The mammalian brain in the electromagnetic fields designed by man.

Leif G. Salford MD, PhD
and the EMF research group, Lund University, Lund, Sweden
"Time Line" For The Origin of Life

Present

500 million

1 billion years ago

First nucleated cells with organelles
marine life / bacteria colonized
algae cells (symbiosis)

2 billion years ago

First photosynthesis
2.2
First photosynthesis
by blue-green algae
2.5

3 billion years ago

3.3 - Earliest unicellular life / bacteria /
stromatolites / cyanobacteria
3.8 - Oldest rocks / zircon crystals, Greenland

4 billion years ago

End of "Heavy Bombardment"

No geologic record

ORIGIN OF LIFE

4.56 - Earth formation

5 billion years ago

Sun formation + 90% of all stars

~15 billion years ago

Age of Universe

Present

~2 million - Homo
Age of Mammals

65 million - Dinosaurs extinct

100 million years ago

Age of Dinosaurs

200 million years ago

300 million years ago

First Reptiles

400 million years ago

First Land Plants and Animals

First Vertebrates

500 million years ago
"Time - Line" For The Origin of Life

Present
- 500 million

1 billion years ago
- First nucleated cells with organelles
  marine life / bacteria colonized
  algae cells (symbiosis)

2 billion years ago
- Oxygen from photosynthesis
  2.2
  First photosynthesis
  by blue-green algae
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5 billion years ago
- Sun formation + 90% of all stars
- 4.56 - Earth formation
- 3.8 - Oldest rocks / zircon crystals, Greenland
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- 2 billion years ago
- 2.5 - First photosynthesis by blue-green algae
- 2.2 - First nucleated cells with organelles
- 1 billion years ago
- First nucleated cells with organelles
- Marine life / bacteria colonized algae cells (symbiosis)
- Present
- 500 million
- Present
- ~2 million - Homo
- Age of Mammals
- ~65 million - Dinosaurs extinct
- 100 million years ago
- Age of Dinosaurs
- 200 million years ago
- 300 million years ago
- First Reptiles
- 400 million years ago
- First Land Plants and Animals
- First Vertebrates
- 500 million years ago
- ~15 billion years ago
- Age of Universe
"Time - Line" For The Origin of Life

Present: ~2 million - Homo
- Age of Mammals
- 65 million - Dinosaurs extinct

100 million years ago:
- Age of Dinosaurs

200 million years ago:
- First Reptiles

300 million years ago:
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- FirstVertebrates

500 million years ago:
- First Nucleated Cells with organelles
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2 billion years ago:
- Oxygen from photosynthesis
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- Earliest unicellular life / bacteria / stromatolites / cyanobacteria
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4 billion years ago:
- End of "Heavy Bombardment"
- No geologic record

5 billion years ago:
- Sun formation + 90% of all stars

~15 billion years ago:
- Age of Universe

Present:
- 500 million years ago
The geomagnetic field (GMF) and the magnetic storms (MS)

MS generated by the sun’s plasma flows 10 times in a month with a 11 year periodicity. They produce alterations of the GMF lasting from hours to days all around the Earth.

Other cycles:
1 day - Earth’s rotation;
6–7 day and 13 -14 days corresponding to the solar winds;
27 days - the Sun’s rotation around its own axis.

29.5 days - the synodic period of the Moon;
1 year – the Earth’s revolution;
Energy discharges from atomic nuclei

(hard X-ray)
Medical applications (soft X-ray)

Visible light
- Violet: 0.400
- Blue: 0.424
- Green: 0.491
- Yellow: 0.575
- Orange: 0.585
- Red: 0.647

Heat lamp

Microwave radar

Television
- FM radio
- AM radio
Earth Radius 4600 km
Ionosphere 80 km
7.8 Hz
(0.001, 0.01, 0.1, 1, 3, 8, 14, 20, 26, 33, 39, 45 Hz)
**GMF-dependence on the Earth**  
(Volpe 2003)

orientation of sea gulls and pigeons, plant branching, orientation of root branches, metabolism and proliferation of root cells; protein synthesis in a number of vegetal cells

**Shielding of the geomagnetic field causes biological alterations**

- decrease of the vital functions in bacteria

- in meristem (cf stemcells in animals) of seedling roots of pea, flax and lentil, electron microscopy reveals changes in the mitochondrial structure,

- a 68–75% reduction of cell proliferation, variation of RNA and protein biosynthetic rates

- change in timing of fibroblast division and increase in sensitivity of *in vitro* cell cultures to poisons

- decrease in erythrocyte sedimentation in rats

- decrease of learning *vs.* an increase of hippocampus catecholamines

- increase of the epinephrine and histamine levels and a decrease of the serotonin level in the blood of guinea-pigs.
Magnetic storms cause additional biological dysfunctions (Volpe 2003)

Bacterial bioluminescent intensity varies according to the amplitude and duration of the MSs,

Medical studies correlate MSs with anxiety and irritability and lower attention and accuracy, with an increment of the probability of road accidents.

Acute attacks of cardiovascular diseases become more frequent

During the strong planetary MS of September 21–23, 1984, investigations in rabbits showed that the normal circadian structure in each cardiovascular parameter was lost; desynchronization increased, and abrupt drop of cardiac activity was observed; as well as degradation of mitochondria in cardiomyocytes.
Since birth of Earth: Extremely Low Frequency EMF

Ionosphere

Schumann vibrations
Extremely Low Frequency EMF from the late 19th century

Volta: the electric battery 1800

Tesla: the induction motor

Morse: the long-range telegraph

Hertz demonstrated radiowaves, "Hertzian, aetherial" waves 1888

Marconi: the wireless receiver 1896

Edison: Commercial electrical networks

Bell: the telephone
Microwaves
5 billion years until 1940
Sir Robert Watson-Watt, descendant of James Watt, created the first workable radar system after searching for a way to predict thunder and lightning to warn aviators. Sir Robert, an unsung hero of World War II, was knighted in 1942.
Sir Robert Watson-Watt, descendant of James Watt, created the first workable radar system after searching for a way to predict thunder and lightning to warn aviators. Sir Robert, an unsung hero of World War II, was knighted 1942.

It was during a radar-related research project around 1946 that Dr. Percy Spencer, noticed something very unusual. He was testing vacuum tube called a magnetron, when he discovered that the candy bar in his pocket had melted. The Microwave oven was born.
Microwaves Today

The original mobile phone from SRA, Ericsson, 1956

Mobile Phones 1980 -
One third of the world’s population now volunteer as guinea-pigs in the World’s largest biological experiment.
Nineteen years of EMF - BBB studies in Lund

- Shivers R et al., 1987 London Ontario  Visited 1988

- 1988 - blood-brain barrier (BBB) albumin leakage using Evans Blue after exposure for NMR imaging magnetic and RF fields.

- 1989 – BBB leakage studies with immunostaining for albumin and fibrinogene using pulse modulated 915 MHz microwaves.

- 1998 – BBB leakage of albumin, neuronal damage, gene expression, cognitive functions using real GSM-900 and GSM-1800 exposure
All mammals have a Blood-Brain Barrier. There are good reasons to believe that the BBB of a rat functions as the human BBB – But there might be differences which make results from animal experiments not directly translatable to the human situation! Enzymatic?
The TEM-cell is enclosed in a wooden box. The outer conductor is made of a brass net and is attached to the inner walls of the box.

The central plate, or septum, is constructed of aluminium and is held up by teflon braces, which are attached at the inner side-walls.

To allow access to the inside of the cell both ends can be removed. The inside of the cell is ventilated through 18 holes (diam. 18 mm) in the side-walls and top of the box, and the brass net allows air to circulate.

Fibre optic probes for monitoring the temperature inside the cell or in the test objects are inserted through these holes.
Block diagram and the four TEM cells used in our investigations of non-thermal biological effects of electromagnetic fields.
Earlier experiments in The Rausing lab:

Albumin leakage through the BBB:

Fischer rats (>1600) exposed to EMF for 2 min - 16 hours (majority for 2 hours). Examined within 30 minutes to 16 hours after exposure.
All our experiments: Non-thermal energy

Specific Absorbed Ratio (SAR) = energy absorbed by the tissue. SAR > 2W/kg can increase the temperature of the tissue and cause thermal effects. Regulations for mobile phones allow only SAR < 2W/kg.
”Biological window”

1/1000 and 1/10000

of the energy at the antenna

=SAR value 0,5 – 1 W/kg

(Specific Absorbed Ratio)

of the mobile phone opens the BBB more efficiently than the

energy at the antenna
"WINDOWED" RELATION BETWEEN INTENSITY OF IRRADIATION AND BBB PERMEABILITY?

1300 MHz fields
20 min exposure
Oscar & Hawkins 1977

The "inverse U"

(0.4 mW/kg)

mW/cm²
Dr. David Begley, Kings College, London, chairman at the FGF/COST 281, Reisensburg, 2-6 Nov 2003: statement based upon the presented results of the Lund and the Bordeaux (Aubineau, Töre) groups.

"It seems clear that RF fields can have some effects on tissues"
Albumin in the Brain Parenchyma: Neuronal degeneration is seen in areas with BBB disruption:

* Intracarotid infusion of hyperosmolar solutions in rats (Salahuddin et al. 1988)

* In the stroke-prone hypertensive rat (Fredriksson et al. 1988)

* In acute hypertension by aortic compression in rats (Sokrab et al. 1988)

* And epileptic seizures cause extravasation of plasma into brain parenchyma. The cerebellar Purkinje cells are heavily exposed to plasma constituents and degenerate in epileptic patients (Sokrab et al., 1990)

Albumin is the most likely neurotoxin in serum (Eimerl et al. 1991)
Albumin in the brain

25 microlitres rat albumin infused into rat neostriatum.

10 and 30, but not 3 mg/ml albumin causes neuronal cell death and axonal severe damage.

It also causes leakage of endogenous albumin in and around the area of neuronal damage.

10 mg/ml is approx. 25% of the serum concentration

“Passive” mobile exposure?
SAR = 1 mW/kg
1.85 metres away from the mobile phone
Effect from base stations?
$SR_{\text{AR}} = \frac{1 \text{ m}}{W/\text{kg}}$
Antenna 1.4 cm from human head, 915 MHz, SAR values derived from Anderson and Joyer 1995 and Dimylow 1994.

<table>
<thead>
<tr>
<th>SAR</th>
<th>W/kg</th>
<th>W/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Salford and Persson
From Gandhi

10.2 cm from the top of the head
DAMAGE TO BRAIN CELLS LONG TIME AFTER ONE EXPOSURE FOR 2 HOURS TO MICROWAVES FROM A GSM MOBILE PHONE???

One exposure for 2 hours. Each exposure group: 8 rats (12-26 weeks old – comparable to human teenagers)

Exposure groups:
0.002 W/kg (1/1000 of the energy at the antenna)
0.02 W/kg (1/100 of the energy at the antenna)
0.2 W/kg (1/10 of the energy at the antenna)

Control rats (8 animals in TEM-cell for 2 hours without GSM irradiation)

The animals were then allowed to survive for 50 days in standard cages. They were then anesthetised and sacrificed by perfusion-fixation followed by histopathological examination for neuronal damage and albumin leakage.
”Dark neurons”
50 days after
2 hours GSM-exposure!
Up to 2% of the neurons are damaged 50 days after a 2-hour GSM exposure. Significance, p=0.002 (Kruskal Wallis)
• “The intense use of mobile phones by youngsters is a serious memento. A neuronal damage of the kind, here described, may not have immediately demonstrable consequences, even if repeated. It may, however, in the long run, result in reduced brain reserve capacity that might be unveiled by other later neuronal disease or even the wear and tear of ageing. We can not exclude that after some decades of (often), daily use, a whole generation of users, may suffer negative effects maybe already in their middle age”.

• Nerve cell damage in mammalian brain after exposure to microwaves from GSM mobile phones. Environmental Health Perspectives online 29/1 2003 and in print June 2003.

Leif G. Salford, Arne Brun, Jacob Eberhardt, Lars Malmgren, Bertil R.R. Persson
• Depts of Neurosurgery, Neuropathology, Medical Radiation Physics and Applied Electronics, Lund University, the Rausing Laboratory and Lund University Hospital, S-22185, Lund, Sweden.
Continued work, completed: Connection albumin leakage – neuronal uptake - damage?

# rats
1600

2 hours exposure

0 14 28 50 days

Neuronal uptake and damage
Albumin leakage

© Salford et al
Exposure scheme, number of animals

<table>
<thead>
<tr>
<th>Recovery time (days)</th>
<th>sex</th>
<th>sham</th>
<th>SAR (mW/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.2</td>
</tr>
<tr>
<td>14</td>
<td>m</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>14</td>
<td>f</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>28</td>
<td>m</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>28</td>
<td>f</td>
<td>8</td>
<td>4</td>
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<tr>
<td>50</td>
<td>m</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>50</td>
<td>f</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>14 d</td>
<td>28 d</td>
<td>50 d</td>
</tr>
<tr>
<td>---------------</td>
<td>------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td><strong>Exposed vs sham</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin foci</td>
<td>0.02</td>
<td>ns</td>
<td>0.04</td>
</tr>
<tr>
<td>Diffuse albumin</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Neuronal albumin</td>
<td>0.005</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Dark neurons</td>
<td>ns</td>
<td>0.01</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Continued work: Long term exposure:

56 male and female Fischer 344 rats have been exposed to GSM 100mW/kg, 1mW/kg, or sham exposed for 2 hours in our TEM-cells once a week for more than a year. Behavioural tests 3-5 weeks after last expos. Exam of perfusion fixed brains and eyes Spared in formaldehyde: testis Spared in -80C: testis, ovary, kidney, spleen, liver, bone marrow, blood
Ongoing analysis

- Different markers for brain ageing
- Gliosis (GFAP staining)
- Pigment in neurons (histological fluorescence)
- Synaptic functionality (immunostaining)
- Apoptosis (but was not found in the 50 day recovery time study)
Behavioural tests
long term experiments (14 months)
2 hours per week GSM 100 and 1 mW/kg

Episodic memory test

- “reollection of a unique past experience in terms of what happened and where and when it happened”
- Episodic memory test for mice and rats has been described in the literature
Episodic memory test

Training 1

Training 2

Test
Results Episodic memory test

- Exposed animals have a significantly (p=0.02) shorter exploration time of the old objects, than the sham exposed which may indicate that the exposed animals have “forgotten” about the old objects.
- No differences between males and females.
- No significant differences between the 2 exposed groups (100 vs 1 mW/kg).
GSM RF non-thermal effects

in vitro

upon gene expression
GSM RF non-thermal effects *in vitro* upon gene expression in human cultured cells.

<table>
<thead>
<tr>
<th>Author</th>
<th>Celltype</th>
<th>RF</th>
<th>time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pacini et al.</td>
<td>Human</td>
<td>GSM phone</td>
<td>1 hour</td>
</tr>
<tr>
<td>2002 fibroblasts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signif. biol.eff. mitogenic signaltransduct. and apoptosis genes upregul.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee et al.</td>
<td>Human</td>
<td>2.45 GHz</td>
<td>2 hours</td>
</tr>
<tr>
<td>2005 HL-60 cells</td>
<td></td>
<td>6 hours</td>
<td></td>
</tr>
<tr>
<td>221 genes altered after 2 hours and 759 after 6 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apoptosis related up- and cell cycle genes downregulated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remondini et al. 2006</td>
<td>6 human cell lines</td>
<td>900 MHz</td>
<td></td>
</tr>
<tr>
<td>REFLEX</td>
<td></td>
<td>1800 MHz Mob. Phone</td>
<td></td>
</tr>
<tr>
<td>3 cell types (endothelial, lymphoblastoma and leukemia) had 12 to 34 altered gene expr for ribosomal proteins upregulating cellular metabolism</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
GSM RF non-thermal effects *in vitro* upon gene expression in human and rat cultured cells.

<table>
<thead>
<tr>
<th>Author</th>
<th>Celltype</th>
<th>RF</th>
<th>time</th>
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</thead>
<tbody>
<tr>
<td>Lezczynski et al.</td>
<td>human endo-thelial cell line</td>
<td>900 MHz</td>
<td>1 hour</td>
</tr>
<tr>
<td>2002</td>
<td></td>
<td>GSM</td>
<td></td>
</tr>
</tbody>
</table>

Altered phosphorylation status hsp27 and p38MAPK (mitogen-activated prot. kinase)

Hypoth: facilitates brain cancer, increase in BBB permeability

<table>
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<th>RF</th>
<th>time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhao et al.</td>
<td>Neurons from new-born rats</td>
<td>1.8 GHz</td>
<td>24 hours</td>
</tr>
<tr>
<td>2006</td>
<td></td>
<td>217 Hz</td>
<td>SAR 2W/kg</td>
</tr>
</tbody>
</table>

34 out of 1200 genes up or down regulated.

Map 2 up regulated, crucial for neuronal function
GSM RF non-thermal effects 
*in vivo*
upon gene expression
Continued work, completed:

Gene response to 915 MHz GSM

- cerebellum: Belyaev et al. 400 mW/kg
- cortex and hippocampus: Salford et al. 25 mW/kg
Gene response to 915 MHz GSM 400mw/kg

8800 rat genes analyzed with Affymetrix Microarray Suite
Cerebellum from 8 Fischer 344 rats, 4 exposed and 4 controls

11 genes upregulated 1.34 – 2.74 fold
1 gene downregulated 0.48 fold
p<0.0025

The induced genes encode proteins with functions including neurotransmitter regulation, BBB and melatonin production

But no induction of PFGE-detectable DNA double stranded breaks or changes in chromatin conformation (AVTD) by 915 MHz GSM

Belyaev I. et al. Bioelectromagnetics 2006
Microarray analysis of 40,000 rat genes (including splicing variants) in cortex and hippocampi of 8 Fischer 344 rats, 4 animals exposed to GSM EMF SAR 25mW/kg for 6 hours in TEM cells and 4 controls kept as long in unexposed TEM cells. Gene ontology analysis of the differentially expressed genes for cortex/hippocampi of the exposed animals versus the control group.
**Top separating categories**

**microarray**

Salford ea 2006

---

**Cortex**

- cell communication e-15
- plasma membrane e-11
- G-protein coupled rec. prot e-11
- extracellular region e-11
- signal transducer activity e-10
- intrinsic to plasma membr e-10
- integral to membr e-10
- membrane e-10
- intrinsic to membrane e-10
- synaptic vesicle amine trpt e-9
- transmembr receptor act -9
- surface receptor linked signal transduct. e-9

**Hippocampi**

- extracellular region e-23
- extracellular space e-22
- signal transducer activity e-15
- transmembrane receptor activity e-15
- receptor activity e-14
- Integral to membrane e-13
- intrinsic to membrane e-13
- organismal physiol process e-11
- rhodopsin-like receptor activity e-9
- G-protein coupled rec. prot sign. pathw. e-9
- cell surface receptor linked sign. trd e-8
- neurotransmitter receptor activity e-8

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Top separating categories

10 of the 12 Hippocampal top categories are the same as 10 of the 19 Cortical top categories (e-)

<table>
<thead>
<tr>
<th>Category</th>
<th># genes</th>
</tr>
</thead>
<tbody>
<tr>
<td>extracellular region e-23 (e-11)</td>
<td>1417</td>
</tr>
<tr>
<td>extracellular space e-22 (e-8)</td>
<td>1188</td>
</tr>
<tr>
<td>signal transducer activity e-15 (e-10)</td>
<td>1455</td>
</tr>
<tr>
<td>transmembrane receptor activity e-15 (e-9)</td>
<td>603</td>
</tr>
<tr>
<td>receptor activity e-14 (e-9)</td>
<td>935</td>
</tr>
<tr>
<td>integral to membrane e-13 (e-10)</td>
<td>1937</td>
</tr>
<tr>
<td>intrinsic to membrane e-13 (e-10)</td>
<td>1949</td>
</tr>
<tr>
<td>organismal physiol process e-11 (e-8)</td>
<td>950</td>
</tr>
<tr>
<td>G-protein coupled receptor prot sign. pathw e-9 (e-11)</td>
<td>467</td>
</tr>
<tr>
<td>cell surface receptor linked sign. transd e-8 (e-9)</td>
<td>118</td>
</tr>
</tbody>
</table>

© Salford et al
The fact that a large number of these categories are connected with membrane functions may have a relation to our earlier observation of albumin transport through the cerebral endothelium.
Mobile phones and Brain tumours
Bioinitiative report July 2007

Lennart Hardell, MD, PhD, Dept of Oncology, Örebro University Hospital, Sweden
Kjell Hansson Mild, PhD, Dept of Radiation Physics, Umeå University, Sweden
Michael Kundi Ph.D., med.habil, Inst. of Env. Health, Vienna, Austria

"In summary we conclude that our review yielded a consistent pattern of an increased risk for acoustic neuroma and glioma after > 10 years mobile phone use. We conclude that current standard for exposure to microwaves during mobile phone use is not safe for long-term brain tumor risk and needs to be revised".
Mobile phone emission modulates interhemispheric functional coupling of EEG alpha rhythms


Compared to sham stimulation, GSM stimulation for 45 minutes modulated the interhemispheric frontal and temporal coherence at alpha 2 (about 8–10 Hz) and alpha 3 (about 10–12 Hz) bands.

Prolonged mobile phone emission affects not only the cortical activity but also the spread of neural synchronization conveyed by interhemispherial functional coupling of EEG rhythms.
The inverted U-function as a response characteristic in connection of RF exposure might explain why, in many studies of pharmacological effects, response is only seen at a certain dose range, and not at higher or lower dosages. It might constitute the basis for window effects observed in connection to RF exposure.

MECHANISMS?
Mechanism behind possible, direct, non-thermal effects of RF radiation upon the central nervous system are not clear. Adey in 1988 suggested the hypothesis that cooperative processes in the cell membrane might be reactive to the low energy of an electromagnetic field. This oscillating field might result in changes of the membrane potential.

Ross Adey, 1922-2004, studied amplitude-modulated radiofrequency fields. “If we made a radio signal look like a brain wave, would it influence behavior? We showed in cats very clearly, and monkeys to some extent, that you could make the brain wave pattern follow the modulation on the radio signal.”
Interaction Between Weak Low Frequency Magnetic Fields and Cell Membranes

C.L.M. Bauréus Koch, M. Sommarin, B.R.R. Persson, L.G. Salford and J.L. Eberhardt
Depts of Radiation Physics, Plant Biochemistry and Neurosurgery - the Rausing Laboratory, Lund University, Lund Sweden


"We show that suitable combinations of static and time varying magnetic fields directly interact with the Ca2+ channel protein in the cell membrane, and we could quantitatively confirm the model proposed by Blanchard"
The effects on pain, nociception and opiate-mediated analgesia constitute one of the most reproducible and reliable effects of EMFs with observed decrease in pain threshold.

The fact that EMFs increase pain perception is of particular interest if one considers our ubiquitous exposure to various EMFs and the prevalence of pain problems in our society.

The physiological mechanisms involved require definition

Based upon > 50 studies in snails, mice and rats
Review: Pain perception and electromagnetic fields
Neuroscience and Biobehavioral Reviews 31 (2007) 619–642
A new theory

**Meyer Overton Correlation**

Charles Ernest Overton (1865–1933) born in England Professor of Pharmacology at Lund University, Sweden 1907 - 1930.
A new theory
Solitons instead of Hodgkin-Huxley?

On soliton propagation in biomembranes and nerves Heimburg, T. and Jackson, AD. (2005) PNAS 102, 9790-9795:

The lipids of biological membranes and intact biomembranes display chain melting transitions close to temperatures of physiological interest. During this transition the heat capacity, volume and area compressibilities, and relaxation times all reach maxima. Compressibilities are thus nonlinear functions of temperature and pressure in the vicinity of the melting transition, and we show that this feature leads to the possibility of soliton propagation in such membranes. In particular, if the membrane state is above the melting transition solitons will involve changes in lipid state. We discuss solitons in the context of several striking properties of nerve membranes under the influence of the action potential, including mechanical dislocations and temperature changes.

The thermodynamics of general anesthesia. Biophys J. 2007 May 1;92(9):3159-65. Anesthetics lower the temperature at which lipids become solid, making it difficult for the waves to form, thereby preventing nerves from sending pain signals.
Fig. 4. Properties of solitons and nerves. (a) Calculated total energy and capacitive energy densities stored in the soliton during the passage. Both functions display similar time dependence. (b) Experimental heat changes during the action potential of garfish olfactory nerve (solid line) and the energy of charging the membrane's capacitor. Both functions display similar time dependence (adapted from ref. 13). (c) Calculated thickness change of a membrane cylinder (displacement) and corresponding voltage changes. Both functions display identical time dependence. (d) Experimentally determined differential displacement of the squid axon and the corresponding action potential (adapted from ref. 27). Both functions display identical time dependence. The different shape of the profiles as compared with b are a consequence of the experimental setup.

John Scott Russell and the solitary wave

In 1834, while conducting experiments to determine the most efficient design for canal boats, a young Scottish engineer named John Scott Russell (1808-1882) made a remarkable scientific discovery, which he described it in his "Report on Waves" after his first sighting of a soliton or solitary wave on the Union Canal near Edinburgh.
In the frame of the pendulum model the kink is the solitary wave of counterclockwise rotation of pendulums through the angle $2\pi$. 
Resonant Microwave Absorption of Selected DNA Molecules

G. S. Edwards and C. C. Davis
Chemical Physics Program and Electrical Engineering Department, University of Maryland, College Park, Maryland 20742

and

J. D. Saffer
Laboratory of Biochemistry, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20205

and

M. L. Swicord
Center for Devices and Radiological Health, Food and Drug Administration, Rockville, Maryland 20857
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The resonant absorption of microwave energy by aqueous solutions containing DNA of known length is experimentally demonstrated. The resonances observed have relaxation times of hundreds of picoseconds. Absorption by linear and supercoiled circular DNA molecules is discussed in terms of a mechanism involving microwave excitation of acoustic modes of the double helix.
In a pioneering paper appeared in 1980, Englander, Kallenbach, Heeger, Krumhansl and Litwin [8] suggested that nonlinear excitations in the DNA double chain could be instrumental in this process and allow the motion of the transcription bubble to occur at near-zero energy cost. In particular, as the fundamental motion undergone by DNA nucleotides in this process is a roto/torsional one, they suggested to model the DNA molecule as a double chain of coupled pendulums; the relevant nonlinear excitations would then be (topological) solitons pretty much like those well known in the sine-Gordon equation. We refer to their work for detail.

Proc. Natl. Acad. Sci. USA
Vol. 77, No. 12, pp. 7222–7226, December 1980
Biophysics

Nature of the open state in long polynucleotide double helices: Possibility of soliton excitations
(hydrogen exchange/DNA dynamics/base pair opening/DNA "breathing")

S. W. Englander*, N. R. Kallenbach‡, A. J. Heeger‡, J. A. Krumhansl*‡, and S. Litwin‡

*Departments of Biochemistry and Biophysics, ‡Biology, and §Physics, University of Pennsylvania, Philadelphia, Pennsylvania 19104; and ¶Institute for Cancer Research, Philadelphia, Pennsylvania 19111

Communicated by Bruno H. Zimm, September 2, 1980

*Departments of Biochemistry and Biophysics, ‡Biology, and §Physics, University of Pennsylvania, Philadelphia, Pennsylvania 19104; and ¶Institute for Cancer Research, Philadelphia, Pennsylvania 19111

Communicated by Bruno H. Zimm, September 2, 1980
Transcription Bubble. A schematic representation of a transcription bubble in the elongation of an RNA transcript. Duplex DNA is unwound at the forward end of RNA polymerase and rewound at its rear end. The RNA-DNA hybrid rotates during elongation.
Solitons hiding in DNA and their possible significance in RNA transcription

E. W. Prohofsky

Department of Physics, Purdue University, West Lafayette, Indiana 47907

(Received 16 February 1988)

We find that the hydrogen-bond–stretch bands of the double helix appear to be nonlinear enough to support solitary-wave energy concentration. Coupling this fact to predictions of our self-consistent theory of helix melting gives rise to speculations of a mechanism for base pair melting in RNA transcription which is consistent with the known energy needs of that process.
Soliton excitations in deoxyribonucleic acid (DNA) double helices

Chun-Tiry Zhang

Department of Physics, Tianjin University, Tianjin, the People's Republic of China
(Received 2 September 1986)

Dynamical theory of soliton excitations in deoxyribonucleic acid (DNA) double helices has been studied by a revised Hamiltonian in which the dipole-dipole interaction and the dipole—induced-dipole interaction between two bases in a complementary base pair are taken into account in addition to the hydrogen-bond energy. The motion equations of bases are a set of coupled sine-Gordon equations. The soliton solutions of these equations are studied in detail and the results are compared with the experimental data in the H-D exchange measurements of DNA chains.
Harmonic and subharmonic resonances of microwave absorption in DNA

Chun-Ting Zhang

Center of Theoretical Physics, Chinese Center of Advanced Science and Technology (World Laboratory) and Department of Physics, Tianjin University, Tianjin, China
(Received 4 November 1988; revised manuscript received 10 April 1989)

We have studied theoretically the movement of large molecular groups of DNA double helices in solution, which are driven by the electromagnetic field. The longitudinal vibration of nucleotides and the torsional movement of bases are taken into account at the same time. A set of coupled nonlinear partial differential equations has been established, and we have solved these equations by the method of perturbation. The result shows that there exists resonant absorption of microwave energy for both longitudinal and torsional modes. The resonant frequencies for the former and the latter are in the region of gigahertz and subterahertz, respectively. In addition to an $n$th-harmonic resonance at $\omega_n$, our theory also predicts a subharmonic resonance at $\omega_n/2$. The strength of the latter is proportional to $l^{-3}$, where $l$ is the length of DNA. The necessary conditions to observe these resonances are also discussed.
Three-Wave Interaction between Interstrand Modes of the DNA

V. L. Golo

Moscow State University, Vorobyovy gory, Moscow, 119992 Russia
e-mail: golo@mech.math.msu.su

Received February 21, 2005

Abstract—We consider the regime in which the bands of the torsional acoustic (TA) and hydrogen-bond-stretch (HBS) modes of DNA interpenetrate each other. We propose a simple model accommodating the helix structure of DNA and, within its framework, find a three-wave interaction between the TA and HBS modes. The phenomenon could be useful for studying the action of microwave radiation on a DNA molecule. Thus, using Zhang’s mechanism of the interaction between the system of electric dipoles of a DNA molecule and microwave radiation, we show that the latter could bring about torsional vibrations that maintaining HBS vibrations. We show an estimate of the microwave power density necessary for generating the HBS mode, which significantly depends on the viscous properties of the ambient medium. © 2005 Plenum Publishing, Inc.
Water
Protein and enzymes
Cell membrane
Ca\(^{2+}\)
Ca-proteins
DNA
The soup of life
RNA
Ion channels
Mammalian brain
in man-made EMFs
Solitons solution?
Domo Arigato Masatoshi Murase et al.
ENGlander et al. demonstrated the existence of transiently open states in DNA and synthetic poly-nucleotide double helices by hydrogen exchange measurements; base pairs reversibly separate and reclose, exposing nucleotide protons to exchange with solvent protons.

They considered the possibility that the low energy and slow opening and closing rates observed reflect a deformation involving several adjacent base pairs.

Assuming a mobile open unit capable of diffusing along the double helix, they found that available data are consistent with structures of 10 or so adjacent open pairs. It is further suggested that these structures correspond to thermally induced soliton excitations of the double helix, which retain coherence by sharing the energy of a twist deformation among several base pairs.

**Solitons are nonlinear excitations that can travel as cohererent solitary waves**, and have been recognized as an important mechanism for mediating conformational changes in polymers and condensed systems generally.

Comparison of the double helix with simple mechanical analogs suggests that soliton excitations may well exist within DNA chains, and that the hydrogen exchange open state is consistent with these.
Fig. 3. Mechanical analog of the strands of a double helix possessing soliton excitations. (C) The ground state of the double helix modeled as two linear chains of pendula (the bases) connected by springs (the sugar-phosphate backbones). Each pendulum is of mass $m$ and length $h$, spaced at $l \approx 3.4$ Å along the helix axis. (A) One strand of the duplex capable of undergoing torsional oscillations (angle $\theta$) about the backbone axis in the presence of a restoring force $mg$. (B) Soliton excitation mode involving a large-amplitude excursion of one pendulum with spreading of the excitation to a group of $L$. Note that the system also possesses small-oscillation wave solutions that propagate along the lattice but which damp and do not exhibit non-linear behavior.
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Ionic Movements during the Action Potential

<table>
<thead>
<tr>
<th>Time (milliseconds)</th>
<th>Membrane Potential (millivolts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+60</td>
</tr>
<tr>
<td>2</td>
<td>+50</td>
</tr>
<tr>
<td>3</td>
<td>+40</td>
</tr>
<tr>
<td>4</td>
<td>+30</td>
</tr>
<tr>
<td>5</td>
<td>+20</td>
</tr>
</tbody>
</table>

**Resting Membrane Potential**
- Na\(^+\) concentrated on outside.
- K\(^+\) concentrated on inside.
- Negatively charged proteins found inside the axon only.

**Depolarization Begins**
- Na\(^+\) gates open and sodium begins to flow rapidly into the axon along the concentration and electrical gradients.
- Negatively charged proteins do not move because they are too large to pass through the axonal membrane.

**Depolarization Continues**
- Na\(^+\) continues to flow rapidly into the axon along the concentration and electrical gradients.
- K\(^+\) gates open and K\(^+\) begins to flow slowly out of the axon (along the concentration gradient but against the electrical gradient).

**Depolarization Peaks**
- Na\(^+\) channels close and Na\(^+\) stops flowing into the axon.
- K\(^+\) has only just started to leave the axon.
- Na\(^+\) and K\(^+\) are now both briefly concentrated on the inside of the axon resulting in the inside being (briefly) positive relative to the outside of the axon.

**Hyperpolarization Begins**
- Now that the Na\(^+\) channels are closed, the Na\(^+\) pump forces the Na\(^+\) out of the axon, back to where it started.
- K\(^+\) Channels start to close. Because the positive ions (Na\(^+\) and K\(^+\)) are both concentrated on the outside of the axon, the outside is now more positive than when the axon is at rest. In other words, the inside is more negative than normal.
- The K\(^+\) pump now begins to pump K\(^+\) back into the axon.

**Axon Returns to the Resting State**
- Na\(^+\) has been pumped back outside.
- K\(^+\) has been pumped back inside.
- Negatively charged proteins have stayed inside the axon through this entire process.
Hodgkin - Huxley

synaptic currents

spine
parallel fiber synapse
stellate cell synapse

K⁺
Ca⁺

voltage-gated currents

axial current into out of soma

Soma

Outside

Inside

\[ I_{ca} = g_{ca} \times (V_m - E_{ca}) \]

\[ V_{m_{t+\Delta t}} = V_{m_t} + (I_{\text{leak}} + I_{\text{chan}} + I_{\text{syn}}) \times \Delta t / CM \]
Conduction pathways in microtubules, biological quantum computation, and consciousness

Stuart Hameroff, Alex Nip, Mitchell Porter and Jack Tuszynski 2001
The Rausing Laboratory
for Experimental Neurosurgery and Radiation Physics
The microwave research section

Gustav Grafström
Bertil Persson
Leif G Salford
Lars Malmgren
Jacob Eberhardt

Arne Brun
Tyrosine (from diet) → DOPA can increase supply → Dopamine (DA) via enzyme MA → AMPT can block this reaction

Reserpine can cause leakage from vesicles → Dopamine (DA) release → Amphetamine increases release → Dopamine receptor

Cocaine blocks reuptake. So do methylphenidate and tricyclic antidepressants, but less strongly.

Postsynaptic neuron
1) interference with presynaptic release

2) altering presynaptic re-uptake

3) interference with postsynaptic binding

4) interference with postsynaptic ionic conductance
Main sources of electromagnetic fields
Natural sources of electromagnetic fields
Static
Geomagnetic field
Time-varying
Local thunderstorms
Solar storms
Human-made sources of electromagnetic fields
Static
Static-electric and magnetic fields
Time-varying
Extremely low-frequency electric and magnetic fields
Radio waves
Microwaves
Infra-red
Visible spectrum
Ultra violet radiation (ionizing radiations)
X-rays (ionizing radiations)
Gamma rays (ionizing radiations)
Time-varying complex
Weak complex magnetic fields
Complex neuroelectromagnetic pulse (Cnp)
Ultra Wideband Electromagnetic Pulses (UWB)
Very High Frequency Waves Pass Through the Atmosphere

- Low Frequency Wave Reflected

- Higher Frequency Waves Travel Further Before Being Reflected

- "Skip"
Extremely Low Frequency EMF

Volta: the electric battery 1800
Volpe
The divergences encountered in the literature with respect to the MF-dependence of given biological structures and functions are due not only to the differences of equipment facilities or experimental accuracy, but rather to the intrinsic inadequacy of proposed methodological approaches. In addition, there is still a largely recognized lack of theoretical analysis to explain the mechanisms which underlie the interactions between the MFs and the various cellular targets.
Efter Egna studierna:
Mekanismerna
Egna vesicle forsök
Calcium
Solitonerna DNA enl Xhang och Zvicord
Solitonerna i nervmembran enl Niels Bohr inst.
Overton
Sannolikheten för solitoner kanske bevisas av snigelförsöken (London Ontario) smärta opiater anestesi etc
Kanske mekanismen?
Det fortsatta sökandet efter sanningen
Inside-out membrane vesicle

Ca\(^{2+}\)-ATPase

ATP

Ca\(^{2+}\)

ADP + P\(_i\)

Calcium channel

Ca\(^{2+}\)
Cepaea nemoralis
Results neuropathology

- Very little albumin leakage, no difference between exposed, sham exposed and cage controls.
- Dark neurons were found but no statistical differences between exposure conditions could be detected.
Possible hypotheses for non-thermal effects according to the Lund group:


*Microwaves have effect directly on the protein-conformation (vibration energy levels)  Ref: de Pomeraï et al FEBS Letters 543:93-97, 2003

*Interaction microwaves → water molecules bound in biologically active molecules

*Autooxidative processes which lead to oxidation in the cells  Ref: Ilhan et al Clin Chim Acta 340:153-162, 2004
Top separating categories continued, CORTEX

dopamine biosynthesis e-9
receptor activity e-9
surface receptor linked signal transduction e-9
alpha-type channel activity e-8
channel or pore class transporter activity e-8
signal transduction e-8
organismal physiological process e-8
voltage-gated ion channel activity e-8
regulation of dopamine metabolism e-8
extracellular space e-8
behaviour e-8
ion channel activity e-8
metal ion transport e-7
G-protein coupled receptor activity e-7
plus 14 more with p-values e-7 and e-6
all highly significant

© Salford et al
Top separating categories cont., HIPPOCAMPI

- neurotransmitter receptor activity e-8
- cell surface receptor linked sign. transd e-8
- peptide binding e-8
- peptide receptor activity G-prot coupl. e-8
- extracellular matrix e-8
- extracellular matrix (sensu Metazoa) e-7
- plus 7 more with p-values e-7 and e-6 highly significant
Gene response to 914.8 MHz GSM, of importance for BBB function

<table>
<thead>
<tr>
<th>Affymetrix Probeset</th>
<th>Fold change</th>
<th>Gene symbol</th>
<th>Gene name</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BBB function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M96601_at</td>
<td>1.56 ± 0.23</td>
<td>Slc6a6</td>
<td>Solute carrier family 6, member 6</td>
<td>Taurine transporter. Predominantly glial expression.</td>
</tr>
<tr>
<td>rc_AA800851_s_a t</td>
<td>1.34 ± 0.20</td>
<td>Ces3</td>
<td>Carboxylesterase 3</td>
<td>Expressed in endothelial cells of the brain.</td>
</tr>
</tbody>
</table>

Belyaev I. et.al. Bioelectromagnetics 2006
Lund University

The largest university in Scandinavia
45,000 students
Resonant Microwave Absorption of Selected DNA Molecules

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S. Yomosa

Department of Physics, Nagoya University, Nagoya 464, Japan
(Received 15 December 1982)

We present in this paper a soliton theory for the open states in deoxyribonucleic acid (DNA) and synthetic polynucleotide double helices. Kink and antikink solutions for the equation of motion of the sine-Gordon form correspond to the open states with positive and negative helicities. The energy of open form and the length of the open configuration which are theoretically estimated are in the same order with the values inferred from kinetic experimental data.