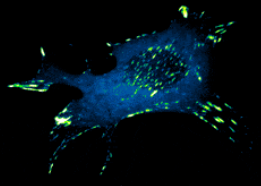


Valore di posizione
sec. Wolpert



NEUROBLASTI

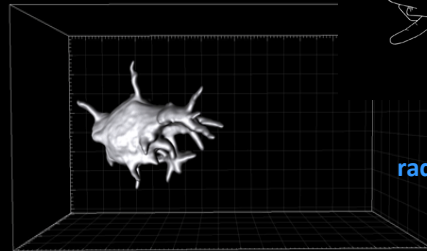
Manti L et al
Effects of modulated microwave radiation at cellular telephone frequency (1.95 GHz) induced chromosome aberrations in human lymphocytes in vitro.
Radiat Res. 2008 May;169(5):575-83.



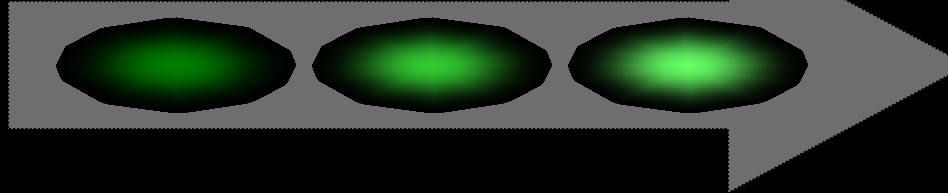
Differenziamento



Marjanović AM
Biological indicators in response to radiofrequency/microwave exposure
Arh Hig Rada Toksikol. 2012



Morfogeni



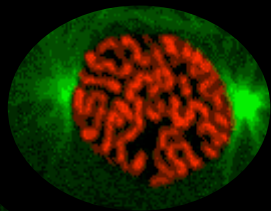
Migrazione

Aly A
Effects of 900-MHz radio frequencies on the chemotaxis of human neutrophils in vitro.
IEEE Trans Biomed Eng. 2008 Feb;55(2 Pt 1):795-7.

Valore di posizione sec. Wolpert

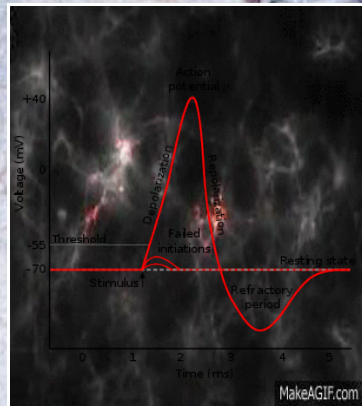


Proliferazione

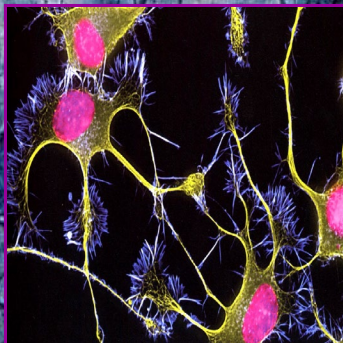
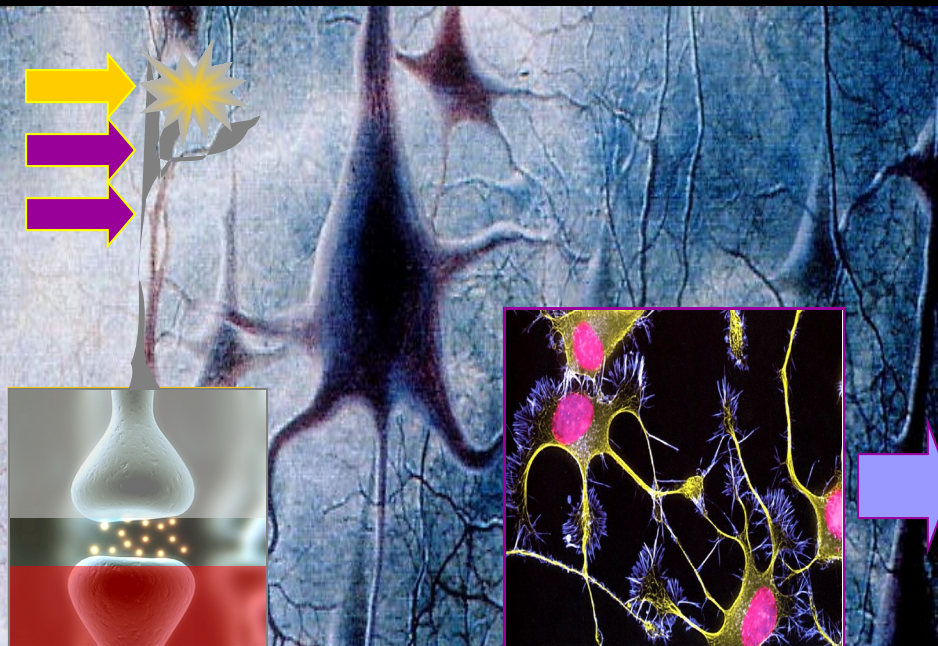


Maes A
Cytogenetic investigations on microwaves emitted by a 455.7 MHz car phone.
Folia Biol (Praha). 2000;46(5):175-80.

SPIKEs

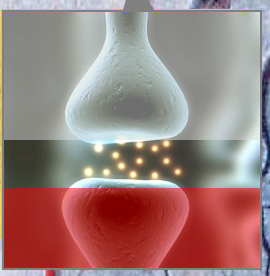
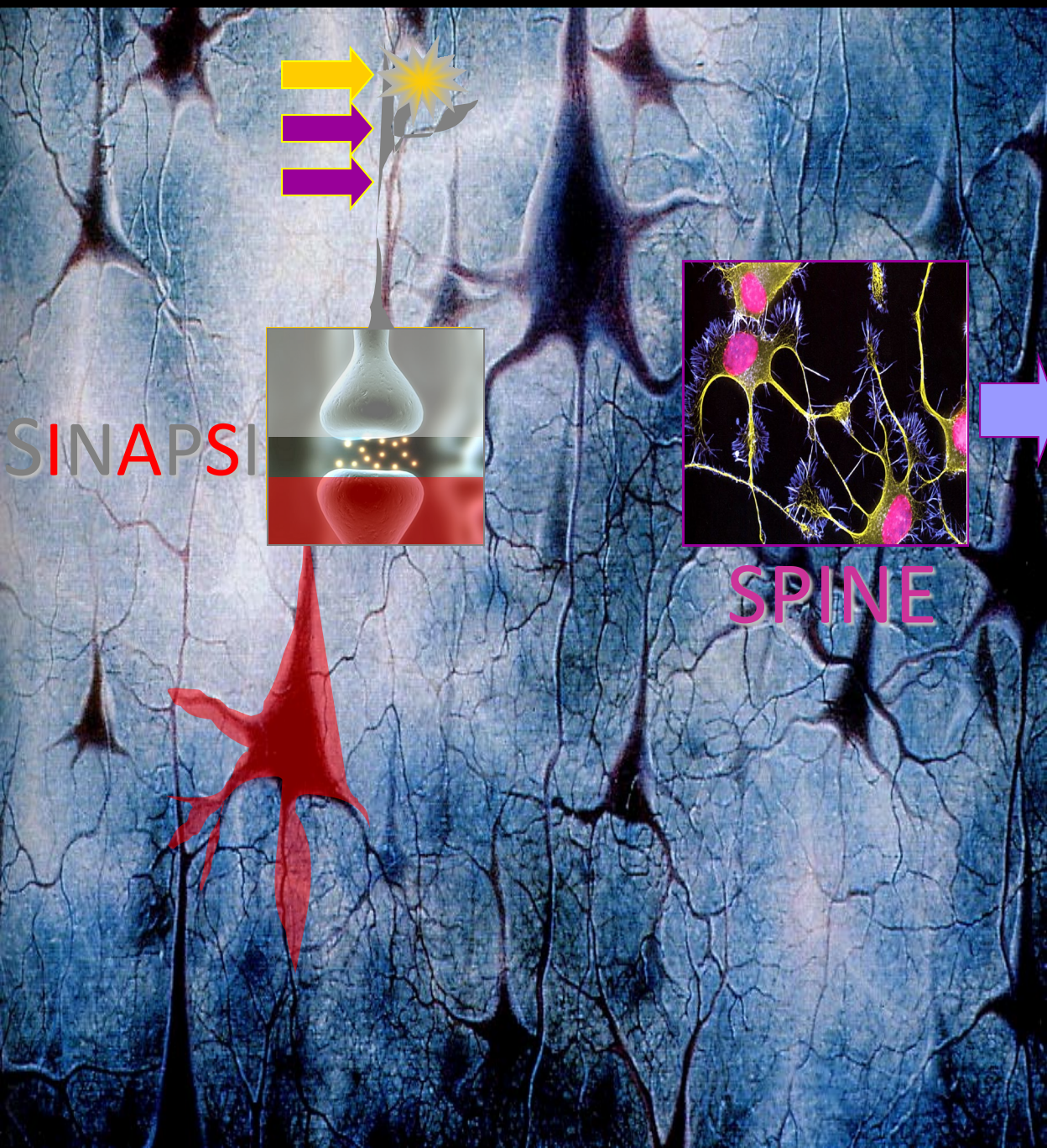


SINAPSI

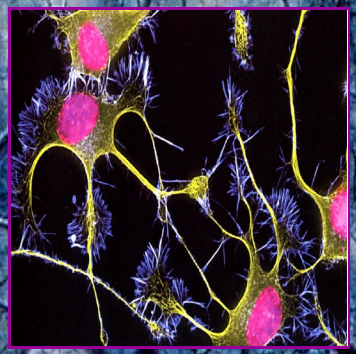


SPINE

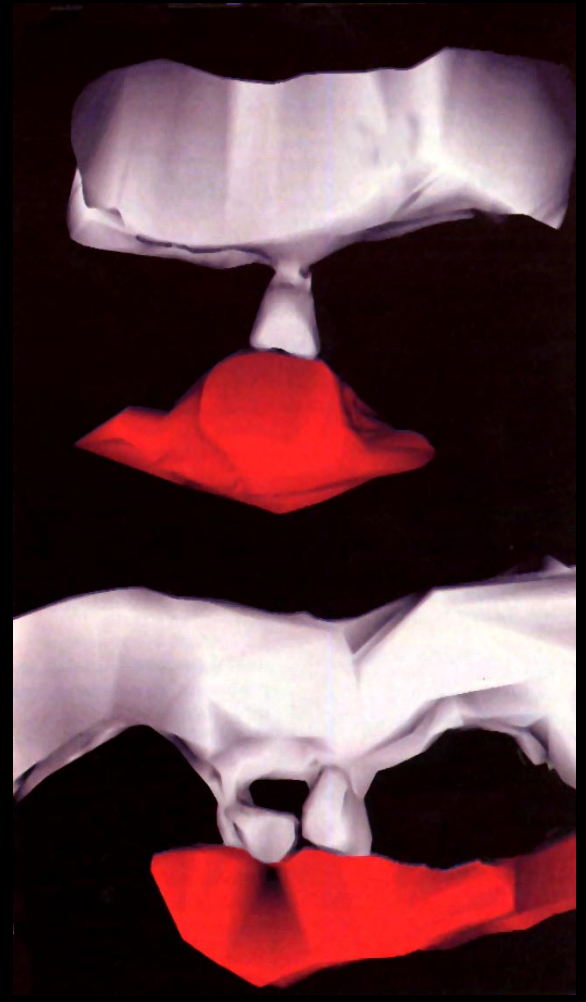




SINAPSI



SPINE



Azione sulle sinapsi che regolano la memorizzazione



SINAPSI

Zhi WJ

Microwave radiation leading to shrinkage of dendritic spines in hippocampal neurons mediated by SNK-SPAR pathway.

Brain Res. 2018 Jan 15;1679:134-143.

Wang H.,

Impairment of long-term potentiation induction is essential for the disruption of spatial memory after microwave exposure.

Int J Radiat Biol. 2013 Dec;89(12):1100-7.

Wang LF

Influence of microwave radiation on synaptic structure and function of hippocampus in Wistar rats

Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 007 Apr;25(4):211-4.

Xu S

Chronic exposure to GSM 1800-MHz microwaves reduces excitatory synaptic activity in cultured hippocampal neurons.

Neurosci Lett. 2006 May 8;398(3):253-7.

Huang X.

Silent synapse: A new player in visual cortex critical period plasticity.

Pharmacol Res. 2019 Mar;141:586-590.

Vincent-Lamarre P

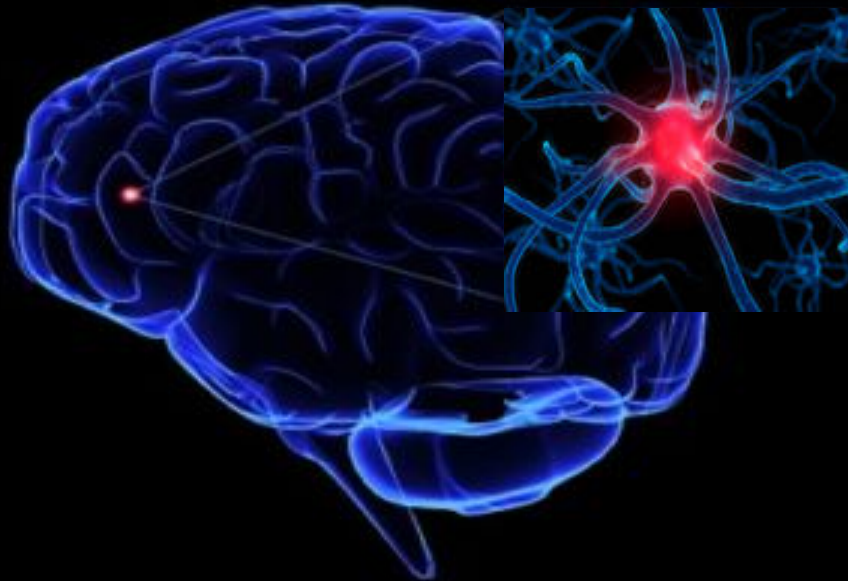
The Eloquent Silent Synapse.

Trends Neurosci. 2018 Sep;41(9):557-559.



Suggestion:

Interferenza sinaptica ?



Malformazioni da anomalie della:

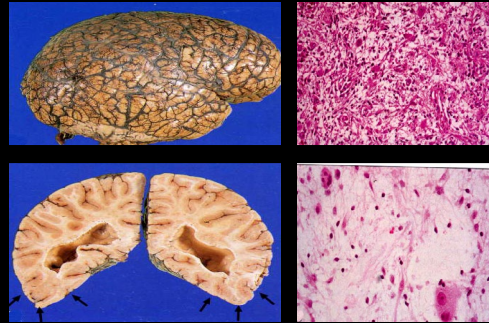
PROLIFERAZIONE

MIGRAZIONE

ORGANIZZAZIONE

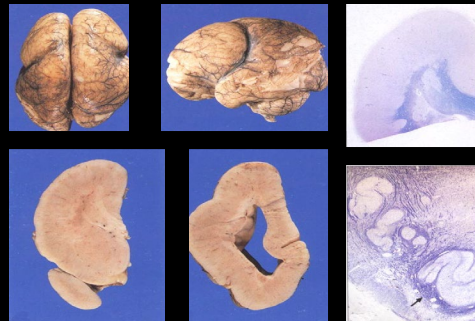
Malformazioni da anomalie della:

PROLIFERAZIONE



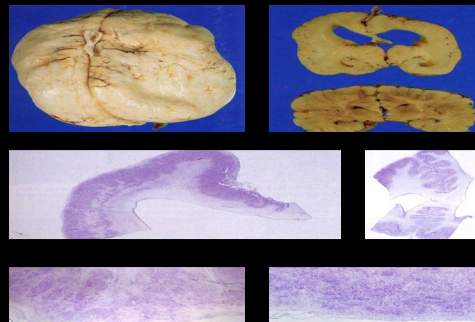
Microcefalie
Megaloencephalia
Amartomi
Gangliomi

MIGRAZIONE

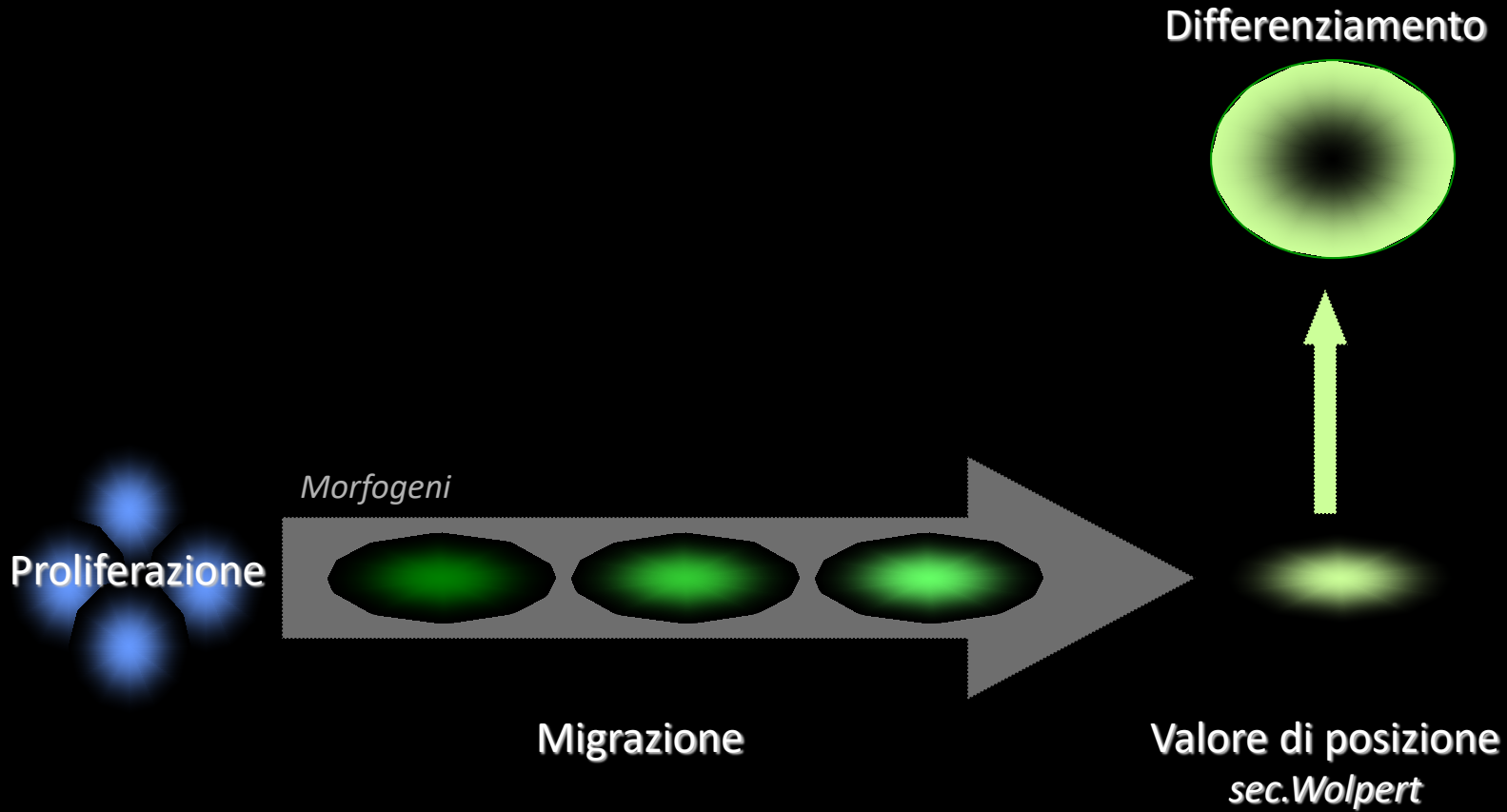


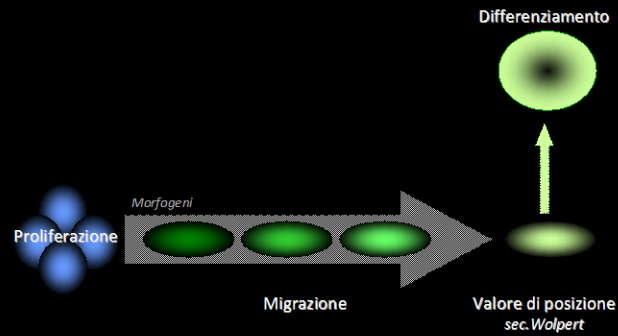
Lissencephalia

ORGANIZZAZIONE



Polimicrogiria
Schizencephalia





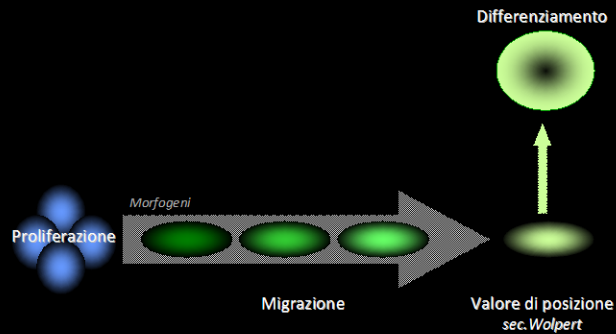
Territorio di migrazione

MORFOGENI

Nature. 2001 Oct 25;413(6858):797-803.

Morphogen gradient interpretation.

Gurdon JB, Bourillot PY



Territorio di migrazione

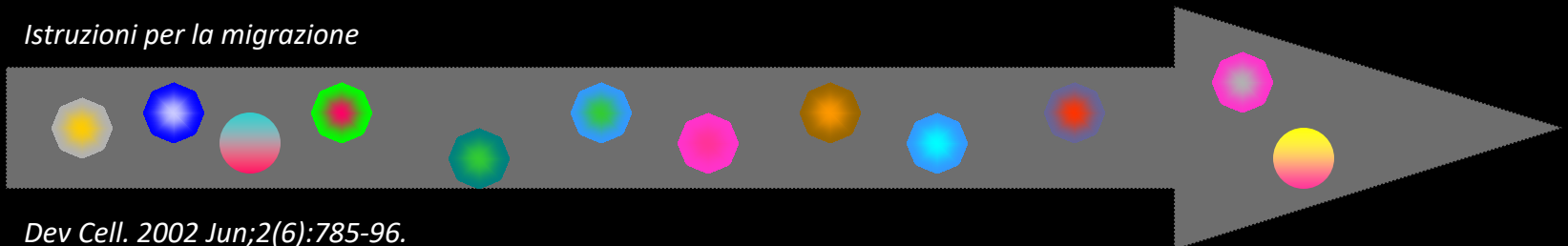
MORFOGENI

Nature. 2001 Oct 25;413(6858):797-803.

Morphogen gradient interpretation.

Gurdon JB, Bourillot PY

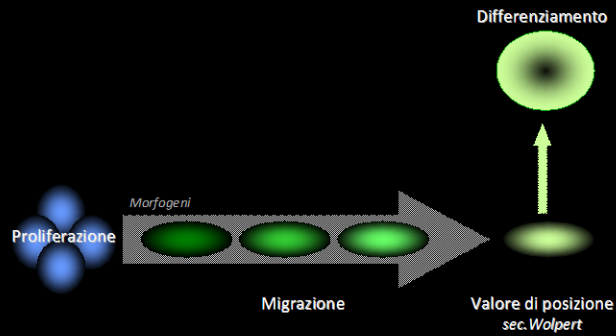
Istruzioni per la migrazione



Dev Cell. 2002 Jun;2(6):785-96.

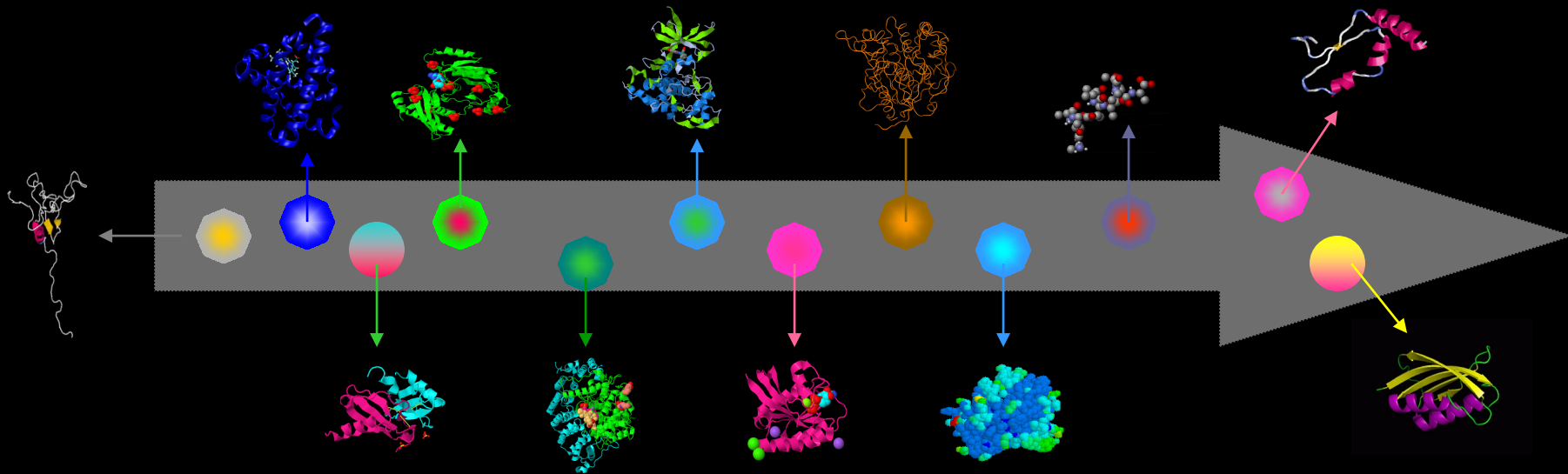
Do morphogen gradients arise by diffusion?

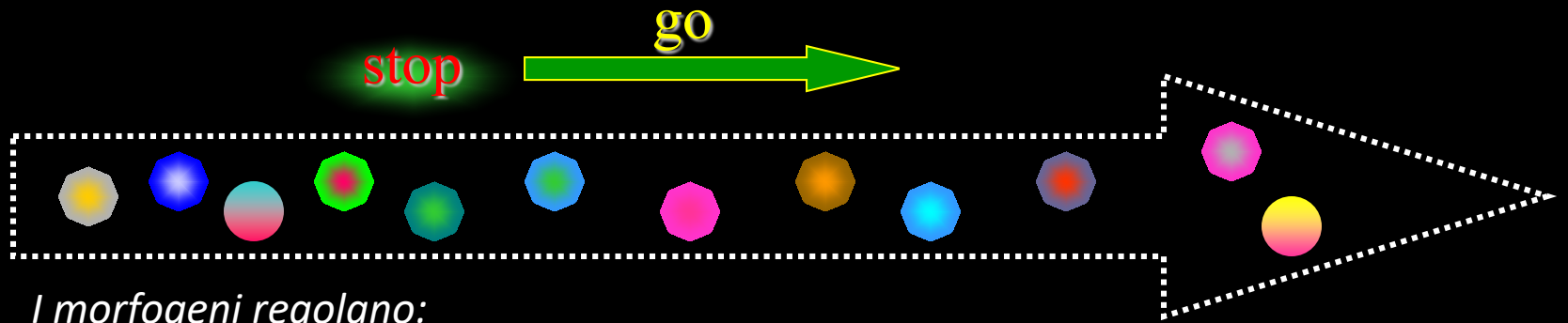
Lander AD, Nie Q, Wan FY.



Territorio di migrazione

MORFOGENI





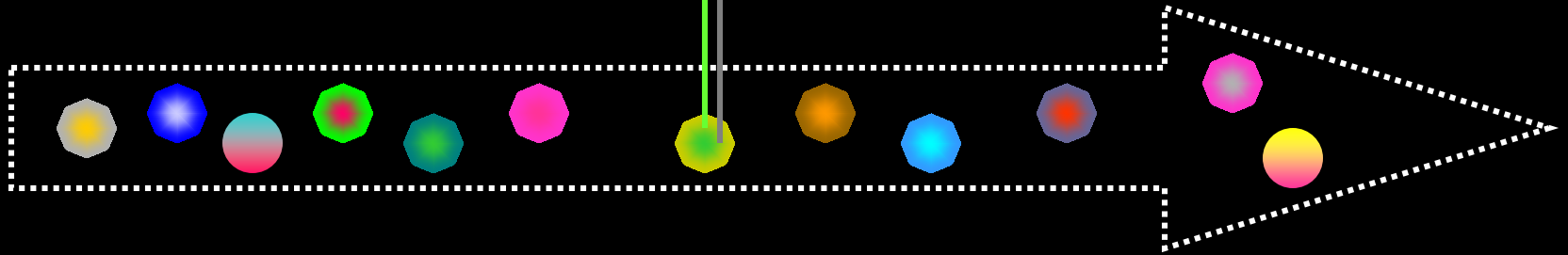
I morfogeni regolano:

Chemiotassi
Chemiocinesi
Pit-Stop

Wolpert L.

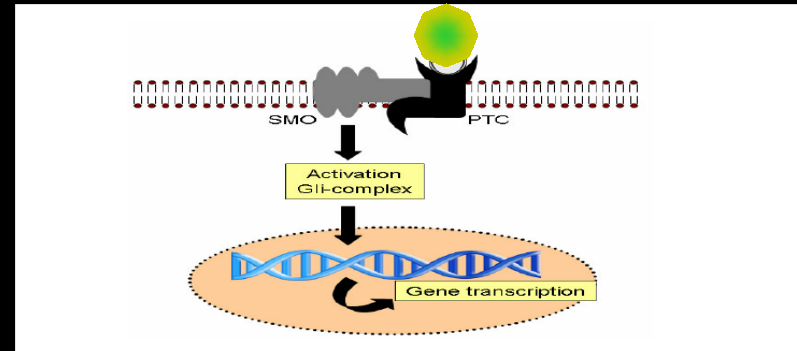
Signals in development: STOP, GO, STAY and POSITION.

J Cell Sci Suppl. 1990;13:199-208.



Roles of SHH signaling:

- Limb development
- **Neural differentiation**
- Facial morphogenesis
- Hair and feather development
- Forming the midline of the body



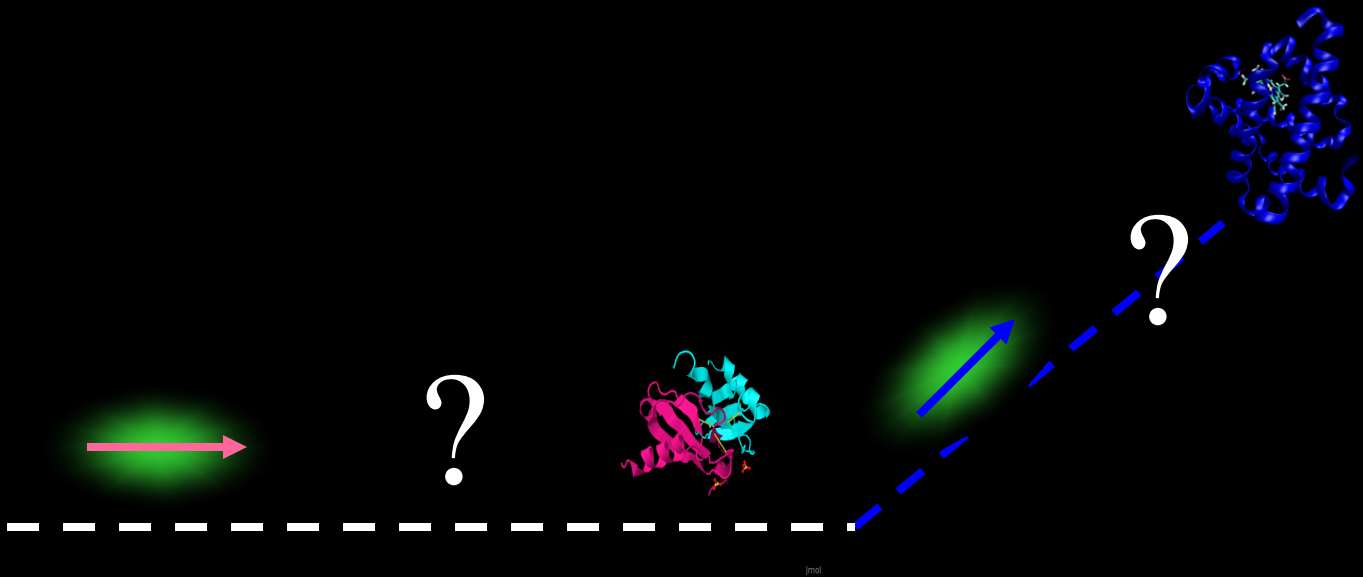
Is a pleiotropic factor in the developing central nervous system (CNS), driving proliferation, specification, and axonal targeting in multiple sites within the forebrain, hindbrain, and spinal cord

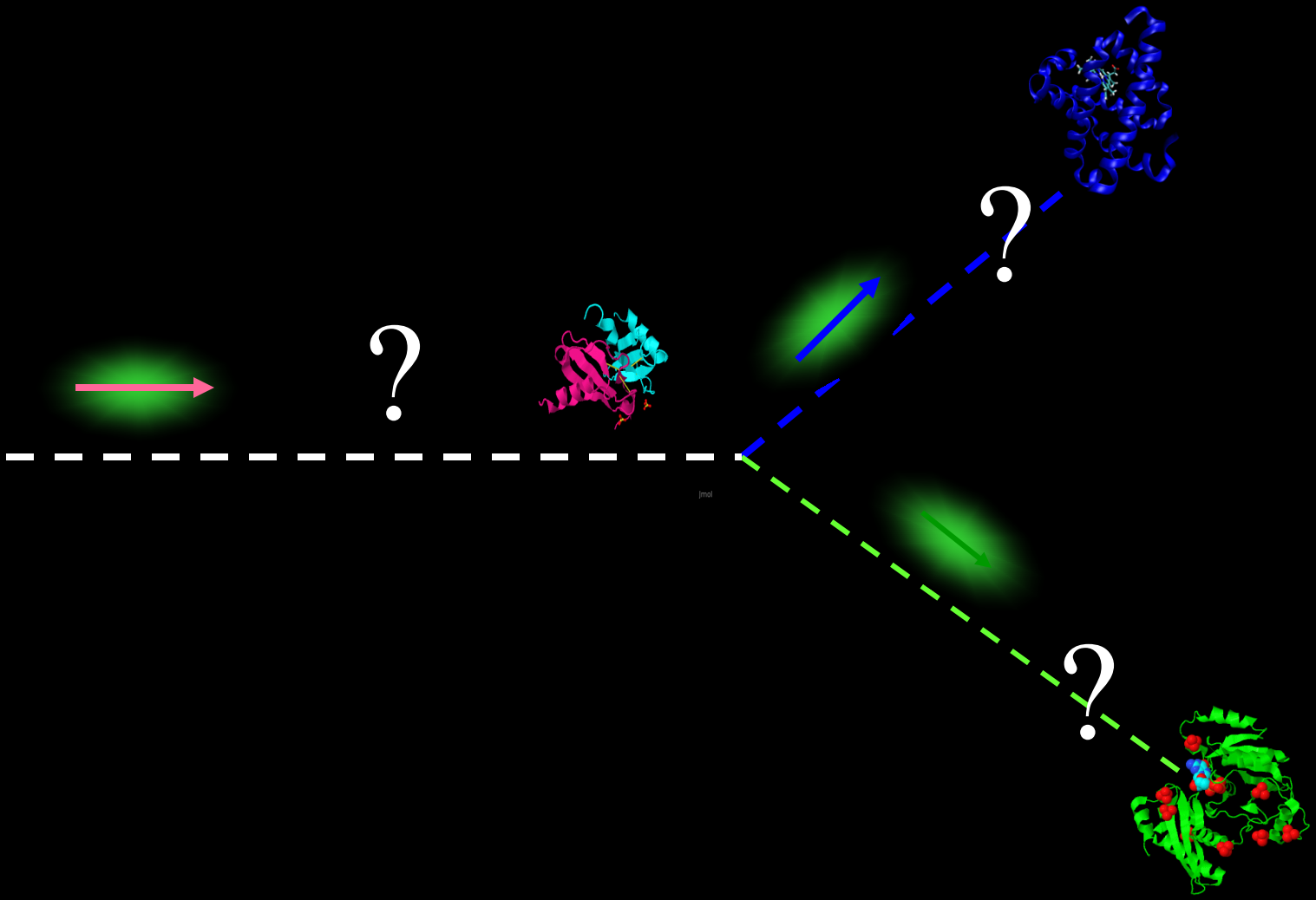


?



mol





Jmol

Jmol

Antenna trasduttrice



Malicki JJ et Al.

The Cilium: Cellular Antenna and Central Processing Unit.

Trends Cell Biol. 2017 Feb;27(2):126-140.

Ostrowski LE et al.

Cilia and models for studying structure and function.

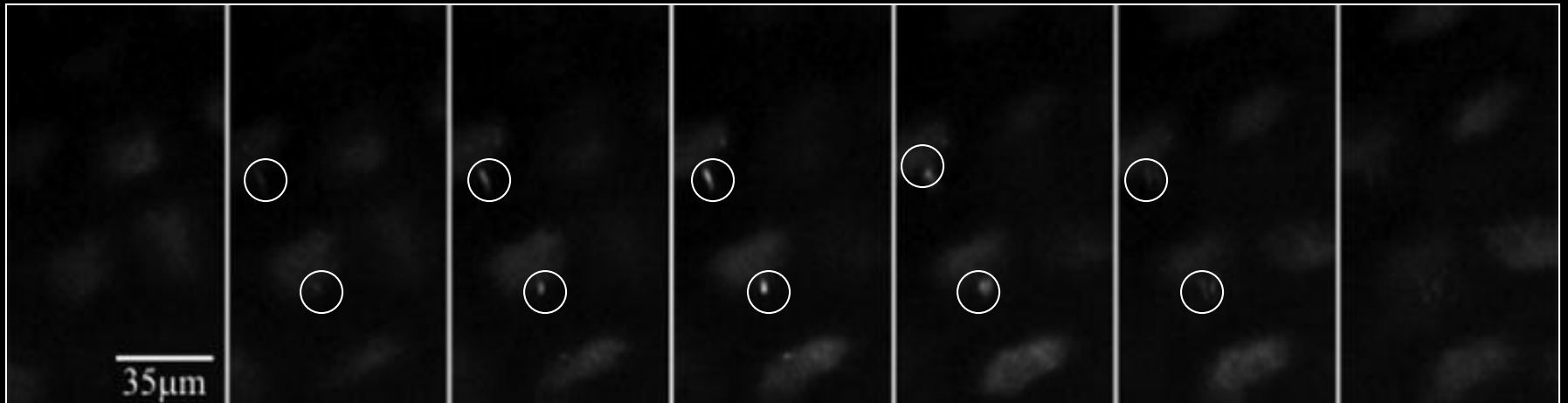
Proc Am Thorac Soc. 2011 Sep;8(5):423-9.

Benmerah A.

The ciliary pocket.

Curr Opin Cell Biol. 2013 Feb;25(1):78-84.

Primary Cilium

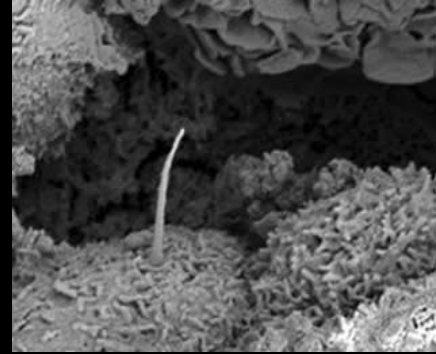
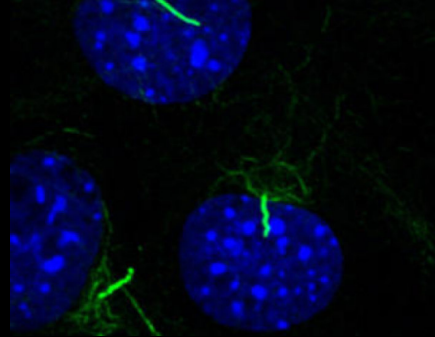


Wheway G et al.

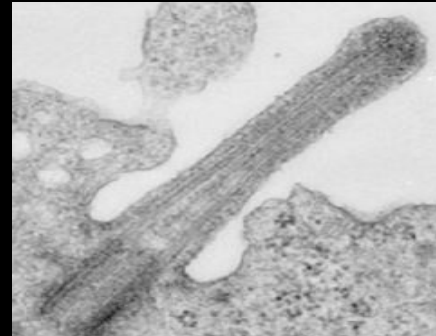
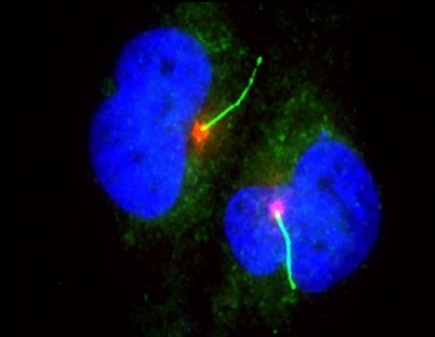
Signaling through the Primary Cilium.

Front Cell Dev Biol. 2018 Feb 8;6:8.

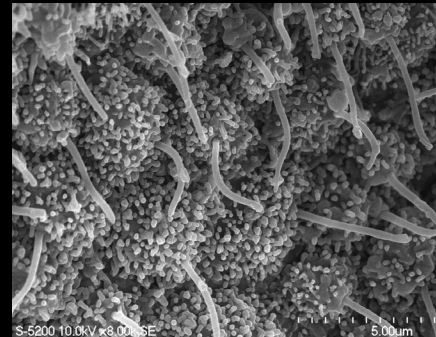
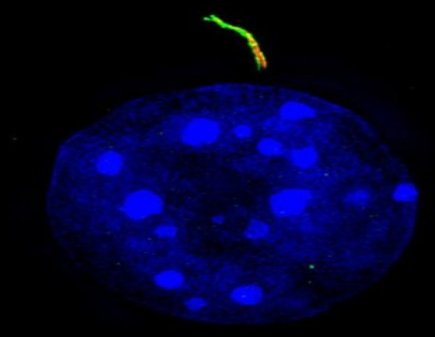
Ciglio Primario:struttura



Pazour GJ et al.
The vertebrate primary cilium is a sensory organelle.
Curr Opin Cell Biol. 2003 Feb 15(1):105-10. Review.



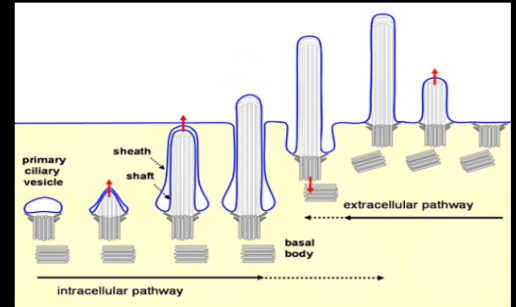
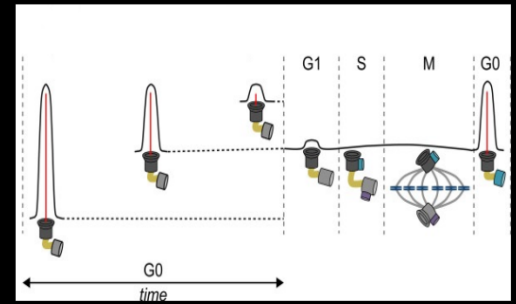
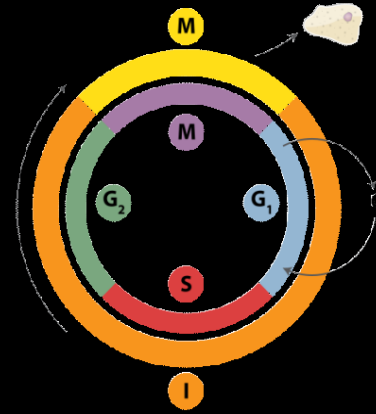
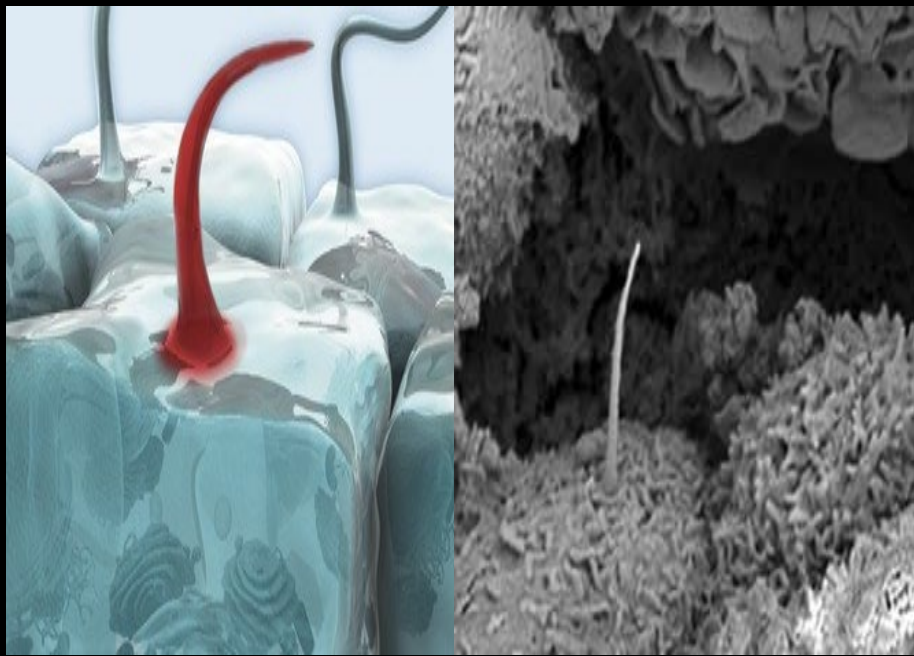
Malicki JJ et Al.
The Cilium: Cellular Antenna and Central Processing Unit.
Trends Cell Biol. 2017 Feb ;27(2):126-140



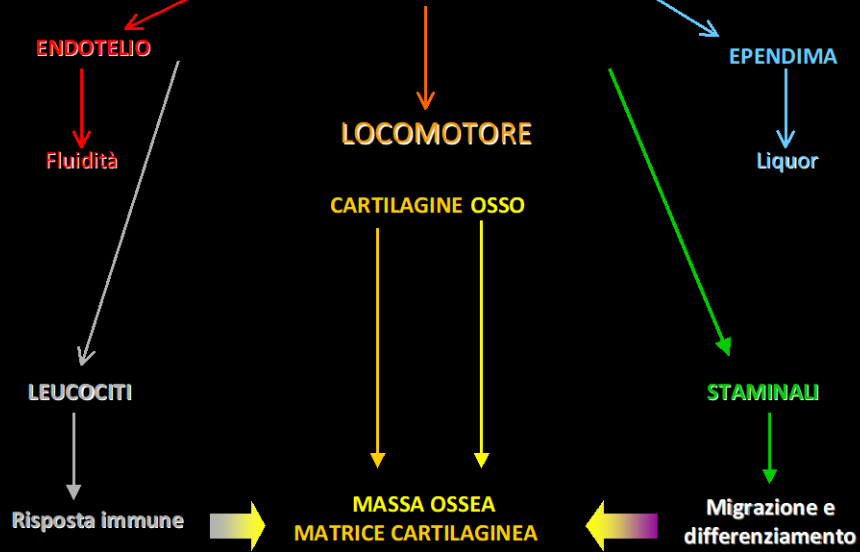
Fry AM et al.
The primary cilium: guardian of organ Development and homeostasis.
Organogenesis. 2014 Jan 1;10(1):62-8.

A cellular cybernetic probe

Pool Ca (1985), Tajana GF (1985)



Funzioni del ciglio primario

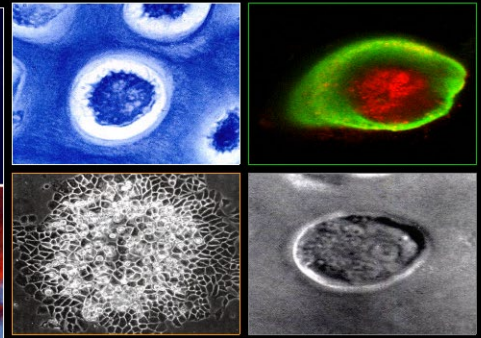


Gianfranco Tajana

IL CONDRONE

Unità morfofunzionale della cartilagine articolare

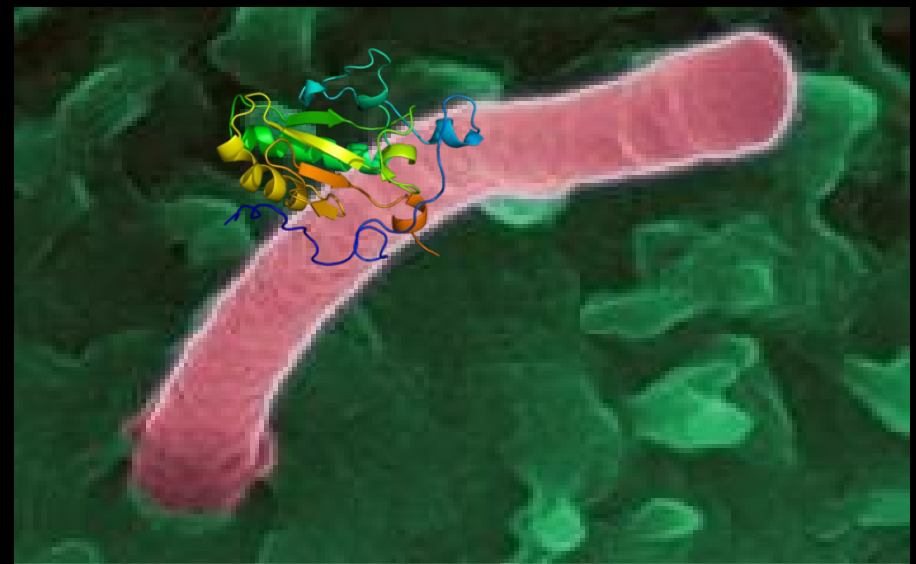
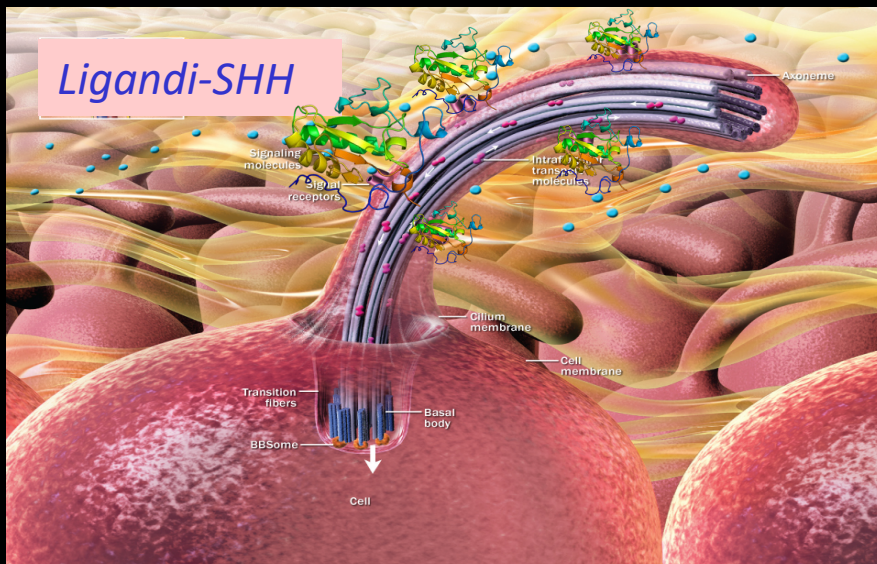
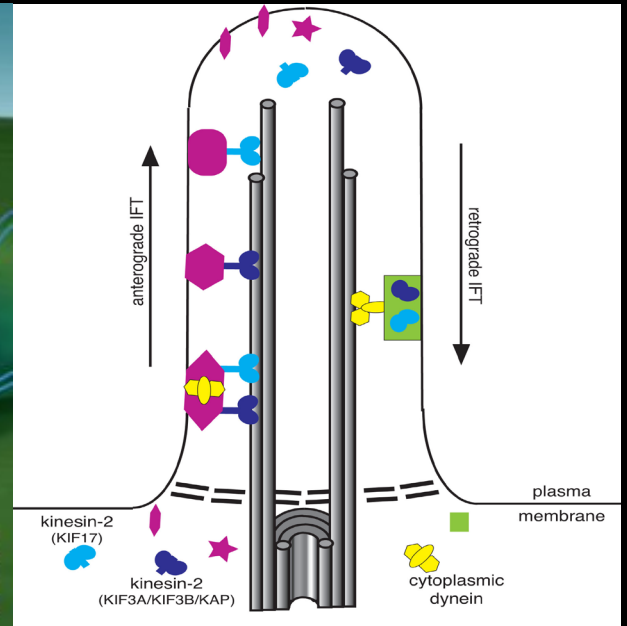
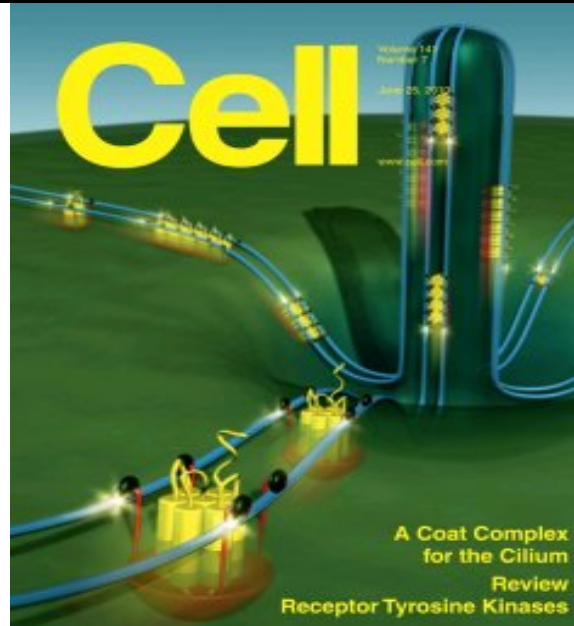
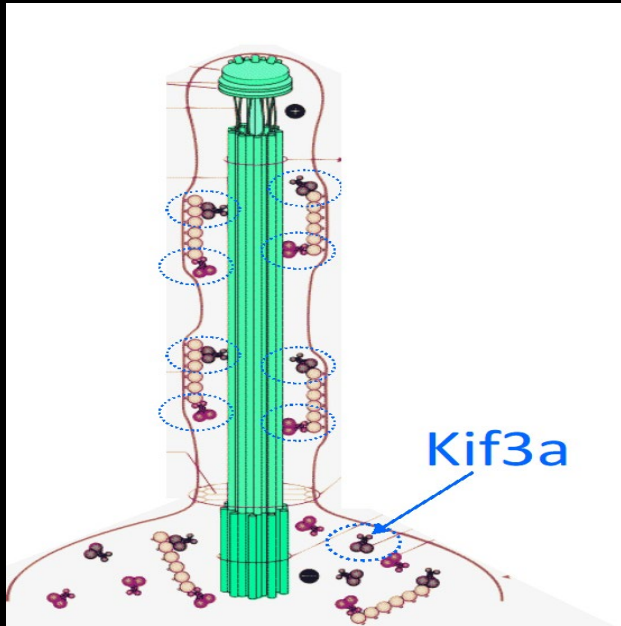
Un modello per la pianificazione delle scelte terapeutiche in corso di osteoartrite

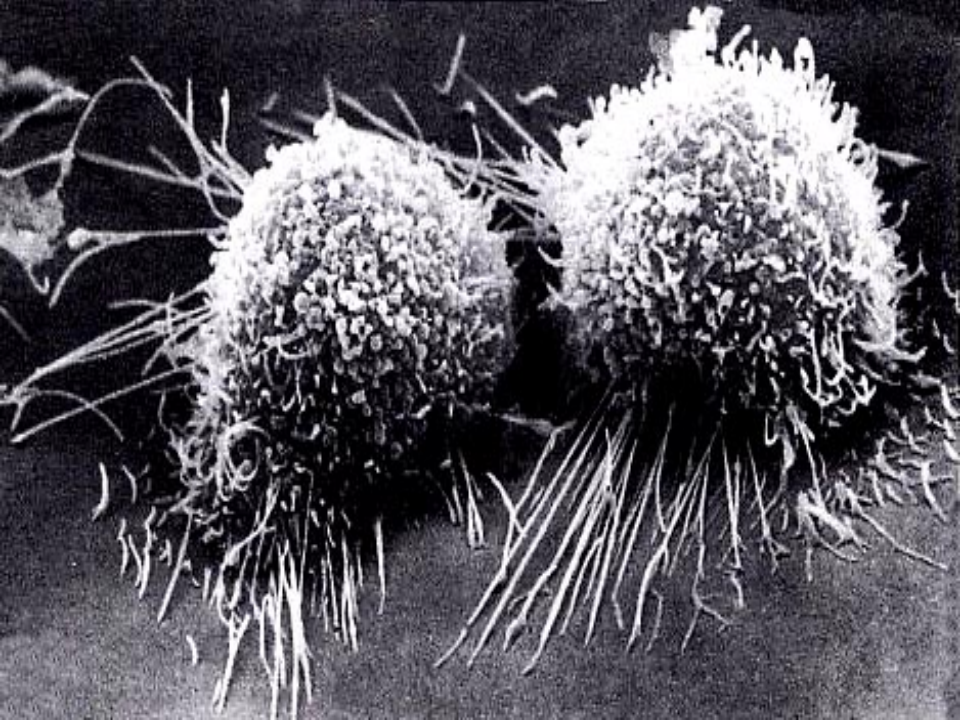


Ciglio "singolo"

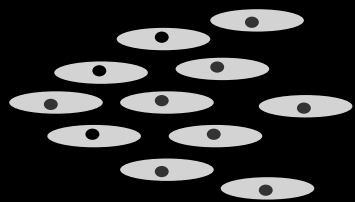
Meccanosensore ?

Ciglio Primario:funzioni

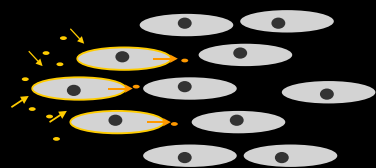




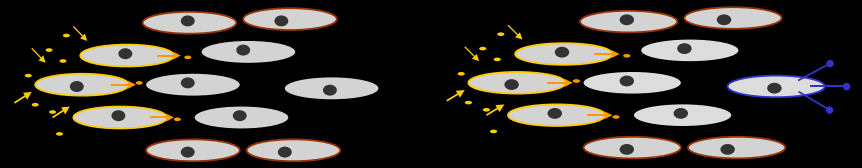
Anilizzatrici



Marginatrici



Cancellatrici

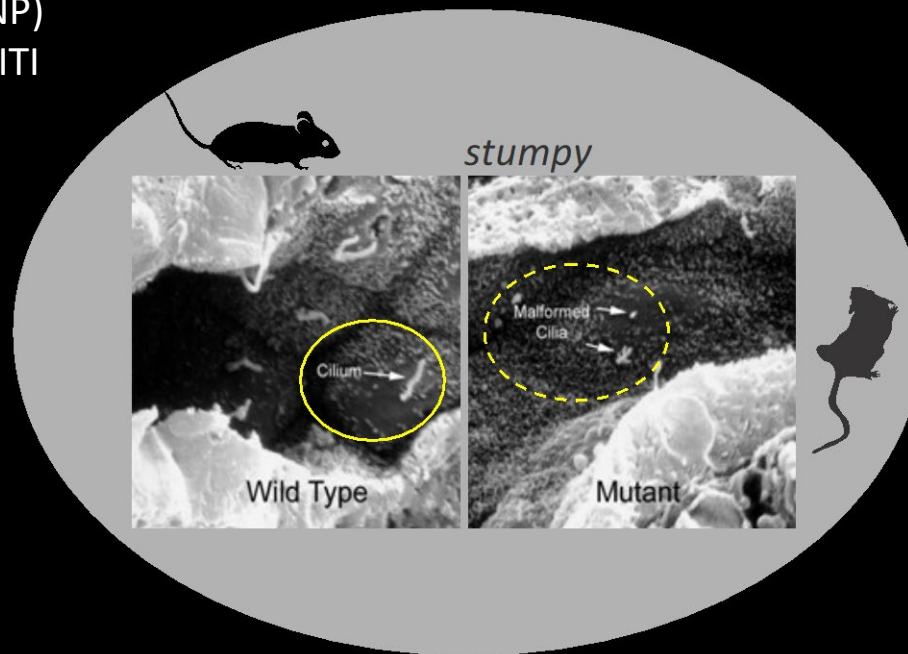
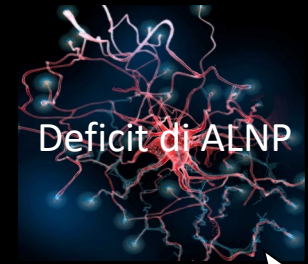
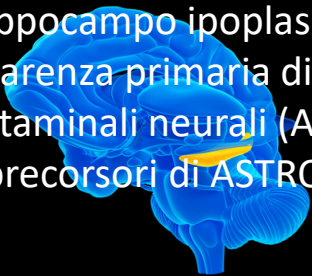


Proc Natl Acad Sci U S A. 2008 Sep 2;105(35):13127-32.

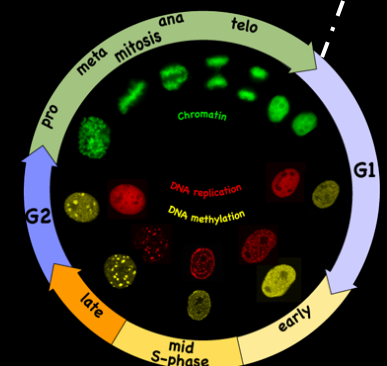
Primary cilia regulate hippocampal neurogenesis by mediating sonic hedgehog signaling.

Breunig JJ et al.

Ippocampo ipoplasico con carenza primaria di cellule staminali neurali (ALNP) precursori di ASTROCITI



Uscita dal ciclo



Il ciglio primario regola il compartimento delle cellule staminali verso il differenziamento ASROCITARIO

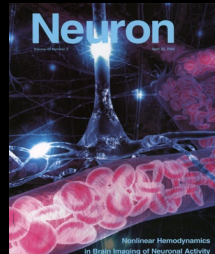
Il ciglio primario è essenziale nello sviluppo del forebrain

J Neurosci. **2008** Nov 26;28(48):12887-900. **A crucial role for primary cilia in cortical morphogenesis.**
Willaredt MA



La trasduzione del segnale Sonic hedgehog (Shh) è dipendente dal CP

Neuron. **2011** Mar 24;69(6):1046-60. **Cilia in the CNS: the quiet organelle claims center stage.**
Louvi A



La Rotatin regola la rotazione assiale dell'embrione attraverso CP

Am J Hum Genet. **2012** Sep 7;91(3):533-40.



IL CP regola la polarità cellulare durante lo sviluppo.

Neuron. **2014** May 7;82(3):511-21. **Primary cilia in the developing and mature brain.**
Guemez-Gamboa A



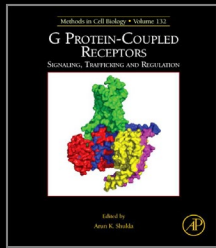
CP regola il differenziamento dei neuroni inibitori ed eccitatori corticali.

Neuroscientist. **2015** Apr;21(2):136-51. **Influences of primary cilia on cortical morphogenesis and neuronal subtype maturation.** Sarkisian MR





Sonic hedgehoggt interviene nella protezione del cervello adulto.
Semin Cell Dev Biol. **2014** Sep;33:105-11. **Sonic hedgehog signaling in the postnatal brain.** Miller M.



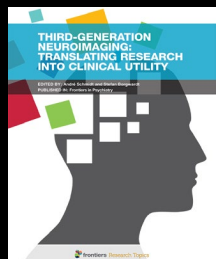
L'intero complesso ciliare può essere trasferito alle cellule figlie.
Methods Cell Biol. **2015**;127:93-129. **Analysis of primary cilia in the developing mouse brain.** Paridaen JT



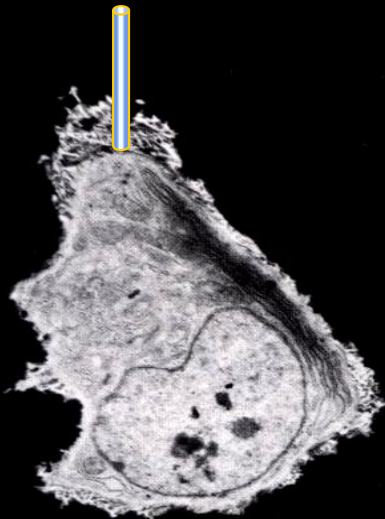
CP regola I livelli di GLI3R durante la formazione del corpo calloso
Hum Mol Genet. **2015** Sep 1;24(17):4997-5014. **The role of primary cilia in corpus callosum formation is mediated by production of the Gli3 repressor.** Laclef C



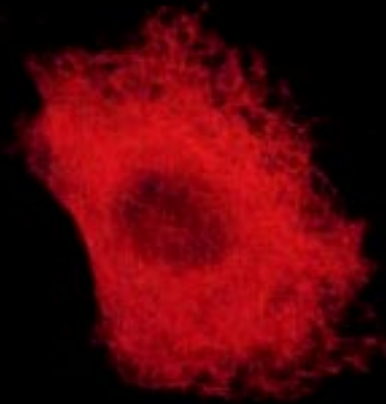
CP controlla il differenziamento delle creste neurali
Dev Biol. **2017** Nov 15;431(2):168-178. **Neural crest cells utilize primary cilia to regulate ventral forebrain morphogenesis via Hedgehog-dependent regulation of oriented cell division.** Schock EN



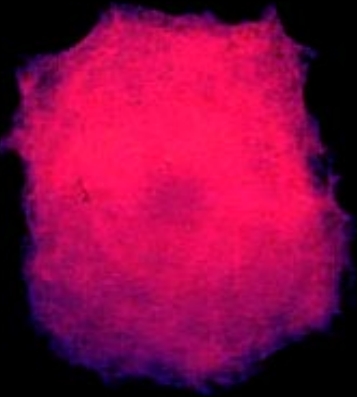
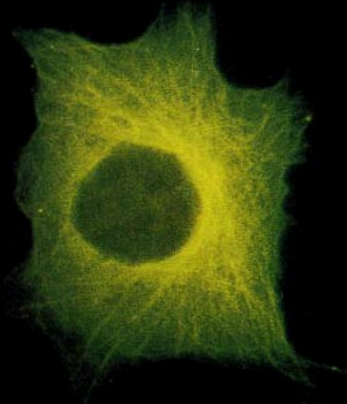
CP per le sue capacità sensoriali potrebbe essere coinvolto nello sviluppo di diverse patologie psichiatriche
Front Psychiatry. **2019** Mar 4;10:104. **Primary Cilia-An Underexplored Topic in Major Mental Illness.** Pruski M



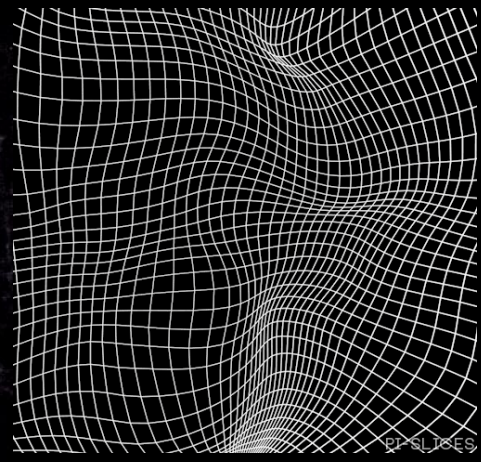
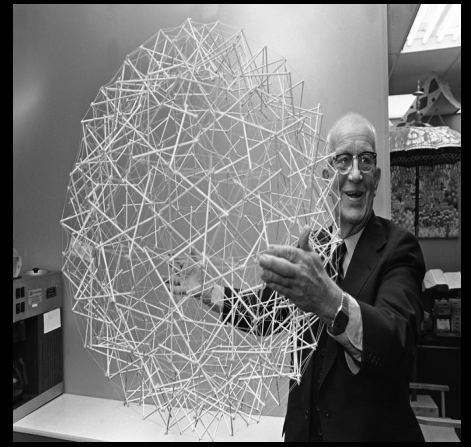
citoscheletro



tensostruttura



Gabbia Fullaranica

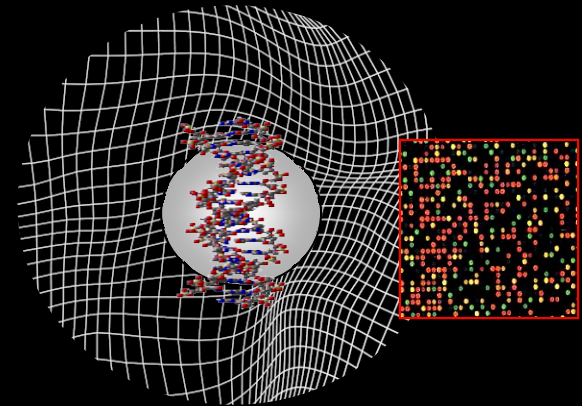
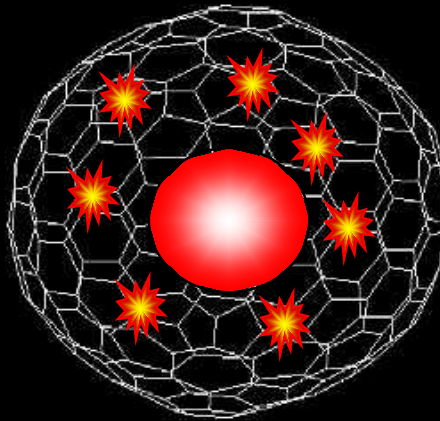
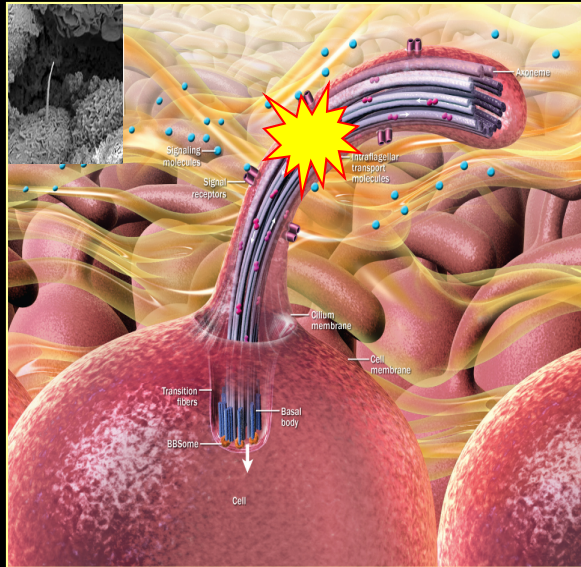


Vibrante...

Malicki JJ et al.

The Cilium: Cellular Antenna and Central Processing Unit.

Trends Cell Biol. 2017 Feb;27(2):126-140.

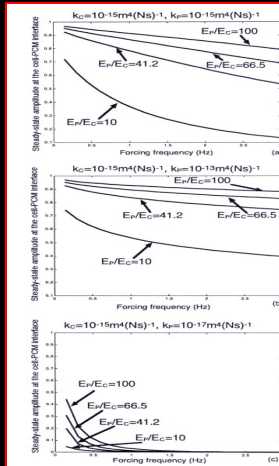
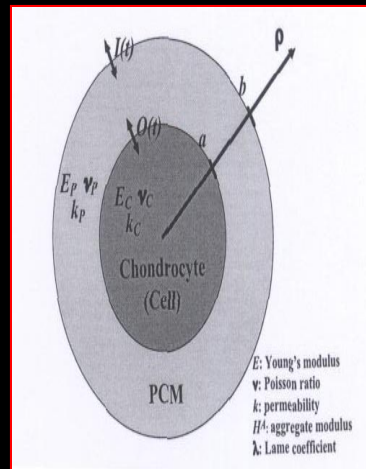


Pienta KJ, Coffey DS

Cellular harmonic information transfer through a cilium system.

Med Hypotheses 1991 Jan; 34:88-95

HARMONIC WAVE →



$$\partial_t u = \begin{cases} k_c H_c^A (\rho^{-2} \partial_\rho (\rho^2 \partial_\rho u) - 2\rho^{-2} u) & 0 \leq \rho \leq a \\ k_p H_p^A (\rho^{-2} \partial_\rho (\rho^2 \partial_\rho u) - 2\rho^{-2} u) & a < \rho \leq b' \end{cases} \quad t > 0 \quad (1)$$

$$p = \begin{cases} H_c^A (2\rho^{-1} u + \partial_\rho u) + f_c(t) & 0 \leq \rho \leq a \\ H_p^A (2\rho^{-1} u + \partial_\rho u) + f_p(t) & a < \rho \leq b' \end{cases} \quad t > 0 \quad (2)$$

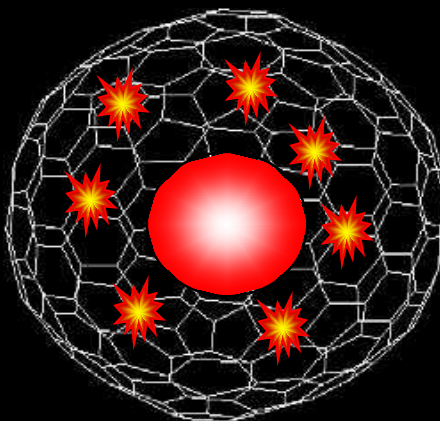
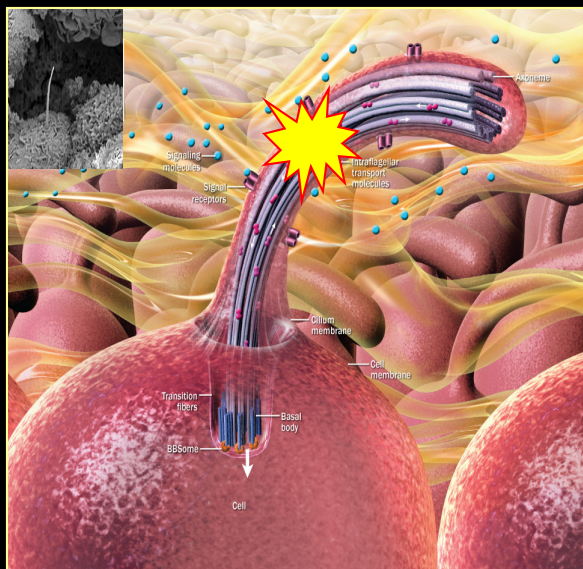
$$\frac{u(\rho, t)}{u_0} = \sum_{j=1}^{\infty} [K_j(\omega) e^{-\gamma_j t} + L_j(\omega) \sin \omega t - K_j(\omega) \cos \omega t] \phi_j(\rho) + M(\rho, t) \quad (5)$$

where: $M(\rho, t) = \sin \omega t \begin{cases} \alpha \rho^2 & 0 \leq \rho \leq a \\ \alpha \rho^2 + \alpha \rho & a < \rho \leq b \end{cases}$

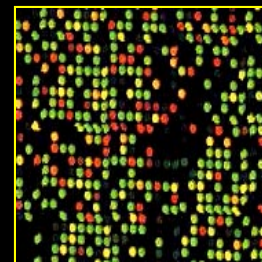
The eigenfunctions in (5) are:

$$\phi_j = \begin{cases} (r_j \rho)^2 [\sin(r_j \rho) - r_j \rho \cos(r_j \rho)] & 0 \leq \rho \leq a \\ (\delta_j (s_j \rho)^2 [\sin(s_j (\rho + \kappa_j)) - s_j \rho \cos(s_j (\rho + \kappa_j))]) & a < \rho \leq b \end{cases} \quad (6)$$

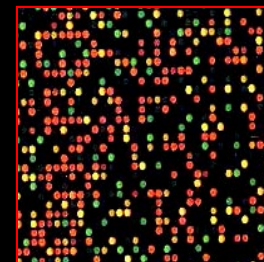
where $r_j = \gamma_j^{1/2} (k H_c^A)^{-1/2}$ and $s_j = \gamma_j^{1/2} (k H_p^A)^{-1/2}$. The constants

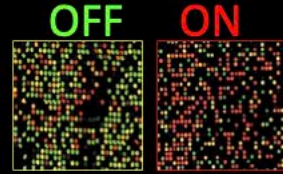
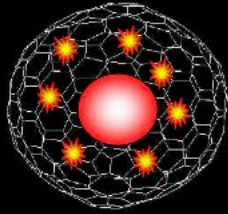
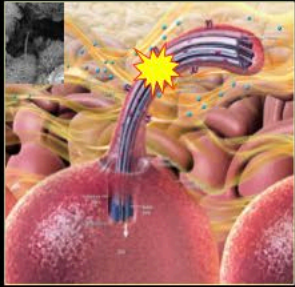


OFF



ON





Geni regolati dal Cilium

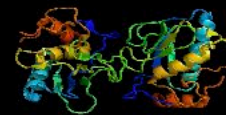
FOSB
Proteina dimerizzante



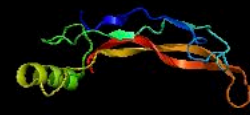
C-FOS
Fattore trascrizione



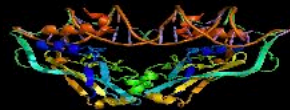
MMP-13
Matrix metalloproteinase



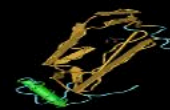
BMP-4
Bone morphogenetic protein



Tbx2
T-box transcription factor 2



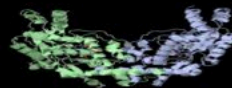
GLAST
Glutamate/aspartate transporter



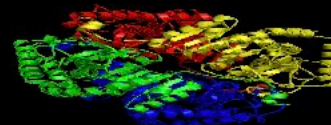
Cx43
Gap Junctional protein



NOS
Nitric Oxide Synthase



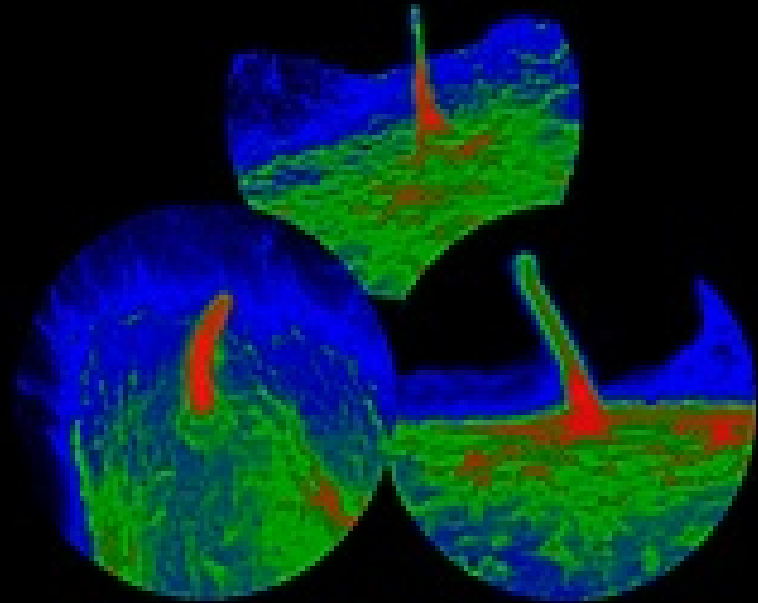
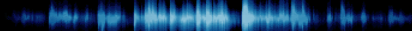
PGHS2
Prostaglandin-endoperoxide synthase 2



SOST
Sclerostin







To be continued...