Chulabhorn Research Institute

Bangkok

Mobile Phones*, WiFi and other wireless devices: are there health effects from exposure?

Denis L Henshaw

University of Bristol
and
Children with Cancer UK

January 2015

*Over 6 billion worldwide

University of BRISTOL

CHILDREN with CANCER UK
Registered Charity No. 298405

I will discuss:

Part 1

- What is an EMF?
- Mobile phones, WiFi and other wireless devices

  - principal health findings

Part 2

- EMF and living systems

  - including power frequency magnetic fields
- Conceptual issues
- Conclusion and precaution

What is an EMF?

Separate Electric and Magnetic fields

Extremely Low Frequency (ELF) EMFS

0 – 3,000 Hz

Electromagnetic fields
and
Electromagnetic radiation (EMR)

Radio frequencies, including mobile phone

Bioelectromagnetics

- the study of EMF interactions with biological systems

- Probably over 100,00 peer-reviewed papers
  - Already 1000s of papers on RF effects

Reported effects from RF EMFs include: DNA damage, cell malformations, apoptotic cell death, changes in chromatin conformation and micronucleus formation in different cell types or organisms

Not all studies report positive findings and some studies report no genotoxic effects

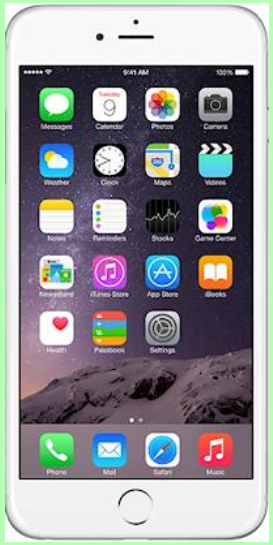
However, mobile phone radiation has been also found to cause broad changes in gene and protein expression in certain cell types

Most common mobile phone systems in use today

GSM
(2G)

Most epidemiological studies have involved phones on the GSM system - 900 & 1800 MHz

3G
4G

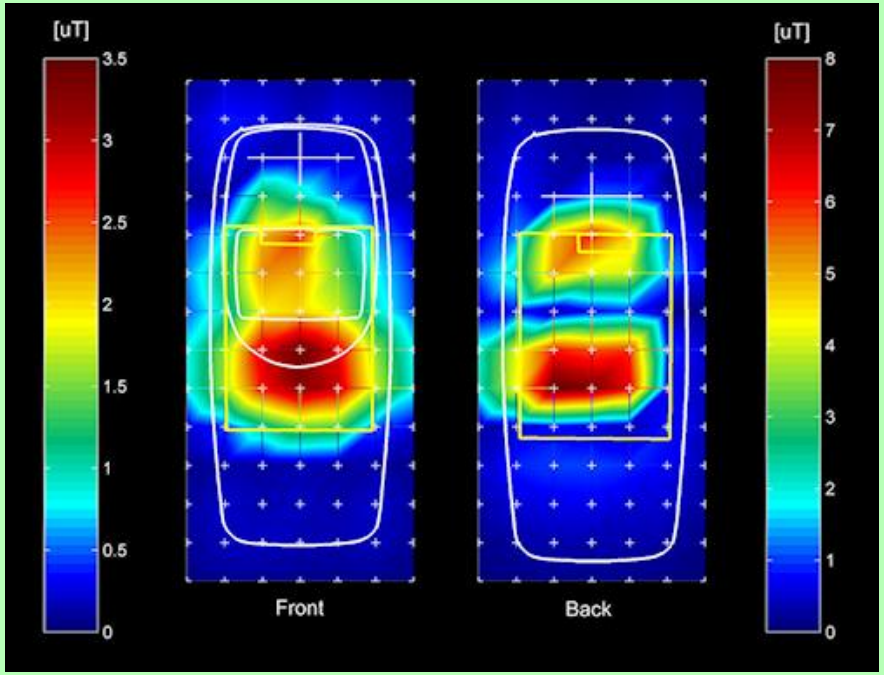


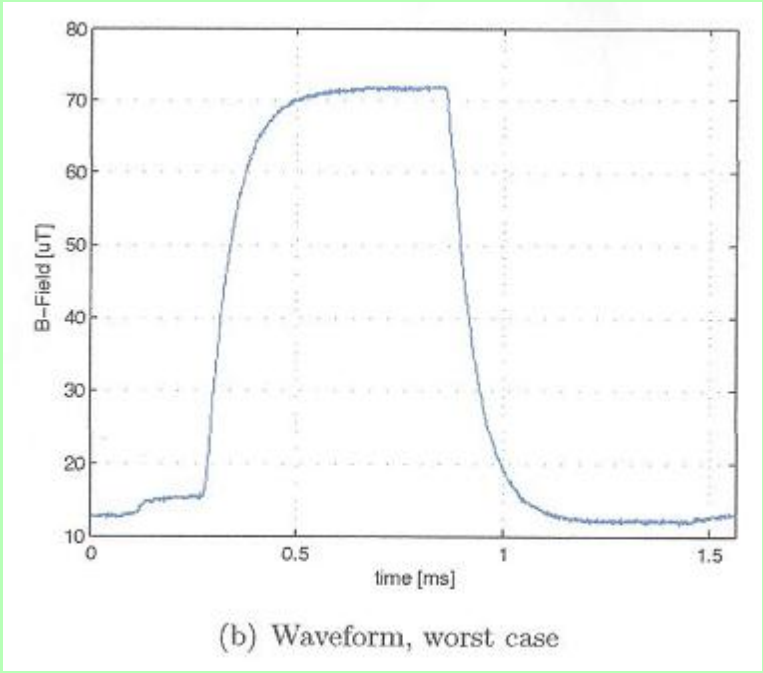
Phones using 3G are far less biologically active than GSM phones - 850, 1900 MHz

Phones using 4G may be more biologically active than 3G

GSM phones have a low frequency magnetic field associated with the battery current*

Nokia 3310





(b) Waveform, worst case

Yellow contour represents the battery

*Tuor et al. Assessment of ELF Exposure from GSM Handsets and Development of an Optimized RF/ELF Exposure Setup for Studies of Human Volunteers. Foundation for Research on Information Technologies in Society, Report: BAG Reg. No. 2.23.02.-18/02.001778, Zurich, January 2005

IARC (2011): Mobile phones and Brain tumours

International Agency for Research on Cancer

World Health Organization

PRESS RELEASE
N° 208

31 May 2011

IARC CLASSIFIES RADIOFREQUENCY ELECTROMAGNETIC FIELDS AS POSSIBLY CARCINOGENIC TO HUMANS

Lyon, France, May 31, 2011 -- The WHO/International Agency for Research on Cancer (IARC) has classified radiofrequency electromagnetic fields as possibly carcinogenic to humans (Group 2B), based on an increased risk for glioma, a malignant type of brain cancer[1], associated with wireless phone use.

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 102: NON-IONIZING RADIATION, PART II: RADIOFREQUENCY ELECTROMAGNETIC FIELDS [INCLUDES MOBILE TELEPHONES, MICROWAVES AND RADAR] Lyon, France: 24-31 May 2011 [480 pages]. See also: The Lancet Oncology, Volume 12, Issue 7, Pages 624 - 626, July 2011

IARC 2B[1] based largely on two major studies:

- Interphone (Int J Epidemiol 2010; 39: 675–94) – 13-country[2] case-control study of mobile phone use, but not including cordless phones

  ≥1640h, or >30 mins per day for 10 years:

  OR =1.40 (95% CI 1.03–1.89) for glioma,

- Hardell *et al* (Int J Oncol 2011; 38: 1465–74) - case-control study of mobile phone use, <u>including</u> cordless phones

  - More than 1 year use: OR for glioma of 1·3 (95% CI 1·1–1·6).
  - OR of 3·2 (2·0–5·1) for more than 2000 h of use.
  - Ipsilateral use associated with higher risk.
  - Similar findings for use of cordless phones.

[1]The IARC committee voted heavily in favour of 2B

[2]Australia, Canada, Denmark, Finland, France, Germany, Israel, Italy, Japan, New Zealand, Norway, Sweden, and the UK.

Recent publications from the Hardell Group

– (Umeå University, Sweden).

1. Hardell L, Carlberg M. Brain Tumour Risk Associated with Use of Mobile and Cordless Phones (Richter K, Ludwig P). Würzburg, Festung Marienberg, 5. April 2014. S. 6-21.

2. Hardell L, Carlberg M, Söderqvist F, Mild KH. Mobile phones and cancer: Next steps. Epidemiology. 2014;25(4):617-618.

3. Hardell L, Carlberg M. Long-term mobile phone use and acoustic neuroma. Epidemiology. 2014;25(5):778.

4. Hardell L, Carlberg M. Mobile and Cordless Phone Use and Brain Tumor Risk. In: Rosch (ed) Bioelectromagnetic and Subtle Energy Medicine. In press.

5. Carlberg M, Hardell L. Decreased survival of glioma patients with astrocytoma grade IV (glioblastoma multiforme) associated with long-term use of mobile and cordless phones. Int J Environ Res Public Health 2014;11:10790-10805; doi:10.3390/ijerph111010790. www.mdpi.com/journal/ijerph

6. Hardell L, Carlberg M. Mobile phone and cordless phone use and the risk for glioma - Analysis of pooled case-control studies in Sweden, 1997-2003 and 2007-2009. Pathophysiology 2014, in press.

7. Carlberg M, Hardell L. Pooled analysis of Swedish case-control studies 1997-2003 and 2007-2009 on meningioma risk associated with use of mobile and cordless phones. Submitted.

Hardell et al 2011 – more detailed breakdown

Hardell, Carlberg & Mild 2011. – (Umeå University, Sweden). Int J Oncol 38:1465-74 Pooled analysis of brain tumours: - 1,251 (85%) cases and 2,438 (84%) controls.

- Risk increased with latency period and cumulative use.
- Highest risk for the most common type of glioma, astrocytoma: >10 year latency for mobile phone use: OR = 2.7, (95% CI = 1.9-3.7) and cordless phone use: OR = 1.8 (95% CI = 1.2-2.9)
- These phone types were independent risk factors for glioma.
- Highest risk for astrocytoma with first phone use before the age of 20: mobile phone use OR = 4.9, (95% CI = 2.2-11), cordless phone use OR = 3.9, (95% CI = 1.7-8.7).

Hardell & Carlberg 2014 Mobile phone and cordless phone use and the risk for glioma – Analysis of pooled case-control studies in Sweden, 1997–2003 and 2007–2009. Pathophysiology (In press)

- 1498 (89%) cases and 3530 (87%) controls.
- Mobile phone use increased risk, OR = 1.3, 95% CI = 1.1–1.6 overall, increasing to OR = 3.0, 95% CI = 1.7–5.2 in >25 year latency group.
- Use of cordless phones, OR = 1.4, 95% CI = 1.1–1.7, highest risk in >15–20 years latency group, OR = 1.7, 95% CI = 1.1–2.5.
- The OR increased statistically significant both per 100 h of cumulative use, and per year of latency for mobile and cordless phone use.
- Highest ORs overall were found for ipsilateral mobile or cordless phone use, OR = 1.8, 95% CI = 1.4–2.2 and OR = 1.7, 95% CI = 1.3–2.1, respectively.
- The highest risk in the temporal lobe. First use before age 20 gave higher ORs

Acoustic neuroma – rare benign tumour behind the ear.

- Incidence only 6 – 10 per million per year

Hardell, Carlberg, Söderqvist, Mild. 2013. Int J Oncol 43: 1036-1044 - Pooled analysis of acoustic neuroma diagnosed 1997-2003 and 2007-2009 and use of mobile and cordless phones - 316 participating cases and 3,530 controls

Analogue phone: OR = 2.9, (95% CI = 2.0 - 4.3), >20 years latency (time since first exposure) OR = 7.7, (95% CI = 2.8 – 21).

2G (GSM) phone: OR = 1.5, (95% CI = 1.1 - 2.1), >15 years: OR = 1.8, (95% CI = 0.8 - 4.2).

Cordless phone: OR = 1.5, (95% CI = 1.1 - 2.1), for latency >20 years, OR = 6.5, (95% CI = 1.7 – 26).

2G, 3G, cordless combined: OR = 1.5, (95% CI = 1.1-2.0) increasing to OR = 8.1, (95% CI = 2.0-32).

For total use, highest risk was for longest latency >20 years: OR = 4.4, (95% CI = 2.2-9.0).

Summary of effects from long-term exposure to mobile phone radiation

- Evidence of increased risk of brain tumours and acoustic neuroma from long-term use/exposure, with long latency
- Brain tumours are rare: ~9,000 cases or 12.5 cases per 100,000 per year in the UK
- Acoustic neuroma is both much rarer and are benign.

The risk to the individual is small

Effects on the male reproductive system - human sperm quality* (a rapidly growing area of research)

Types of study:

- Assessment *in vivo* based on mobile phone usage
- *In vitro* - separated sperm exposed to mobile phone radiation
- Studies in animals

Assays:

- Motility, Viability, Number, Generation of ROS, DNA damage

Effects also include:

- increased generation of seminal ROS & reduction in antioxidant enzymes leading to oxidative stress,
- chromosomal damage and micronuclei formation,
- altered spermatozoal membrane potential & signal transduction (decreased calcium efflux, histone kinase and protein kinase C),
- altered sperm proliferative activity, increased caspase activation leading to apoptosis,
- suppression of testicular steroidogenesis & reduced testosterone levels, leading to decreased spermatogenesis

***Note that this is concerned with acute, short-term exposure**

Adams *et al* 2014: Effect of mobile telephones on sperm quality: A systematic review and meta-analysis. Environment International 70:106–112

Table 1
Study characteristics from mobile phone exposure and sperm quality meta-analyses. (– denotes information not provided).

Sperm parameters										
Reference	Sample size	Study design	Participant group	Motility	Viability	Concentration	Radio-frequency (MHz)	SAR (W/kg)	Exposure time	Comments
Agarwal et al. (2008)	361	*In vivo*	Fertility clinic	✓	✓	✓	–	–	–	Exposed to commercially available mobile phones
Agarwal et al. (2009)	64	*In vitro*	Fertility clinic	✓	✓	✓	850	1.46	60 min	Exposed to Sony Ericsson w300i
Ahmed and Baig (2011)	44	*In vitro*	Population	✓			900	1.3	60 min	Exposed to Nokia 112 in talk mode
Dkhil et al. (2011)	40	*In vitro*	Population		✓		850	1.46	60 min	Nokia 73 in talk mode
De Iuliis et al. (2009)	8	*In vitro*	Population	✓	✓		1800	1	16 h	Exposed using a waveguide, connected to a function generator and RF amplifier.
Erogul et al. (2006)	54	*In vitro*	Population	✓		✓	900	–	5 min	Exposed to commercially available mobile phones
Falzone et al. (2008)	24	*In vitro*	Population	✓			900	2	60 min	RF-EMR chamber
Feijo et al. (2011)	343	*In vivo*	Fertility clinic	✓	✓	✓	–	–	–	Exposed to commercially available mobile phones
Fejes et al. (2005)	254	*In vivo*	Fertility clinic	✓		✓	–	–	–	Exposed to commercially available mobile phones
Sajeda and Al-Watter (2011)	300	*In vivo*	Fertility Clinic	✓		✓	–	–	–	Exposed to commercially available mobile

Adams et al 2014 contd..

- Participants were from fertility clinics and research centres. Sperm quality outcome measures were motility, viability & concentration. 10 studies in meta-analysis - 1492 samples.

Exposure to mobile phones was associated with :

- reduced sperm motility (mean difference −8.1% (95% CI −13.1, −3.2)) and
- viability (mean difference −9.1% (95% CI −18.4, 0.2)),
- effects on concentration were more equivocal.

The results were consistent across experimental in vitro and observational in vivo studies

Adams *et al* 2014 contd..

- extract from figure 1

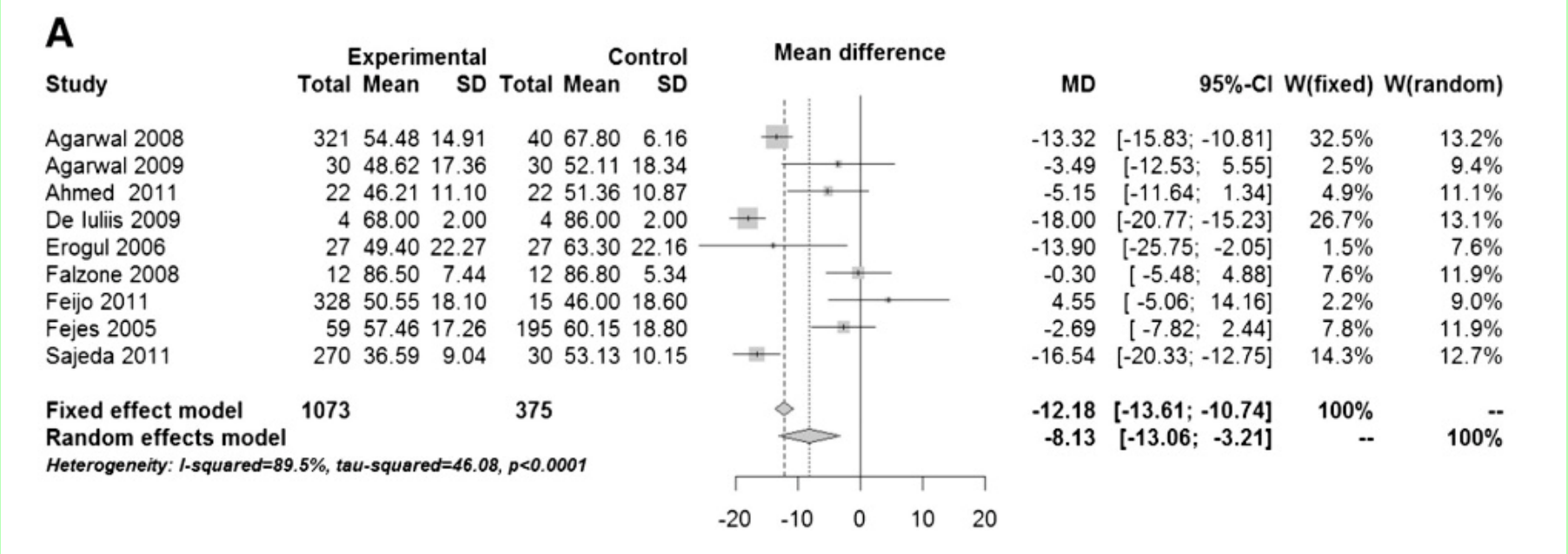


Fig. 1. Forest plot showing the effect of mobile phone exposure on human sperm motility (A)

Recommended reading

Open Access

INVITED RESEARCH HIGHLIGHT

Asian Journal of Andrology (2015) 17, 1–2

Are men talking their reproductive health away?

Ashok Agarwal[1], Damayanthi Durairajanayagam[1,2]

[1]Center for Reproductive Medicine, Cleveland Clinic, Cleveland, Ohio, USA.
[2]MARA University of Technology, Sungai Buloh, Malaysia.
Correspondence: Dr. A Agarwal (agarwaa@ccf.org)

Effects on the female reproductive system

- effects on flies as a bio-marker of exposure

- **Oogenesis** is the creation of an ovum (egg cell) - the female equivalent of the male spermatogenesis

- **Fecundity** - similar to fertility - the *actual* reproductive capacity, measured by the number of eggs

Drosophila oogenesis as a bio-marker responding to EMF sources

- Margaritis *et al* 2014 Electromagn Biol Med. 33(3): 165–189

(Work supported by the European Union, EU & Greek National Science funding)

Drosophila melangaster
(common fruit fly)

Drosophila virilis

Whole flies Exposed to:

- GSM 900/1800 MHz mobile phones
- Cordless (*DECT) handset
- 2.44 GHZ WiFi
- 2.44 GHz blue tooth
- 27.15 MHz baby monitor
- Microwave oven, 44 GHz RF

*Digital Enhanced-European-Cordless Telecommunication

More than 240 replicates were performed. Exposures ranged from 6 – 60 mins per day for 3-7 d depending on protocol

Assayed for:

- Reproductive capacity (fecundity)
  - by counting the number of pupae
- Apoptotic cell death
  - acridine orange staining signal (DNA fragmentation of follicles)

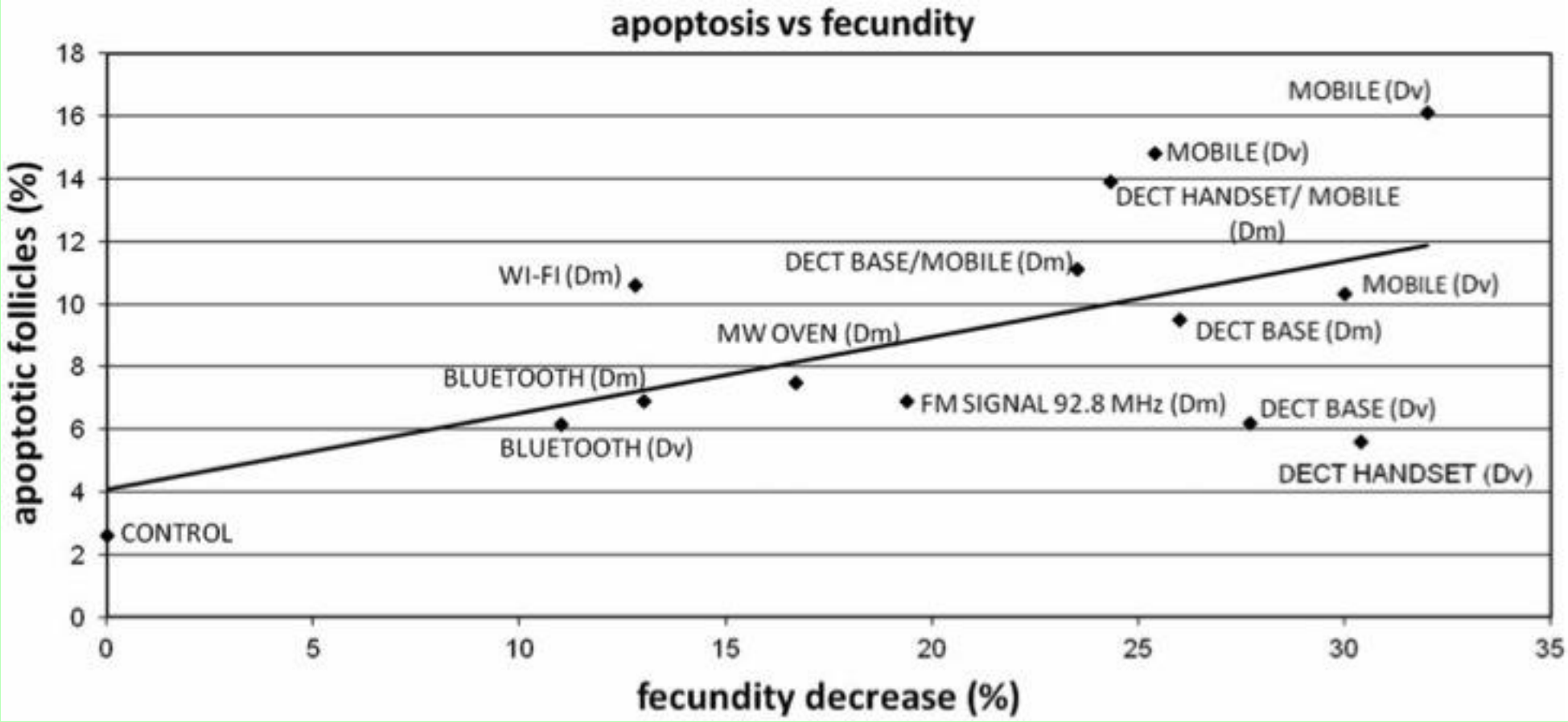
More than 240 replicates were performed. Exposures ranged from 6 – 60 mins per day for 3-7 d depending on protocol

Sample findings from Table 2

EMF SOURCES vs. EFFECT ON FECUNDITY

EMF SOURCE	BIOLOGICAL MODEL SYSTEM	Average E-field intensity EXPOSURE PROTOCOL	FECUNDITY CHANGE AFTER EXPOSURE COMPARED TO SHAM EXPOSED Numbers in brackets correspond to bar numbers in Figure 23	*p* Value one-way ANOVA statistical analysis exposed vs. sham exposed
MOBILE PHONE GSM 900 MHz (see Figures 7A, 8A, 8B and 8D)	*D. virilis*. For more exposure protocols and results see Figures 20, 21, 23	22 V/m 6 min per day for 7 d	−30.0 ± 2.5 [1]	<0.005
		22 V/m 12 min per day for 7 d	−32.0 ± 8.8 [2]	<0.005
DECT BASE 1880–1900 MHz (see Figures 1A, 1B, 7B and 9)	*D. melanogaster*	2.7 V/m 30 min per day for 5 d	−26.0 ± 3.7 [3]	<0.005

Margaritis et al 2014 – Figure 25



Almost every kind of radiation had an impact in the reproductive capacity of Drosophila melanogaster (Dm) and Drosophila virilis (Dv). The maximum reduction was observed after exposure to mobile phone and the DECT handset.

Magnetic fields, evolution and living systems

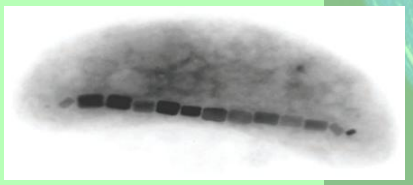
Earth forms (4.5 bn)

Big bang (13.2 bn)

Present day

10^{11} 10^{10} 10^{9} 10^{8} 10^{7} 10^{6} 10^{5} 10^{4} 10^{3} 10^{2} 10^{1} 1

Time (years)



Earth forms (4.5 bn)

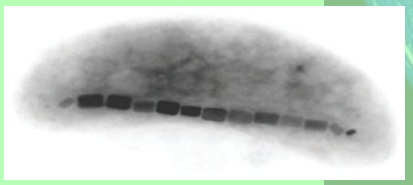
Magnetotactic bacteria (2 bn)

Big bang (13.2 bn)

Present day

10^{11} 10^{10} 10^{9} 10^{8} 10^{7} 10^{6} 10^{5} 10^{4} 10^{3} 10^{2} 10^{1} 1

Time (years)



Earth forms (4.5 bn)

Magnetotactic bacteria (2 bn)

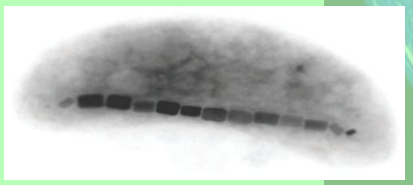
Bird compass (90 m)

Big bang (13.2 bn)

Present day

10^{11} 10^{10} 10^{9} 10^{8} 10^{7} 10^{6} 10^{5} 10^{4} 10^{3} 10^{2} 10^{1} 1

Time (years)



Earth forms (4.5 bn)

Magnetotactic bacteria (2 bn)

Bird compass (90 m)

Early man (6 m)

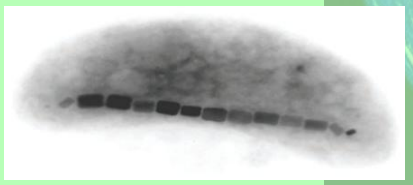
Present day

Big bang (13.2 bn)

10^{11} 10^{10} 10^{9} 10^{8} 10^{7} 10^{6} 10^{5} 10^{4} 10^{3} 10^{2} 10^{1} 1

Time (years)

Chao-praya
Chorn Phon Surasakmontri



Earth forms (4.5 bn)

Big bang (13.2 bn)

Magnetotactic bacteria (2 bn)

Bird compass (90 m)

Early man (6 m)

Electrification (1884)

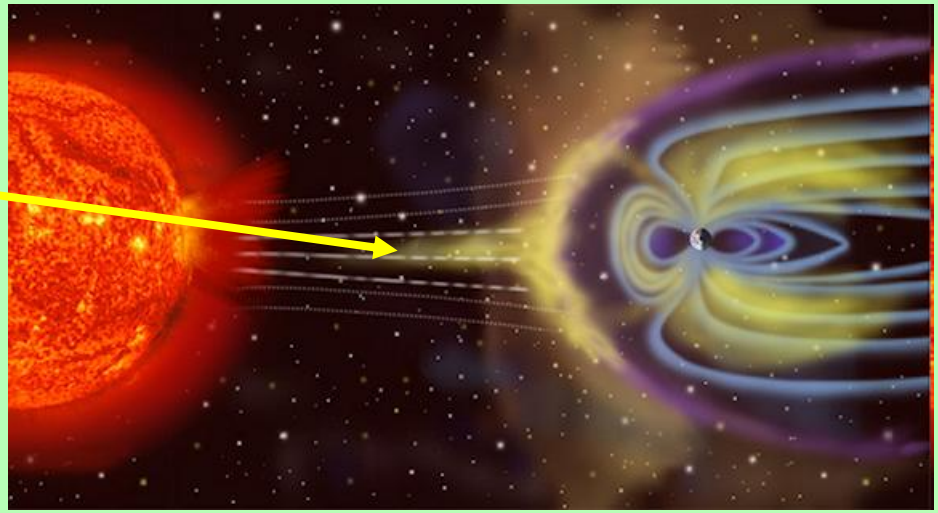
Present day

10^{11} 10^{10} 10^{9} 10^{8} 10^{7} 10^{6} 10^{5} 10^{4} 10^{3} 10^{2} 10^{1} 1

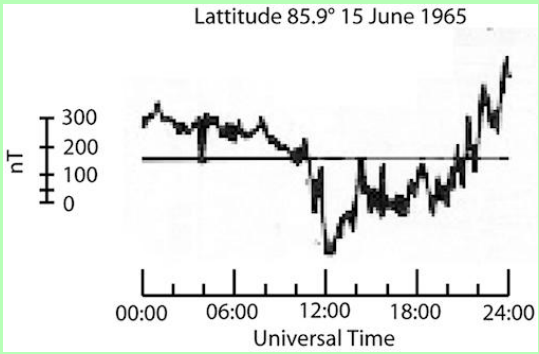
Time (years)

Geomagnetic Storms*

- Arising from charged particles from the sun



Typical MF profile (Campbell 2003)
(K-value – maximum fluctuation over a 3-hour period)



Storms of interest last 1–5 days and have a magnitude of about 100 nT

Acute health effects include*: increase in depressive illnesses, melatonin disruption, heart rate variability, blood pressure changes.

However, only 10-15% of the population seem affected

Strength of the Storm* (nT)	Frequency
> 100	**4.6 per year**
> 200	9.4 per 10 years
> 400	9.73 per 100 years

*Superimposed on the static GM field which in Bangkok is 37.3 μT

***Pigeon migration is also disturbed by GM storms** (Schiffner & Wiltschko 2011 J Comp Physiol A DOI 10.1007/s00359-011-0640-y

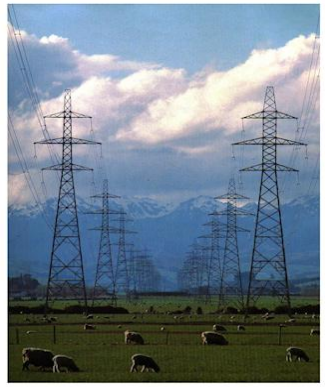
See: http://www.ngdc.noaa.gov/stp/GEOMAG/kp_ap.html

Love & Gannon Ann. Geophys. 27:3101-3131 (2009)
http://en.wikipedia.org/wiki/Geomagnetic_storm

Power frequency electric & magnetic fields
- especially magnetic fields, MFs†

Appliances: can be tens of μT close to

(Richard Box's 'FIELD' February 2004 Photo: Stuart Bunce, www.richardbox.com)



Under powerlines MFs can be several μT or evens tens of μT

Doubling of Childhood Leukaemia risk associated with average 0.3/0.4 μT*

Average MF home levels 0.05 μT

*and 30% increase in risk above 0.2 μT – Zhao et al 2014

*Robust association reiterated in 2014 EU SCENIHR Report

†Magnetic fields are an IARC Class 2B Possible Carcinogen

Review bodies' assessments of MF association of various diseases.

- IARC has classified Power Frequency MFs as Class 2B – 'possible carcinogen'.

	Disease	NIEHS 1999[1]	IARC[2] 2002	California* 2002	EU: SCENIHR 2014[3]	EMF & Health 2011[4]
1.	Childhood Leukaemia	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**
2.	Adult Leukaemia[5]	**Yes**		**Yes**		**Yes**
3.	Adult brain cancer[5]			**Yes**		**Yes**
4.	Miscarriage			**Yes**		**Yes**
5.	ALS[6]			**Yes**		**Yes**
6.	Alzheimer's disease				**Yes[7]**	**Yes**

[1]US National Institute of Environmental Sciences

[2]International Agency for Research on Cancer

[3]EU: Scientific Committee on Emerging and Newly Identified Health Risks: Possible effects of Electromagnetic Fields (EMF) on Human Health.

[4]EU: EMF & Health, Brussels Nov 2011

[6]Motor neurone disease

[7]Studies more recently published

[5]Aggregated data is highly significant:

O'Carroll and Henshaw 2008. Risk Analysis 28:225-234.

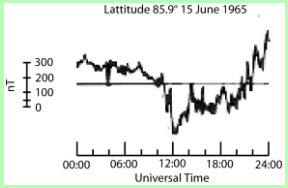
Kheifets et al. 2008. JOEM 50:677-688.

*http://www.ehib.org/emf/RiskEvaluation/riskeval.html

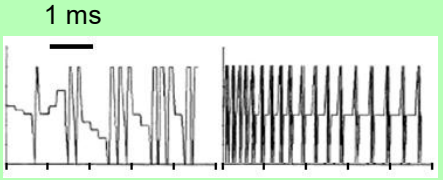
Common question: Given that we are all exposed to the geomagnetic field of **50 μT**, **how can a 100 nT fluctuation or a 50 Hz 0.4 μT field make any difference?**

"Real" magnetic fields are noisy – and appear particularly biologically active

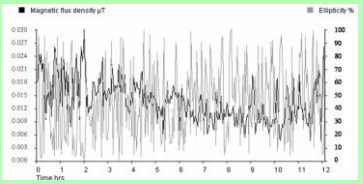
- Effects of GM storms - increase in depressive illnesses, melatonin disruption, heart rate variability, blood pressure changes.
- Animal navigation – disruption by GM anomalies & stroms and stray MFs
- Pain threshold – reviewed in del Seppia et al 2007 Neuroscience & Biobehavioral Reviews 31;619–42
- Patterned field effects – e.g. St-Pierre et al. *IJRB*. 2008. 84: 325-335
- Alternative exposure metrics - Lee *et al*. (2002) and Li *et al*. (2002) - higher ORs for miscarriage for RCM compared to TWA



Typical GM storm profile

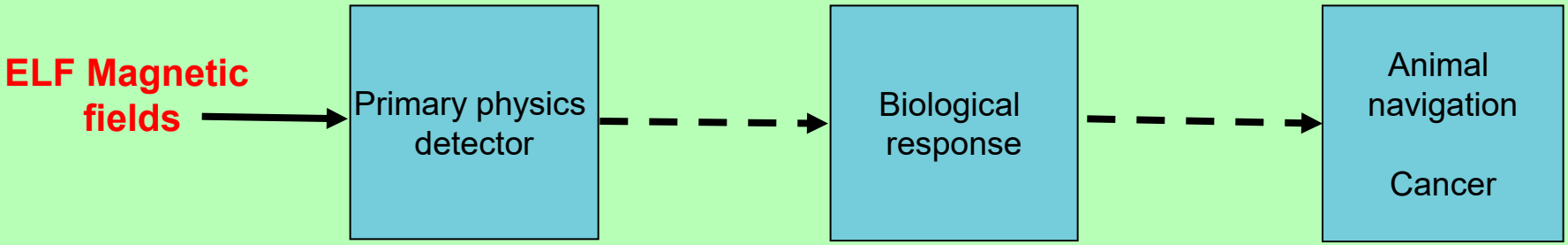


Patterned MF associated with increased cellular anomalies at 0.09 μT – St-Pierre et al. *IJRB*. 2008. 84: 325-335



Ainsbury & Henshaw 2006 Phys Med Biol 51:6113–23

► **Lee, GM. *et al.*** *Epidemiology.* 2002; **13**: 21-31. **Li, D. *et al.*** *Epidemiology.* 2002; **13**: 9-20.



The primary physics detector, only has to detect

It is the subsequent biological response that matters - In animal navigation, evidence suggests MF processing is in the brain

MF adaptation

Pigeons

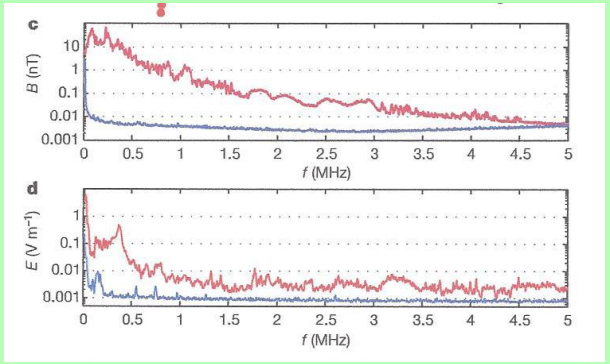
Mora and Walker 2012 doi:10.1016/j.anbehav.2012.05.005

- Homing pigeons with 2,500 μT magnets on their beaks.
- Released from 26 sites up to 42 km from their loft.
- Initially flew to the right of their homing direction
- This was corrected within 2.5 km
- No effect on the speed or success of homing

NdFeB magnets, 2,500 μT, 50 times GMF
1-4 year olds, trained to home from 40 km
Up to 40 pigeons in repeated releases

EMF Interference:

Magnetic orientation of European robins disrupted by RF EMFs



Engels *et al* 2014 doi:10.1038/nature13290

Question: Where in the body do navigation disruption effects occur?

What links these apparently disparate EMF health outcomes?

- Childhood leukaemia
- Adult leukaemia
- Adult brain tumours
- ALS (motor neurone disease)
- Miscarriage & adverse birth outcomes
- Depression & depressive symptoms
- Alzheimer's disease
- Breast cancer

They could all be explained by Melatonin & circadian rhythm disruption by electric & magnetic fields*

*Henshaw DL, Reiter RJ. 2005. Do magnetic fields cause increased risk of childhood leukaemia via melatonin disruption? Bioelectromagnetics Supplement 7:S86-S97.

Magnetite* and other iron-mineral particles in animals and man

(Magnetic intensity)

All possess biogenic magnetite* or other membrane bound iron-mineral particles (magnetosomes) used for navigation

*Magnetite: Fe_3O_4

(magnetic sensitivity exists in all major groups of vertebrate animals, as well as in some molluscs, crustaceans and insects, including flies, chickens and mole rats)

Particles of interest:

Single domain

30 – 200 nm

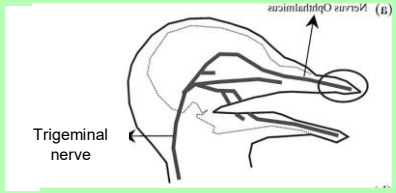
Whole particle rotates

Superparamagnetic (sp)

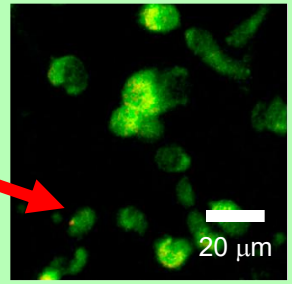
<30 nm

Particle remains stationary but MF vector flips

Pigeons
(Upper beak)



Trout
(Olfactory epithelium)



→ μm-sized candidate magnetoreceptor cells
Eder et al. 2012 PNAS DOI:10.1073/pnas.1205653109

In pigeons, the inclination sensitivity is 0.02 - 0.17 degrees, down to 0.01 μT (~10 nT) - Gould 2010 Current Biol 21;R206

Magnetic particles in human brain and ferritin

(Kirschvink et al. (1992) PNAS 89:7683-7 and Allen et al. 2000 Biochimica et Biophysica Acta 1500;186-196)

1. Human brain: Kirschvink et al. characterised magnetite biomineralisation in adult human brain:

- Sizes **10 – 70 nm** & **90 – 200 nm**, some **600 nm**. 5 million single-domain crystals/g for most brain tissues, >100 million crystals/g for pia and dura – the layers near the skull.
- Particles in clumps of between **50** and **100** particles; **U/*kT* values between 20 and 150.**
- **The larger particles could respond to a 50 Hz field at 0.4 μT** - putting mechanical stress on neighbouring cells

2. Ferritin:

- has a natural ferrihydrite nano-particle, ~8 nm, superparamagnetic, SP at room temperature.
- 1 – 200 mT fields in their vicinity; ~1 mT at 50 nm away
- SP particle would effectively **"amplify"** a 0.4 μT 50 Hz field by induced magnetisation **- Binhi 2008 IJRB 84:569-579**

Superparamagnetic (SP)

<30 nm

Particle remains stationary but MF vector flips

A second mechanism of low level MF detection

(Magnetic compass)

- The process known as the Radical Pair Mechanism, RPM

- Low intensity MFs can increase the lifetime of free radical pairs

They do so by altering the spin states of radical pairs- Increasing the rate of transition from the short-lived **singlet (S)** to the longer-lived **triplet (T)** state

- Purported to act on cryptochromes, leading to changes in chemical reaction products which can form the basis of a chemical magnetic compass
- Could also act in cryptochromes to disrupt circadian rhythms?
- The process also results in free radicals becoming more available to cause biological damage

Now let's look at a second mechanism of MF detection in animals

– a chemical compass in the eye based on the RPM*

***Note that in salamanders the MF compass is housed in the pineal gland. The gland is also involved in the light-dependent compass in frogs, lizards and some fish**

Proposal by Ritz et al. 2000

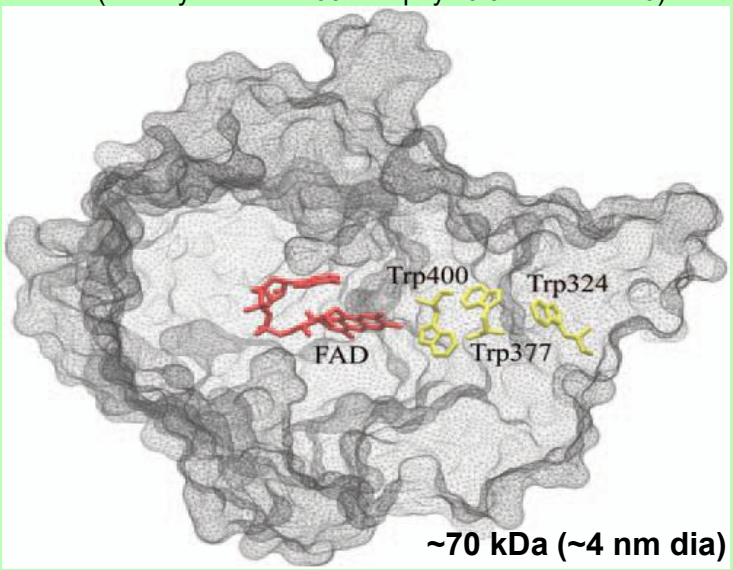
(Biophys J 78:707-718)

-proposed that the MF reception in birds was mediated via the RPM on cryptochromes in the eye

-50–90 kDa blue-light photoreceptor; flavoproteins - **best known for their role in controlling circadian rhythms**. High sequence-homology to DNA photolyases.

- Ritz proposed that RF fields ~1 MHz might interfere with the MF compass
- Proposed that since the time scale of the RPM was ~1 μs, this could be disrupted with RF-EMFs in the MHz region
- A series of experiments in birds and insects have confirmed compass disruption with fields as low as 20 nT

Schematic view of cryptochrome
(Solov'yov et al. 2007 Biophys J 92:2711–2726)



FAD = flavin-adenine dinucleotide

Radical pair consisting of $FADH^{\bullet}$ and the terminal Tryptophan residue of the cryptochrome Trp-triad, RP separation is ~1.9 nm (Efimova & Hore 2008)

[1]Liedvogel et al. 2007 *PLos One* 2(10): e1106; [2]Cry1a located in UV/V-cones Niessner et al. 2011 PLoS ONE 6(5): e20091

Are human cryptochromes magnetosensitive? - Yes

Foley, Gegear & Reppert 2011 Nature Comm ncomms1364:

"Human cryptochrome exhibits light-dependent magnetosensitivity"

- **Study:** Magnetic behavioural response of CRY-deficient and hCRY2 *Drosophila melanogaster* (10 – 12 groups of 100-150 individual flies per test), under control of *tim*-GAL4 *driver.*
- **Methods:** Flies exposed between 10 – 500 μT with full spectrum and blocked (>500 & >400 nm) light
- **Findings:** (i) CRY-deficient flies showed no MF response; (ii) Human CRY-rescued flies showed light-dependent magnetosensitivity: positive response under full spectrum light was blocked at >500 nm but partially restored at >400 nm.

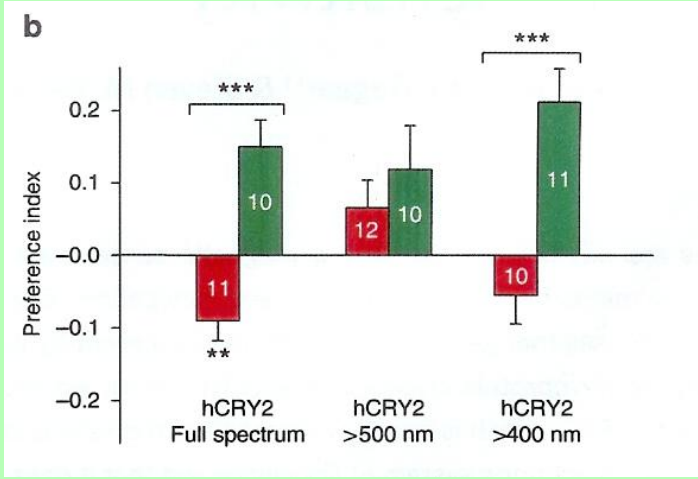


Figure 1b

Summary on ELF MFs

- MFs may induce damage to biological cells directly
- Simultaneously, they may also disrupt circadian rhythms.
- We have (at least) two candidates for mediating the initial MF interaction, **magnetic particles** and the **RPM**
- There are number of conceptual issues to address

Do these findings apply to mobile phone radiation?

- Magnetite particles may respond to mobile phone EMFs
- However, the effect of mobile phone EMFs on the RPM is very hard to judge
- Overall, the primary interactions mechanisms are poorly understood

Precaution against mobile phones & WiFi

- Use by young children should be discouraged
- Use a hands-free kit where possible
- Avoid keeping your mobile phone in your trouser pocket
- At night, avoid keeping your mobile phone by the bedside – better to keep it further away or keep switched off
- In relation to the nocturnal production of melatonin, sleep in the dark

Acknowledgements

Children with Cancer UK

University of BRISTOL

CHILDREN with CANCER UK
Registered Charity No. 298405

Effects of animal magnetic compass orientation with RF and ELF EMF exposures (GMF = geomagnetic field).

Study	MF and light exposure	Findings
Ritz et al. 2004: European robins, *Erithacus rubecula*: 12 individually tested in spring migration season.	Local GMF 46 μT, inclination 66° and 565 nm light (control) plus: (i) broadband 0.1 – 10 MHz, 0.085 μT; (ii) single frequency 7 MHz, 0.47 μT; all parallel, 24° or 48° to GMF vector.	Birds exhibited seasonally appropriate migratory orientation with no applied RF or when the RF field was parallel to the geomagnetic field, but were disoriented when it was presented at an angle of 24° or 48° at **0.085 μT**.
Thalau et al. 2005: As in Ritz et al. 2004 using 12 robins in spring and 16 robins in autumn.	As in Ritz et al. 2004, but applying RF at the local Larmor frequency of **1.315 MHz** at 0.485 μT, parallel and at 24° to GMF vector.	Birds exhibited seasonally appropriate migratory orientation in both spring and autumn with no applied RF or when the RF field was parallel to the geomagnetic field, but were disoriented when applied at 24° at **0.485 μT**.
Wiltschko et al. 2007: Domestic chickens, *Gallus gallus*; 36 in total, between 12 and 22 days old.	Local GMF 55.9 μT, inclination 62° , artificially orientated East as control; and white, 465 nm blue or 645 nm red light plus: (i) local **Larmor frequency 1.566 MHz* at 0.48 and 0.048 μT** vertical (28° from GMF vector); (ii) 50% weaker and stronger: 27.9 μT and 83.8 μT and (iii) 25%, weaker and stronger: 41.9 μT and 69.9 μT.	1. Chickens orientated well in control field, but in general not in the weaker and stronger fields, suggesting a functional window around the GMF. 2. Tendency to orientate well under white and blue light, but not red, but results not statistically significant. 3. Exposure to **1.566 MHz** led to disorientation suggestive of an underlying radical pair mechanism.
Stapput et al. 2008: European robins, *Erithacus rubecula*; 12-16 per test	Local GMF 46 μT, inclination 66° and 565 nm green light or total darkness, alone (control) or plus 1.315 MHz at 0.48 μT, 24° to GMF vector.	Normal seasonal migratory orientation under 565 nm light. In total darkness, birds orientated NW, not the migratory direction, and were not disrupted by 1.315 MHz fields, although were disrupted by anesthesia of the upper beak. Findings suggestive of two magnetic compass systems: (i) an inclination compass based on radical-pair processes allowing orientation in the migratory direction and (ii) an iron-based system that, aside from providing ‘‘map’’ information, can affect orientation in ‘‘fixed directions’’ in the absence of light, but is normally dormant when the radical-pair mechanism is operating.
Keary et al. 2009: Zebra finches, *Taeniopygia guttata.* 10 for MF orientation; 7 for visual perception	Local GMF 43 μT, inclination 67° daylight. Local Larmor frequency 1.156 MHz at 0.47 μT, horizontal component of GMF shifted 90° clockwise (control), RF added in same vector direction. Separately, birds were trained to orientate with respect to visual clues.	Birds exhibited migratory orientation in the 90° shifted control field, but this was disrupted when the RF field was added. Birds trained for visually guided orientation were unaffected by either the static or RF fields.

*This corresponds to the Larmor frequency for the **free electron** in the local GMF

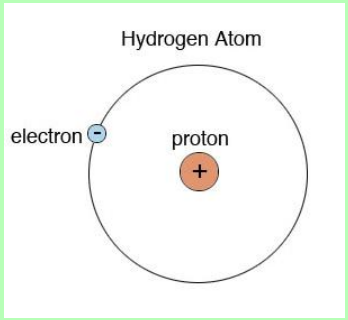
Ritz *et al.* 2004 Nature 429:177-180, Thalau *et al*. 2005 Naturwissenschaften 92:86–90, Wiltschko *et al.* 2007 J Exp Biol 210:2300-2310. Stapput *et al.* 2008 Curr Biol 18:602–606, Keary *et al*. 2009

Effects of animal magnetic compass orientation with RF and ELF EMF exposures (GMF = geomagnetic field). Continued:

Study	MF and light exposure	Findings
Vacha et al. 2009: American cockroaches: 11 individually isolated from each other.	Local GMF 42.9 μT, inclination 64˚ , white light: (i) These conditions as control (ii) GM North was rotated 60˚ in 5 min intervals Adding vertically to both of these: (iii) 1.2 MHz, 0.044 μT, reducing (iv) 2.4 MHZ, 0.044 and 0.018 μT (ii) 7 MHz, 0.044 μT	Cockroaches were tested for locomotive activity using double-blinded procedure. 1. Changes in activity between stable and 60˚ periodic field rotations, indicating functionality of basic MF sense; 2. 1.2 MHz interfered with above changes, disruption threshold between **12 – 18 nT**; 3. 2.4 MHz interfered with above changes, disruption threshold between **18 - 44 nT**; 4. 7 MHz produced no disruption at 44 nT.
Ritz et al 2009: European robins, *Erithacus rubecula*: 12 individually tested in spring migration season	(i) Local GMF 46 μT, inclination 66˚ 565 nm green light, plus 8 frequencies from 0.01 to 7.0 MHz, including **Larmor 1.3 15 MHz***, 0.47 – 0.48 μT (ii) GMF artificially doubled to 92 μT, plus 1.315 and **(matched Larmor) 2.63 MHz**	1. GMF of 46 μT: (i) GMF alone: well orientated; (ii) 0.01 and 0.03 MHz: no interference; (iii) 0.1 and 0.5 MHz: weak axial response characteristic of compass on its limit of operation; (iv) 0.658 MHz and higher: disorientation; (v) Larmor frequency of **1.315 MHz***: disoriented even at **15 nT**, not affected at 5 nT. 2. Static field set artificially at 92 μT: (i) 92 μT alone: well orientated; (ii) 1.315 MHz at 150 or 48 nT orientation no longer affected; (iii) **2.63 MHz**.: disorientation at **15 nT**.
Begall et al. 2008: Worldwide satellite observations: 8,510 **Domestic cattle** in 308 pastures and 2,974 **Roe deer** at 241 localities	The natural GMF, daylight observations.	Domestic cattle across the globe, and grazing and resting red and roe deer, **align their body axes in roughly a N-S direction**. Roe deer orient their heads northward when grazing or resting. At high magnetic latitudes, magnetic North was a better predictor of alignment than geographic North.
Burda et al. 2009: As in Begall et al. 2008, including 153 localities/herds (cattle) and 47 localities/herds (roe deer) within 150 m of high voltage powerlines	Separate analysis of orientation of animals near high voltage powerlines, exposed to the GMF and power frequency electric and magnetic fields and corona ion disturbances of the atmospheric electric field.	The natural N-S orientation of cattle and deer was disrupted, with random orientation within 150 m of high voltage powerlines. However, directly under powerlines animals aligned themselves E-W under E-W lines, N-S under N-S lines and randomly under NE-SW or NW-SE lines. Furthermore, the alignment of cattle as a function of distance from E-W lines progressively rotated from **E-W under the line to N-S at distances >150 m away**. In the case of E-W powerlines, **cattle and deer oriented better on the north side compared with the south side**. Overall, the evidence supports a magnetic compass in cattle and deer based on an intensity-dependent mechanism.

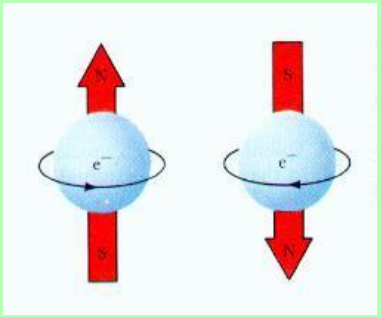
*This corresponds to the Larmor frequency for the **free electron** in the local GMF

Vácha *et al*. 2009 J Exp Biol 212:3473-3477. Ritz *et al*. 2009 Biophys J 96:3451–3457, Begall *et al*. 2008 PNAS 105:3451-13455 Burda *et al.* 2009 PNAS 106:5708-13

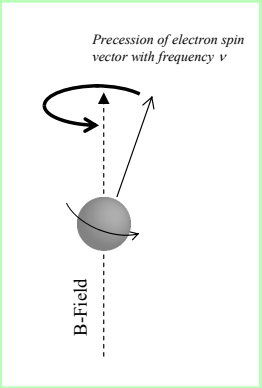


$H^{\bullet}$

Electron spins: angular momentum ½h/2π



Spin “up” Spin “down”



Classical model - electron spin vector precesses at the Larmor frequency of 1.4 MHz at 50 μT

Joseph Larmor (1857-1942

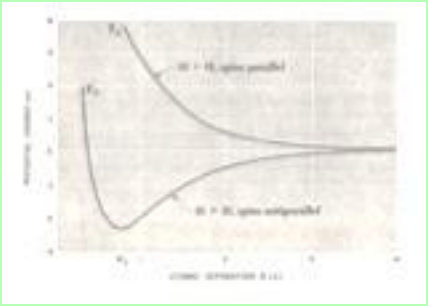
Hydrogen atom:

-has a single electron – with no partner (unpaired).

- an example of a “radical”

- electron spins about its axis either “upwards” or “downwards”

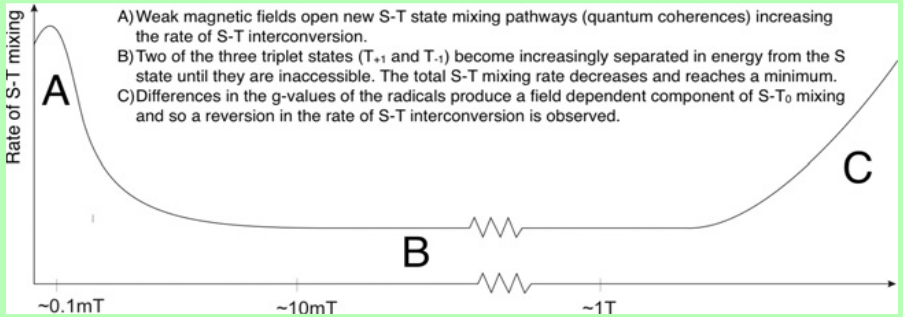
- also “precesses” in a magnetic field



$(H\uparrow + H\downarrow) \rightarrow H_2$

The hydrogen molecule forms by the addition of two hydrogen atoms whose electrons have opposite spins

RPM and the Low Field Effect



Woodward et al. 2009 Biochem Soc Trans 37(2):358-62.

Blue-light photon

$D^{\downarrow\uparrow} + A$

Electron transfer

S↔T mixing

$(D^{\uparrow} + A^{\downarrow})^{S}$ $(D^{\uparrow} + A^{\uparrow})^{T}$

Magnetic nuclei + external field

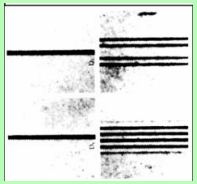
Singlet products

Triplet products (Different products)

At low fields* get an increased rate of S-T conversion
T-state radical pairs cannot recombine, so they react elsewhere, e.g. with DNA

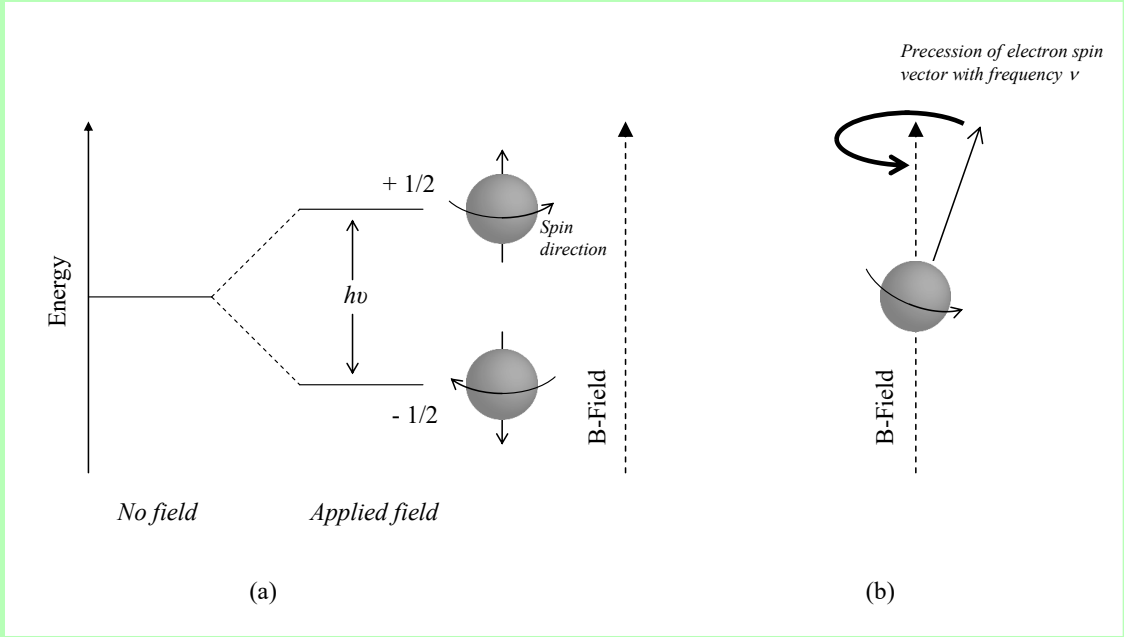
*for GM field sensitivity, requires RP lifetimes ~1 μs

Introduction to RPM – Zeeman splitting and Larmor precession



Zeeman Effect 1896

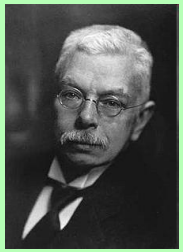
In a static MF, get splitting of spectral lines due to the electron spin



The equivalent classical model has the electron spin vector precessing at the Larmor frequency of 1.4 MHz at 50 μT

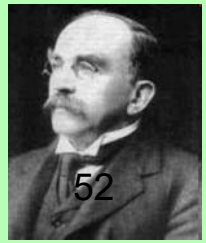
Get resonant absorption (ESR) at frequency ν = 1.4 MHz at 50 μT

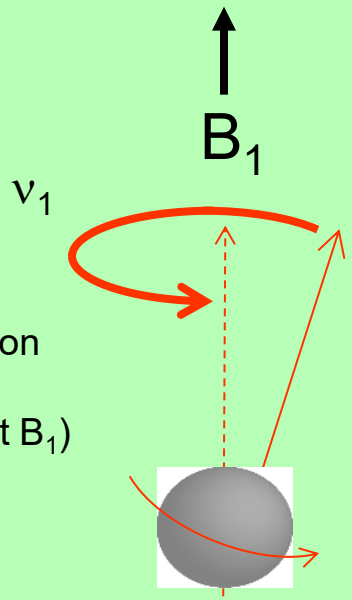
At the GM field in London, 48.7 μT:
- hν is ~10^{-7} of thermal energy *kT*



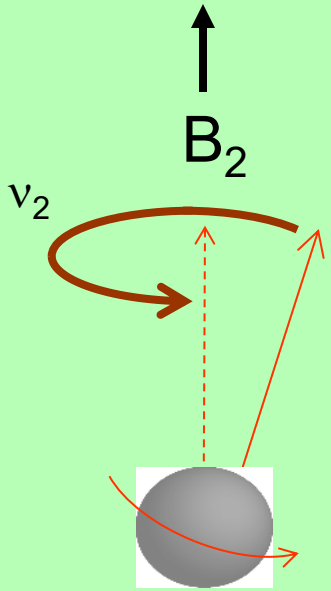
Pieter Zeeman (1865-1943)

Joseph Larmor (1857-1942)





Unpaired electron
- radical 1
(precesses about B_1)



Unpaired electron
- radical 2
(precesses about B_2)

Maximum sensitivity when:

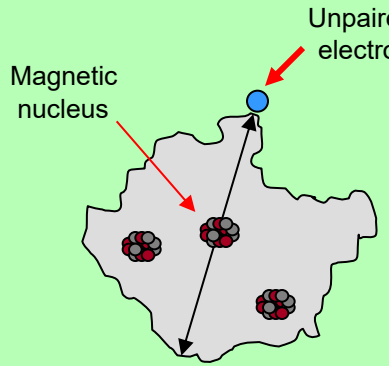
$B_{int} >> B_{ext}$
(Earth's field has little influence)

$B_{int} = 0$,
(only influence is the Earth's field)

The field vector, B comprises:

1) Internal field, B_{int} due to high-abundance magnetic nuclei e.g. ^{1}H ^{14}N

2) External field, B_{ext} – the Earth's field



Hyperfine interactions with the magnetic nucleus (<10 – 1000 μT or 28 kHz μT^{-1}):

- s-orbital (isotropic) – part of wave function inside the nucleus
- dipole (anisotropic) – gives compass directionality

Direct MF effects of Magnetic Fields *in vitro*

1.Release of reactive oxygen intermediates in human cord blood-derived monocytes **(1 mT, 50 Hz: Lupke et al 2004. Free Rad. Res. 38:985–993)**

2.Stress response induced in HL-60 cells human leukaemia cells **(10 μT, 50 Hz: Tokalov & Gutzeit 2004. Environ. Res. 94:145–51)**

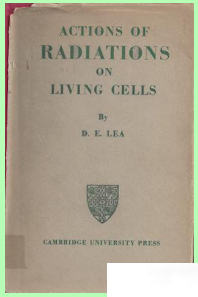
Mattsson & Simkó 2014. **(Frontiers in Public Health 2:Article132)**

The authors reviewed **41** studies, **36** of which reported an MF-induced oxidative response

"The conclusion from the work is that ELF MF (modulated or unmodulated) consistently can influence the oxidative status, at or above 1mT, in a broad range of cell types and independent of exposure duration. A response at lower flux densities is seen in certain studies, although not consistently."

See now:

Luukkonen et al 2014 Mut Res/Fundamental & Molecular Mechanisms of Mutagenesis 760;33– 41.



D E Lea 1946: Actions of Radiations on Living Cells Chapter VI

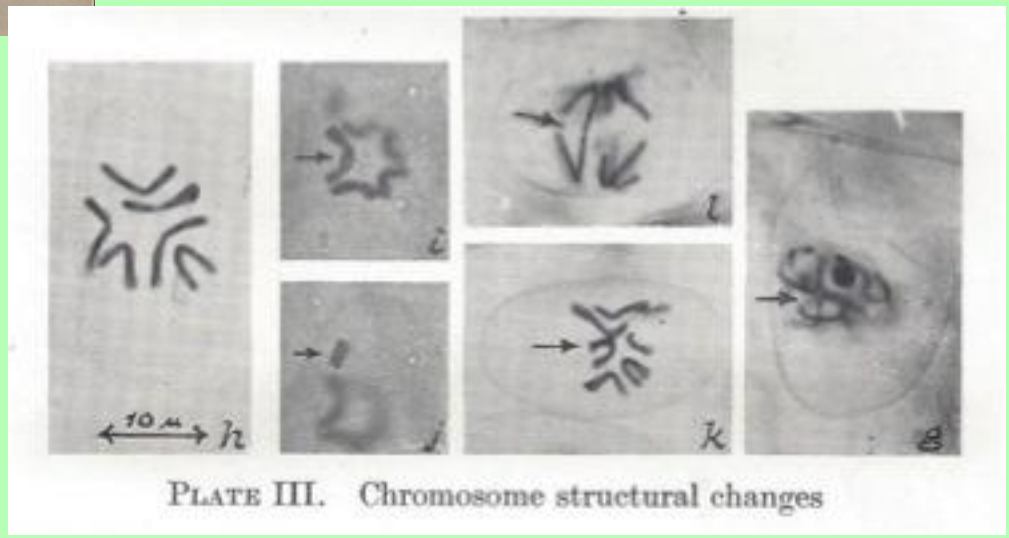


PLATE III. Chromosome structural changes

Chromosome structural changes/rearrangements on Drosophila following the passage of X-rays

"Aberrations seen, for example, in metaphase are then due to radiation which was given to the cell at a stage prior to metaphase corresponding to the time interval which elapsed Between irradiation and fixation."

But later:

"When chromosome **breaks** are being studied…. [The action of the radiation appears to be **direc**t , in the sense that **breakage** is caused by an ionising particle passing **through** or in the immediate vicinity of the chromosome at the point where the breakage occurred]."

Statement:

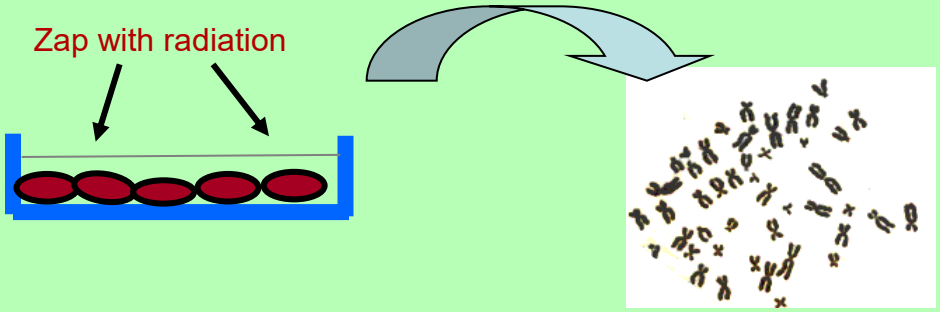
MFs do not have the quantum energy to cause DNA strand breaks, so they cannot cause cancer

An obvious flaw:

If this is true, how then do asbestos particles, cancer viruses or carcinogenic chemicals cause cancer – because they do not ionise like ionising radiation !

The Bystander Effect & Genomic Instability

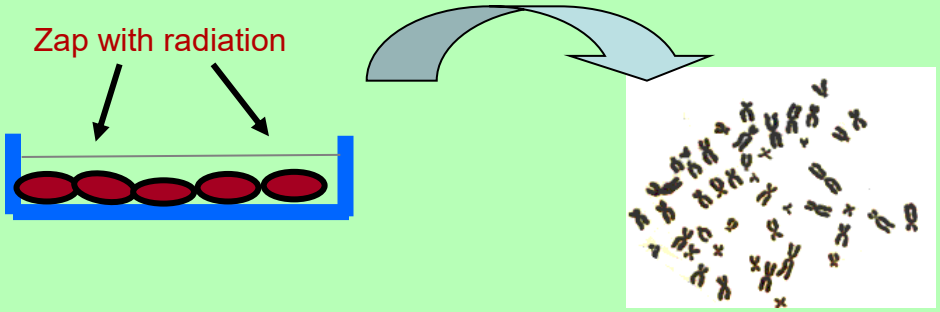
50 years of dogma



Look at the chromosomes at metaphase and note the damage ("DNA strand breaks")

The Bystander Effect & Genomic Instability

50 years of dogma

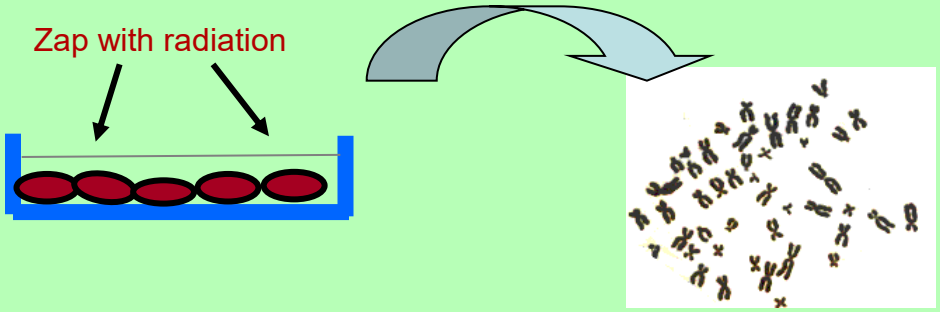


Look at the chromosomes at metaphase and note the damage ("DNA strand breaks")

Bystander effect (c1992)

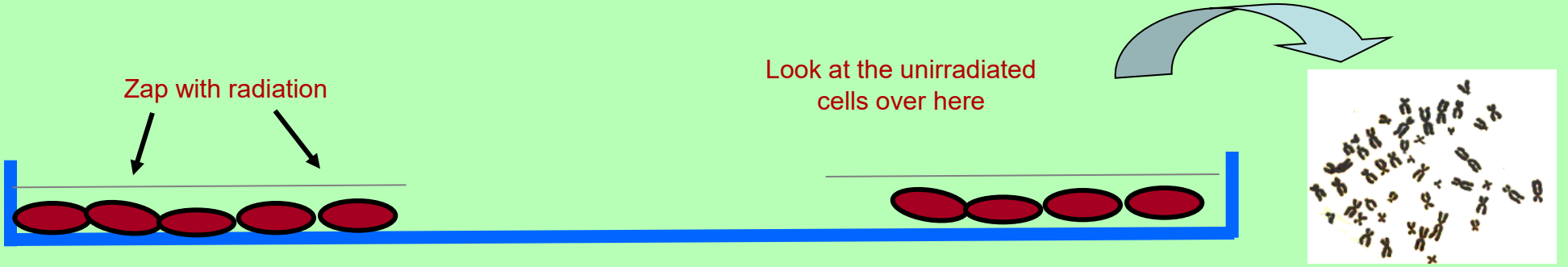
The Bystander Effect

50 years of dogma



Look at the chromosomes at metaphase and note the damage ("DNA strand breaks")

Bystander effect (c1992)



We also get DNA strand breaks

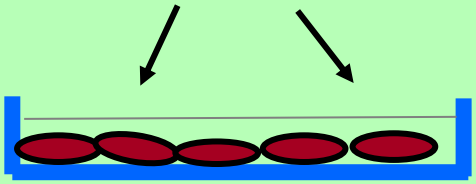
See the work of Prof Carmel Mothersill at the Dublin Institute of Technology

Mothersill et al 2006: *Dose-Response*, 5:214–29: "It is concluded that bioelectric or magnetic effects may be involved in producing bystander signaling cascades commonly seen following ionizing radiation exposure."

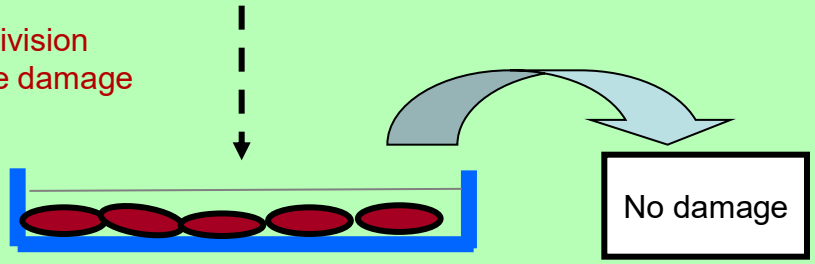
Genomic instability (1992)

50 years of dogma

Zap with low dose radiation

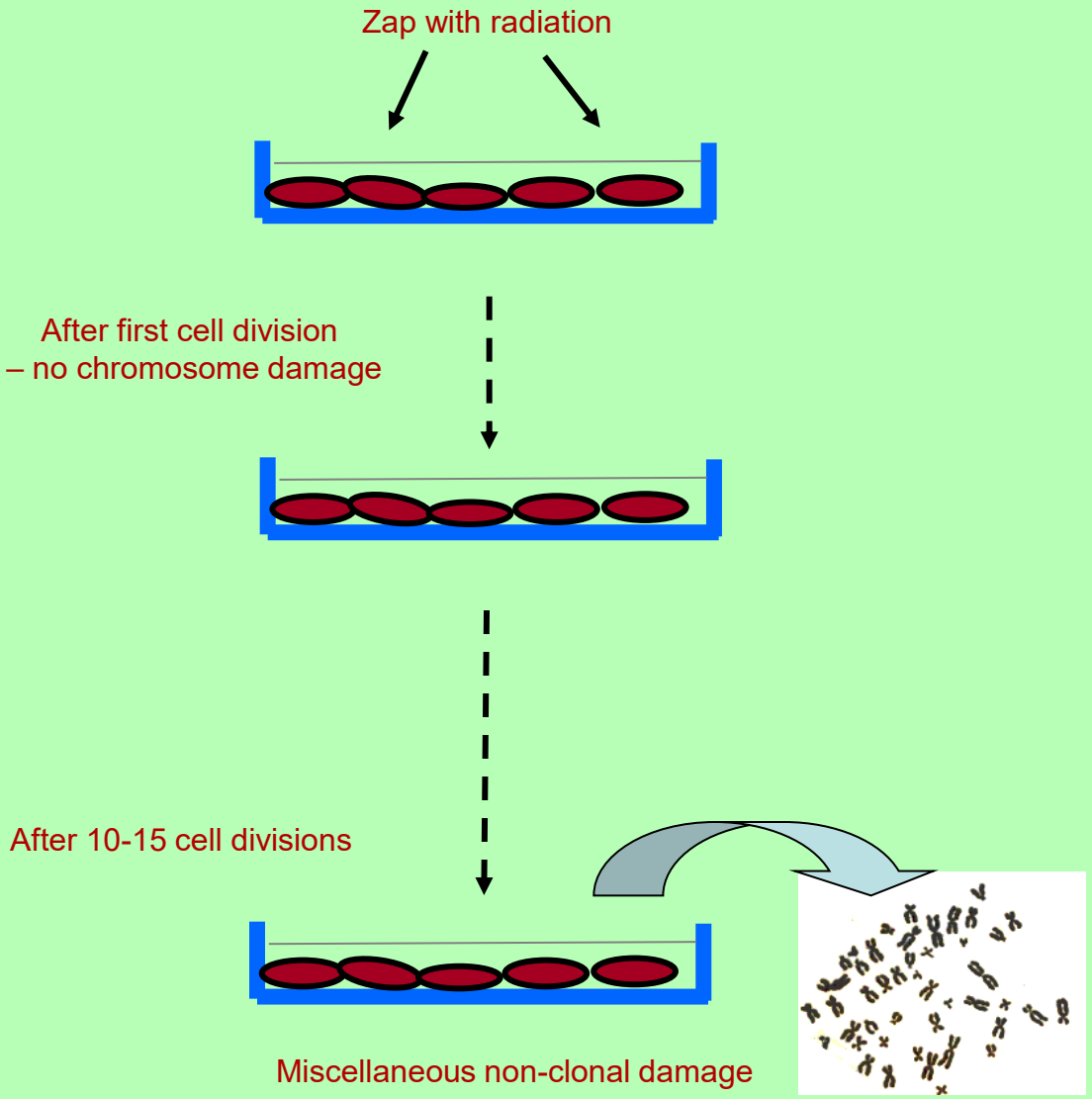


After first cell division
– no chromosome damage



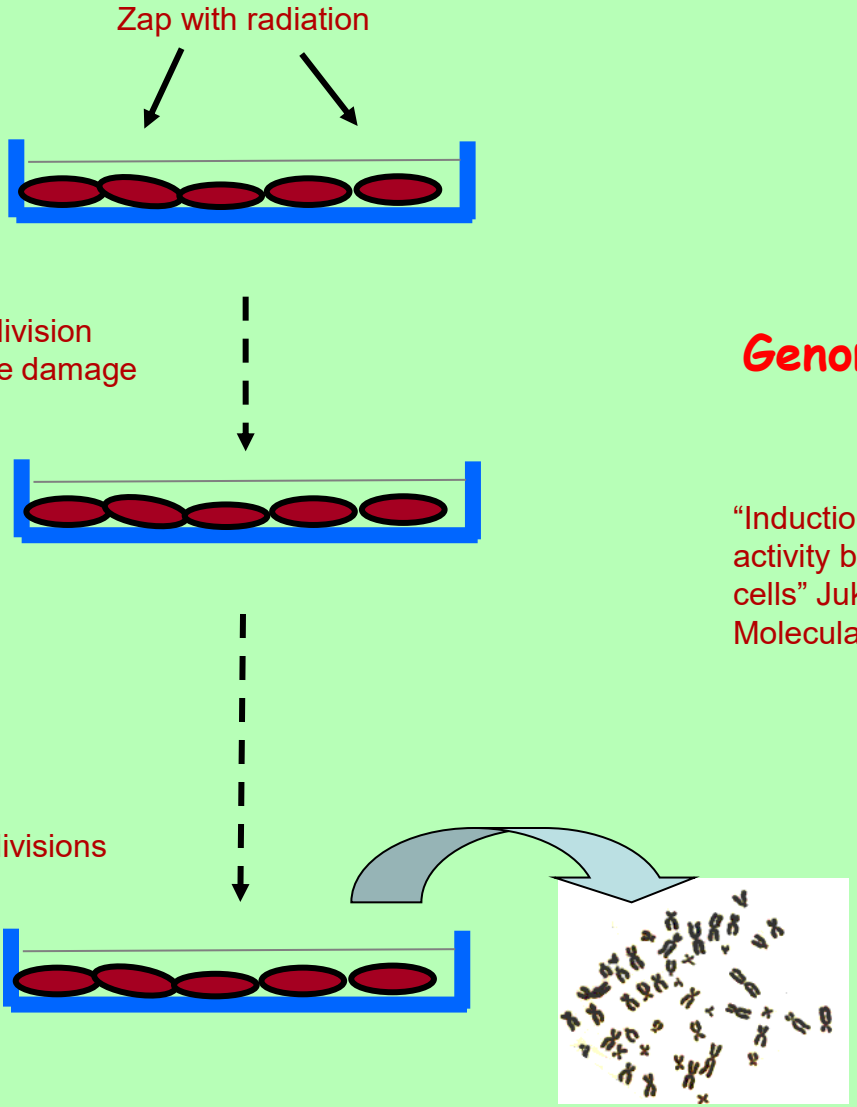
Genomic instability (1992)

Kadhim *et al*. 1992 Nature, 355;738-740.



First seen with ionising radiation,
but since seen with metals and chemicals

Genomic instability (c1994)



2014:

Genomic instability observed with magnetic fields:

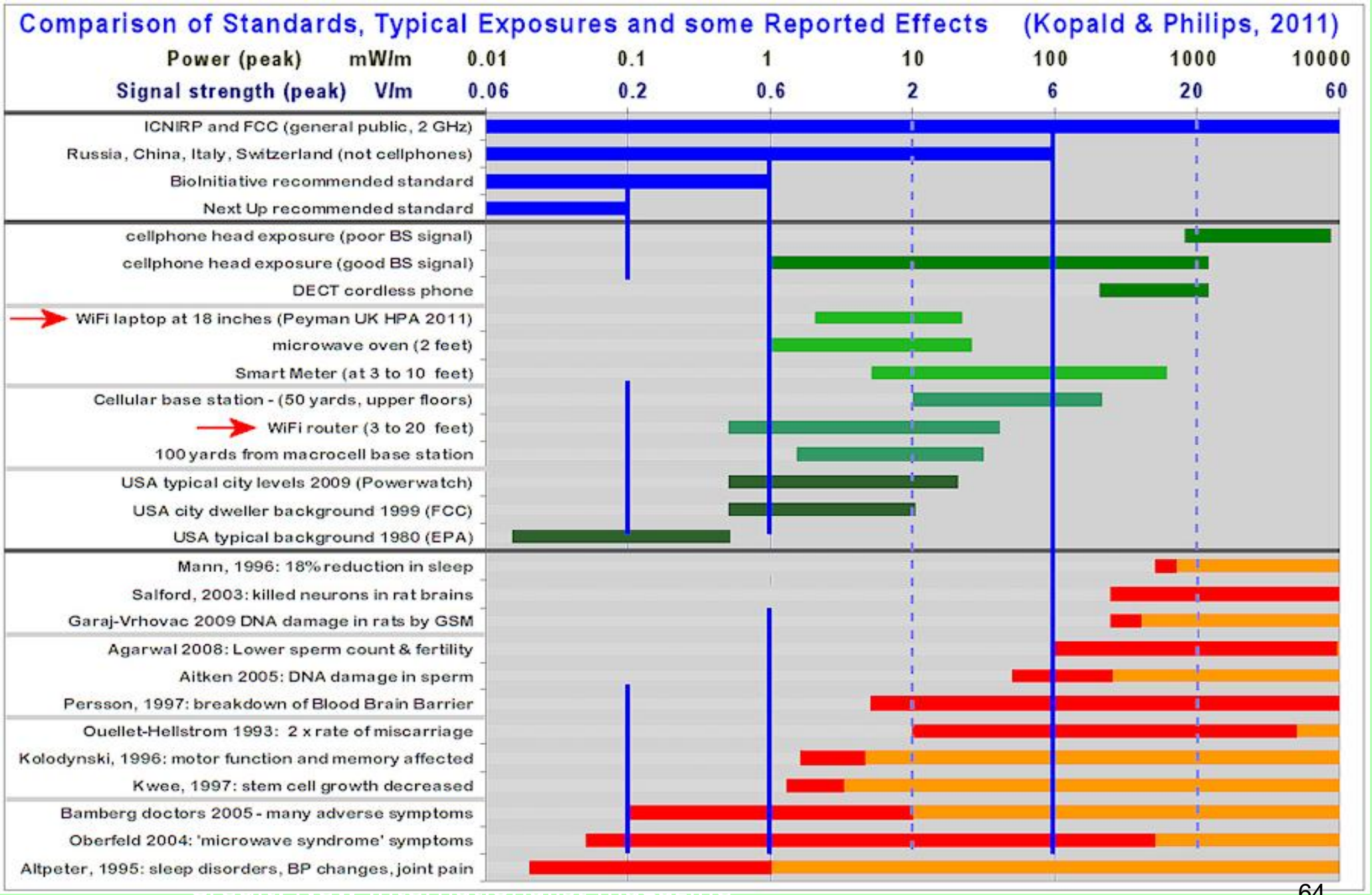
"Induction of genomic instability, oxidative processes, and mitochondrial activity by 50 Hz magnetic fields in human SH-SY5Y neuroblastoma cells" Jukka Luukkonen et al 2014 Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis 760:33-41

First seen with ionising radiation,
but since seen with metals and chemicals

Magnetic fields and routes to cancer

(i)	Magnetic particles	Mechanical stress or free radical damage via the RPM
(ii)	Cryptochromes (in the eye)	Circadian rhythm disruption
(iii)	Cryptochromes (in peripheral blood cells)	Free radical damage by the RPM
(IV)	Genomic instability	Clearly relevant to cancer as it might lead to accumulation of mutations required for cancer formation*

*Luukkonen et al 2014 Mutation Research 760:33-41



Credit: New Internationalist Magazine

International exposure guidelines

1800 MHz Public Exposure Guidelines		Equivalent	c.f. speed	
	uW/m2	**V/m**	**m.p.h.**	
NRPB prior to IEGMP (Stewart) Report	100,000,000	194	9479	A
ICNIRP (1998), WHO	9,000,000	58	2847	B
Belgium (ex Wallonia)	1,115,000	21	1002	C
Italy (sum of frequencies)	100,000	6	300	D
Russia, PRChina	100,000	6	300	E
Switzerland, Lichtenstein, Luxembourg	95,000	6	292	F
Belgium Wallonia	24,000	3	147	G
Wien (sum GSM)	10,000	1.9	95	H
Italy (single frequency)	1000	0.6	30	I
Salzburg 1998 (sum GSM)	1000	0.6	30	J
EU-Parl, GD Wissenschaft, STOA GSM (2001)	100	0.2	9	K
Salzburg GSM/3G outside houses (2002)	10	0.06	3	L
Salzburg GSM/3G inside houses (2002)	1	0.02	1	M
Bürgerforum BRD proposal, waking areas (1999)	1	0.02	1	N
Bürgerforum BRD proposal, sleeping areas (1999)	0.01	0.002	0.1	O
Mobile phone handsets can work down to about	0.000 002	0.000 03	0.0015	