First I will demonstrate a magnetic field and an electric field. They are quite distinct. At power frequencies, the two fields are essentially independent and can be treated separately.
When the Earth was formed 4.5 billion years ago magnetic fields were already present, and had been since the Big Bang some 9 billion years earlier.

2 billion years ago aquatic magnetotactic bacteria evolved which contain a chain of magnetite particles enabling them to swim along the Earth’s magnetic field lines to find food.

Over 90 million years ago the avian magnetic compass developed, enabling pigeons to detect magnetic field changes around 0.02 muT, 20 nT, or even lower.

Some 6 million years ago, man evolved, some of whom appear sensitive to solar storm fluctuations in the geomagnetic field of around 0.1 muT or 100 nT.
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So, by the time the Dublin electric light company was established in 1880 and, soon after, an experimental public light was erected outside the offices of the Freeman’s Journal in Prince’s St. Dublin, it was already the case that wide sections of the animal kingdom had evolved to detect and exploit magnetic fields at levels below those associated with this new invention, and with hindsight, a hint that there might be adverse health effects in humans.

Notes only:
The species whose magnetic compass has been analyzed so far are not at all closely related. Chickens belong to an ancient line of birds, the Galloanseres, that separated from the remaining modern birds, the Neoaves, more than 90 million years ago in the beginning of the Late Cretaceous Finding the same type of
magnetic compass in species of all three groups suggests that this compass mechanism may have already been present in their common ancestor.

From: **Turn On The Lights** Electrification Comes To Rural Ireland:
In 1880, Thomas Edison invented the electric filament lamp in the US. In the same year, the Dublin Electric Light Company was established and, soon after, an experimental public light was erected outside the offices of the Freeman’s Journal in Prince’s St. Dublin, followed by seventeen public lights in the vicinity of Kildare St., Dawson St. and St. Stephen’s Green. In 1889, Carlow became the first provincial town in Ireland to get public electric lighting, supplied from a generator in a flour mill some four miles away.
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

---


http://en.wikipedia.org/wiki/Geomagnetic_storm

---

So, start by taking as quick look at Geomagnetic storms

Superimposed on the Earth’s static magnetic field of 49.1 μT in Dublin, are small fluctuations caused by storms of charged particles emitted by the Sun

They are categorised by their K-value, their maximum variation over a three hour period.

The storms of interest are those around 100 nT, there being about 4.6 such events per year.

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

Much of this research was carried out as part of the US and Russian Space Programme
Health effects of Geomagnetic storms

*Reviews of studies

Here is a short list of some of the studies of health effects resulting from geomagnetic storms, the first two are reviews
So, let's now look at power frequency magnetic fields. In 2002 these were classified by The International Agency for Research on Cancer (IARC) as a Class 2B Possible carcinogen – similar to coffee: drinking 3-8 cups of coffee per day in pregnancy can lead to a 2-3 fold increase in childhood leukaemia risk in offspring.

The average exposure to power frequency magnetic fields in the home is only 0.05 microtesla (μT) or 50 nanotesla (nT). However, close to certain appliances, levels can be tens of μT. Under powerlines MFs can be several μT or even tens of μT.

Crucially a doubling of childhood Leukaemia risk is associated with average exposure of 0.3/0.4 μT. Further analyses of international epidemiological studies indicate a 30% increase in childhood leukaemia risk associated with average magnetic field exposures above 0.2 μT (Zhao et al 2013. Leukaemia Research In press – online early).
What are the adverse health effects linked to power frequency electric & magnetic fields?

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

*Including newly emerging finds: De Vocht et al 2014 Bioelectromagnetics, in press
Here is what various review bodies have said about Magnetic Field and adverse health effects

IARC 2002 must have had a bad day because their own listing of studies shows strong evidence of association (See O’Carroll & Henshaw 2008 and also Kheifets et al 2008). In fact the MF link with adult leukaemia is, if anything, even stronger than the link with childhood leukaemia

Representative results from 33 independent adult leukemia studies tabled by IARC yielded 23.5 positives \((p \approx 0.01)\) and 9 significant-positives \((p<10^{-7})\). From 43 representative results from CDHS, there were 32 positive \((p<0.001)\) and 14 significant-positives \((p<10^{-12})\). There were no significant-negative results in either list. Results for adult brain cancer gave a similar, but less clear message.
Features of the above Reports

- Not peer-reviewed (although the California report* used a structured assessment procedure)
- Dominated by epidemiology and not underlying science
- Cite at most only a few 100 papers against possibly over 100,000 available
- Do not discuss (out of remit):
  - Magnetoreception in microorganisms and fungi
  - Magnetoreception in plants
  - Animal magnetoreception and navigation
  - EMF effects on pain threshold in animals
  - Health effects of geomagnetic storms
  - Use of EMF in health treatment including cancer

But it is in these areas that significant advances in understanding how EMFs interact with biology have been made.

*http://www.ehib.org/emf/RiskEvaluation/riskeval.html
Review bodies’ assessments of MF association of various diseases.
- IARC has classified Power Frequency MFs as Class 2B – ‘possible carcinogen’.

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</tr>
</thead>
<tbody>
<tr>
<td>1. Childhood Leukaemia</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2. Adult Leukaemia</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3. Adult brain cancer</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
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<tr>
<td>4. Miscarriage</td>
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<tr>
<td>5. ALS</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td></td>
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<tr>
<td>6. Alzheimer’s disease</td>
<td></td>
<td></td>
<td>Yes</td>
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</tbody>
</table>

*US National Institute of Environmental Sciences
EU: Scientific Committee on Emerging and Newly Identified Health Risks: Possible effects of Electromagnetic Fields (EMF) on Human Health.
*EU: EMF & Health, Brussels Nov 2011
*Motor neurone disease
*Studies more recently published

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IARC & California assessment of epidemiological studies
Why the difference for adult leukaemia & brain cancer?

How epidemiology works

- The epidemiological studies look at cancer rates near MF sources and compare these with rates well away from MF sources.

- We obtain risk ratio, RR:
  - If cancer rates are the same near and away from MF sources, RR = 1.
  - If cancer rates are doubled near MF sources, RR = 2.

We also look at the probability of the finding being just due to chance (being just a fluke).
- This is known as the “p-value”.

If the probability of the finding being due to chance is better than 1 in 20 (p<0.05) we say the finding is statistically significant.

Sometimes p-values, especially for many studies considered together, can be far more significant:
- e.g. p<0.001 or 1 in 1000 probability of the finding being just chance.
The Nobel Prize in Physics 2013 was awarded jointly to François Englert and Peter W. Higgs "for the theoretical discovery of a mechanism that contributes to our understanding of the origin of mass of subatomic particles, and which recently was confirmed through the discovery of the predicted fundamental particle, by the ATLAS and CMS experiments at CERN's Large Hadron Collider."

Following the discovery at CERN, Geneva of the new particle known as the Higgs boson, confirmed (established) when the probability of the finding being just due to chance was less than 1 in 10 million or p-value < 10^{-7} or 99.99999% "proof"
By any accepted definition, there is an established association between magnetic fields from the electricity supply and adult leukaemia and brain cancer.
Bioinitiative 2012: 
- a biologically-based EMF Report
http://www.bioinitiative.org

- Highly authoritative – 12 authors representing world-class leading EMF scientists including three former Presidents of the International Bioelectromagnetics Society
- Concentrates on the underlying biology of ELF and RF EMF
- Special chapters on melatonin disruption, childhood cancers, breast cancer & Alzheimer's disease
- Cites approximately 1800 peer-reviewed studies
- Strongly recommends precaution against EMF exposure at levels well below current International guidelines.
These surveys were carried out in three estates with very similar private housing, away from major roads or sources of industrial pollution. While this is not a professional survey, the findings closely mirror those published in the peer-reviewed literature.
Increased incidence of childhood leukaemia near HV powerlines, beyond the range of the direct AC fields (~100 m)

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Cases</th>
<th>Increased risk to</th>
</tr>
</thead>
<tbody>
<tr>
<td>Draper et al. 2005</td>
<td>222</td>
<td>600 m</td>
</tr>
<tr>
<td>Lowenthal et al. 2007</td>
<td>304</td>
<td>100 m</td>
</tr>
<tr>
<td>Field &amp; Armit 2007</td>
<td>60</td>
<td>300 m</td>
</tr>
<tr>
<td>Sohrabi et al. 2010</td>
<td>180</td>
<td>600 m</td>
</tr>
</tbody>
</table>

The literature includes four studies showing increased leukaemia risk up to 600 metres from powerlines which is well beyond the range of the AC fields, although well within range of corona ion emission. The findings could be explained by two possible models: that corona ions attach to particles of air pollution making them more likely to be retained in the lung when inhaled, and that corona ion disturbance of the natural electric field of the Earth results in melatonin and circadian rhythm disruption.
EMF effects on cattle

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

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

Lee et al. (2002) and Li et al. (2002) – higher odds ratios for miscarriage for RCM compared to TWA

There is a key difference between the initial detector which senses magnetic fields, and the subsequent biological response. For example, the ear senses music, but the brain decides whether it likes it or not.
Some underlying biology........
Navigation across the Earth
- requires two measurements

Humans use latitude & longitude

Many animals use magnetic intensity and compass direction of the Earth's magnetic field
Magnetic intensity

Magnetic sensitivity is widespread throughout the animal kingdom, and these are some of the animals which possess biogenic magnetite or other iron-mineral particles used for navigation.

Notes:

Lohmann: magnetic sensitivity is phylogenetically widespread; it exists in all major groups of vertebrate animals, as well as in some molluscs, crustaceans and insects. The list includes groups such as flies, chickens and mole rats, none of which migrate.
Particles of interest:

**Pigeons** (Upper beak)

Fleissner et al. 2007 Naturwissenschaften 94:631–42

but see Treiber et al Nature doi:10.1038/nature11046

In pigeons, the inclination sensitivity is 0.02–0.17 degrees, down to 0.01 μT (~10 nT)

Gould 2010 Current Biol 21;R226

**Trigeminal nerve**

**Trout** (Olfactory epithelium)

μm-sized candidate magnetoreceptor cells

Eder et al. 2012 PNAS DOI:10.1073/pnas.1205653109

20 μm

---

Single domain permanent magnets, particles >50 nm where the whole particle physically rotates in an MF

And

Superparamagnetic particles which remains stationary but the MF vector quantum flips

Flessner et al 2007 Goethe-Universität, Frankfurt

Treiber et al 2012 1Institute of Molecular Pathology, Dr Bohr-Gasse, 1030 Vienna, Austria

Eder & Michael Winklhofer Ludwig-Maximilians-University Munich

Notes:


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

Notes:

Binhi 2008 IJRB 84:569-579

In horse spleen ferritin, up to 30% of the core exhibits magnetite/maghemite structure (Brem et al 2006)

See also, magnetite in the brain of Alzheimer’s patients and human heart, liver and spleen (Dobson 2001, Brem et al. 2006, Collingwood et al. 2008), (Grass-Schultheiss et al. 1997).


Allen et al. 2000. Low-frequency low-field magnetic susceptibility of ferritin and Hemosiderin Biochimica et Biophysica Acta 1500;186-196
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∗
  - This leads to changes in chemical reaction products which can form the basis of a chemical magnetic compass
  - The process also results in free radicals becoming more available to cause biological damage

∗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 – details at end of talk

A full explanation of the RPM may be found in slides at the end of this talk.
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.

These species all have a light-dependent compass with evidence that it is based on the RPM. Notice that in some cases, this is in addition to magnetite. Notice also the involvement of the pineal gland in some species.

From Lohmann 2010: Figure 1 | Animal magnetism. Diverse species have magnetic compasses, including (clockwise from top left) the European robin, the loggerhead sea turtle, the brown bat, the Caribbean spiny lobster and the red-spotted newt. A few, including turtles, lobsters and newts, also have magnetic maps.
Ritz et al 2000 proposed that the avian compass was based on cryptochrome molecules in the eye and that as an experimental test, this might be interfered with by application of an appropriate RF field.

RP lifetimes up to 20 ms – five orders of magnitude higher than 1 mS required have been observed: Liedvogel et al. 2007, Chemical magnetoreception: bird cryptochrome 1a is excited by blue light and forms long-lived radical-pairs” PLoS One 2(10): e1106; and

Cry1a located in UV/V-cones in robins and chickens, in ordered bands along the membrane discs (Niessner et al. 2011 PLoS ONE 6(5): e20091)

FAD = flavin-adenine dinucleotide
Birds: European robins, *Erithacus rubecula*: 12 individually tested in spring migration season.

**RF exposure**: 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.

**Results**:  
- RF magnetic fields disrupt the magnetic orientation behaviour of migratory birds.  
- Robins were disoriented when exposed to a vertically aligned broadband (0.1–10 MHz) or a single-frequency (7 MHz) field in addition to the geomagnetic field.  
- In the 7 MHz oscillating field, effect depended on the angle between the oscillating and the geomagnetic fields.  
- 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.

**Conclusion**:  
These results are consistent with a resonance effect on singlet-triplet transitions and suggest a magnetic compass based on a radical pair mechanism.

These findings have been replicated in robins and seen in chickens, zebra finches and American cockroaches.

FAD = flavin-adenine dinucleotide
Effects of animal magnetic compass orientation with RF and ELF EMF exposures (GMF = geomagnetic field).

<table>
<thead>
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<th>MF and light exposure</th>
<th>Findings</th>
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<td>Ritz et al. 2000</td>
<td>1 MHz, 0.42 T; RF single frequency 2 MHz, 0.47 T</td>
<td>Birds exhibited orientation propensity against GMF when applied by itself. Birds were not disrupted by applied RF or ELF EMF when applied in combination with GMF.</td>
</tr>
<tr>
<td>Stapput et al. 2005</td>
<td>3 MHz, 0.42 T</td>
<td>Birds exhibited orientation propensity against GMF when applied by itself. Birds were not disrupted by applied RF or ELF EMF when applied in combination with GMF.</td>
</tr>
<tr>
<td>Wiltschko et al. 2007</td>
<td>5 MHz, 0.47 T; RF single frequency 3 MHz, 0.47 T</td>
<td>Birds exhibited orientation propensity against GMF when applied by itself. Birds were not disrupted by applied RF or ELF EMF when applied in combination with GMF.</td>
</tr>
<tr>
<td>Keary et al. 2009</td>
<td>8 MHz, 0.45 T</td>
<td>Birds exhibited orientation propensity against GMF when applied by itself. Birds were not disrupted by applied RF or ELF EMF when applied in combination with GMF.</td>
</tr>
</tbody>
</table>

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

This and the next slide:

The findings of Ritz et al 2000 have now been repeated in robins and also in chickens, zebra finches and American cockroaches.

The table is very busy but I just want to point out the very low level of RF fields that disturb the compass and at frequencies corresponding to the Larmor precessional frequency of the free electron


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

**Continued:**

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<tr>
<td>Vácha et al. 2009</td>
<td>Local GMF 46 µT and horizontal 500 MHz radio light</td>
<td>1. Changes in activity between control and GMF exposed groups dependent on latitude; (i) Local GMF alone: well orientated; (ii) 0.01 and 0.03 MHz: no effect; (iii) 0.06 and 0.09 MHz: weak axial response characteristic of compass on interference; (iv) 0.1 and 0.5 MHz: weak axial response characteristic of compass on interference; (v) 1.315 MHz*: disoriented even at 15 nT exposure; (vi) 18 MHz produces no disorientation at 92 µT exposure.</td>
</tr>
<tr>
<td>Ritz et al. 2009</td>
<td>(i) Local GMF 46 µT and horizontal 1.315 MHz radio light; (ii) GMF alone: well orientated; (ii) 0.01 and 0.03 MHz: no effect; (iii) 0.06 and 0.09 MHz: weak axial response characteristic of compass on interference; (iv) 0.1 and 0.5 MHz: weak axial response characteristic of compass on interference; (v) 1.315 MHz*: disoriented even at 15 nT exposure; (vi) 18 MHz produces no disorientation at 92 µT exposure.</td>
<td></td>
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<tr>
<td>Begall et al. 2008</td>
<td>(i) Local GMF 46 µT, inclination 66°; (ii) GMF artificially doubled to 92 µT, plus 1.315 MHz; (iii) 1.2 MHz, 0.044 µT; (iv) 2.4 MHz, 0.044 and 0.018 µT; (v) 2 MHz, 0.044 and 0.018 µT; (vi) 7 MHz, 0.044 µT, reducing interference; (vii) 0.1 and 0.5 MHz: weak axial response characteristic of compass on interference; (viii) 1.315 MHz*: disoriented even at 15 nT exposure; (ix) 18 MHz produces no disorientation at 92 µT exposure.</td>
<td></td>
</tr>
<tr>
<td>Ritz et al. 2010</td>
<td>(i) Local GMF 42.9 µT, inclination 64°, 565 nm green light, plus 8 frequencies from 0.01 to 7.0 MHz, including Larmor (matched Larmor) 2.63 MHz; (ii) GMF of 46 µT: (i) Local GMF alone: well orientated; (ii) 0.01 and 0.03 MHz: no effect; (iii) 0.06 and 0.09 MHz: weak axial response characteristic of compass on interference; (iv) 0.1 and 0.5 MHz: weak axial response characteristic of compass on interference; (v) 1.315 MHz*: disoriented even at 15 nT exposure; (vi) 18 MHz produces no disorientation at 92 µT exposure.</td>
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I point also to the findings of Begall et al 2008 and Burda et al 2009

The ICNIRP Exposure Limit is:

- 0.92 µT at 1 MHz
- 0.092 µT between 10 – 400 MHz
- 0.2 µT at 2 GHz

Note that RF disruption of the animal compass occurs at levels below the ICNIRP limit


CHECK !!!!!
I point also to the findings of Begall et al. 2008 and Burda et al. 2009

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

Continued:

- GMF alone: well orientated
- 0.01 and 0.03 MHz: no activity disruption
- 0.03 and 0.05 MHz: weak axial response characteristic of compass on functionality of basic MF sense
- 0.658 MHz and higher: disorientation
- Larmor 1.3 15 MHz:

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

The ICNIRP Exposure Limit is:

- 0.92 muT at 1 MHz
- 0.092 muT between 10 – 400 MHz
- 0.2 muT at 2 GHz

Note that RF disruption of the animal compass occurs at levels below the ICNIRP limit


CHECK !!!!!
More underlying biology........
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
Circadian rhythm & melatonin* disruption
- could potentially explain many of the EMF health effects

- Melatonin, a key component of circadian rhythms, is produced in the pineal gland mainly at night when light levels fall below ~200 lux
- Broad-spectrum, ubiquitously-acting antioxidant and anti-cancer agent, highly protective of oxidative damage to the human haematopoietic system* - relevant to leukemia
- Disruption by light-at-night associated with (i) increased cancer risk in animals and in humans, (ii) with depression, Alzheimer's disease and possibly miscarriage
- Stevens (1987) proposed that exposure to light at night and EMF may increase breast cancer risk, by melatonin disruption
- Night-shift workers have about 50% increased risk of breast cancer
- IARC 98 (2010) has classified night-shift work as a Class 2A Probable carcinogen

The adverse health effects associated with ELF MF exposure could all potentially be explained by circadian rhythm disruption

Melatonin is a broad-spectrum, ubiquitously-acting antioxidant and anti-cancer agent. Which also reduces growth of human myeloid leukemia cells and whose disruption by light-at-night is associated with increased cancer risk.
Magnetic field disruption of melatonin, pineal cells, cryptochromes and circadian rhythms

- in humans
  Not revealed in volunteer short exposures to pure AC MFs
  Seen in populations exposed to "real" EMFs – down to 0.2 µT

- in animals
  Most effects observed with non-smooth AC MFs
  Strong findings in cows and sheep with "real" EMFs
  Down to 0.2 µT

- on pineal cells
  Small but detailed literature – action in synthesising melatonin
  Disrupted. Some animals have MF compass in the pineal gland

Circadian rhythms are controlled by Clock genes
- the gene CRY1 codes the Cryptochrome protein molecule, CRY1, in the eye, which in turn is involved in the regulation of circadian rhythms.

Cryptochrome acts as the magnetic compass in animals


So what about magnetic field effects on melatonin, pineal cells, cryptochromes and circadian rhythms?

Melatonin disruption in humans is really seen in populations exposed to "real" fields – down to 0.2 µT

Similarly in animals, effects are seen in "real" fields, both in the laboratory and outdoors

There’s a small but detailed literature – that MFs interfere with the action of pineal cells in synthesising melatonin.

The human light-detection threshold is sensitive to MF exposure

But most importantly, cryptochrome, expressed by the CRY genes controls the mammalian circadian clock and acts as the magnetic compass in animals.

And I will be saying more about that later.
Note:
There are 8 Clock genes in humans: PER1, PER2, CLOCK, BMAL1, CRY1, CKId/e, CRY2, BMAL2 (see Cermakian & Boivin 2003)

Gu Age of Eukaryotes & Prokaryotes 2.1-2.9 billion yrs Mol Biol Evol 14;861-66
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 tin-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
Electric fields also affect circadian rhythms in humans

Wever (1979)*: In a long series of experiments, human volunteers were exposed for several weeks to 10 Hz square wave electric fields of only 2.5 V/m. The 24 h circadian rhythm was disrupted. Volunteers were immediately entrained to the external signal. Effect lasted for a few days, indicating E-fields acting as zeitgebers.

Magnetic fields and routes to cancer

<table>
<thead>
<tr>
<th></th>
<th>Magnetic particles</th>
<th>Circadian rhythm disruption</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i)</td>
<td>Cryptochromes (in the eye)</td>
<td>Magnetic particles</td>
</tr>
<tr>
<td>(ii)</td>
<td>Cryptochromes (in peripheral blood cells)</td>
<td>Mechanical stress or free radical damage via the RPM</td>
</tr>
<tr>
<td>(iii)</td>
<td>Genomic instability</td>
<td>Free radical damage by the RPM</td>
</tr>
</tbody>
</table>

*Luukkonen et al 2014 Mutation Research 760:33-41*
Some other key MF effects relevant to childhood leukaemia and cancer

MFs Release reactive oxygen intermediates in human cord blood-derived monocytes (Lupke et al 2004. Free Rad. Res. 38:985–993) - This alone would provide a model of how MFs increase childhood leukaemia risk*

Induction of genomic instability, oxidative processes, and mitochondrial activity by 50 Hz magnetic fields in human SH-SY5Y neuroblastoma cells. Luukkonen et al 2014 Mutation Research 760:33-41 - Clearly relevant to cancer, first observed with ionising radiation, now with magnetic fields

*IARC Report no 102, 2013 states that there are well performed studies showing induction of ROS and oxidative DNA damage by RF EMFs
The Bystander Effect & Genomic Instability

Zap with radiation

Look at the chromosomes at metaphase and note the damage
("DNA strand breaks")
The Bystander Effect & Genomic Instability

50 years of dogma

Bystander effect (c1992)

Zap with radiation

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

Zap with radiation

Look at the unirradiated cells over here
The Bystander Effect & Genomic Instability

50 years of dogma

Bystander effect (c1992)

We also get DNA strand breaks

Mothersill et al 2006: Dose-Response, 5:214–28: "It is concluded that bioelectric or magnetic effects may be involved in producing bystander signaling cascades commonly seen following ionizing radiation exposure."
Genomic instability (c1994)

50 years of dogma

Zap with radiation

After first cell division
- no chromosome damage
Genomic instability (c1994)

Zap with radiation

After first cell division
– no chromosome damage

After 10-15 cell divisions

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

After 10-15 cell divisions

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

- Biological studies show that magnetic fields have key hallmarks of a carcinogen.
- Epidemiological studies strongly associate magnetic field exposure with a range of adverse health outcomes.
- Precaution against EMF exposure is highly warranted and cost-beneficial.

In the case of high voltage overhead powerlines, the solution is to bury the lines over populated areas. This eliminates the electric fields and corona ions, and can strongly attenuate magnetic fields.
Acknowledgements

Marian Harkin MEP and her colleagues

Ilia Solov’yov (Illinois)
Jonathan Woodward (Tokyo)
Mike O’Carroll

and

Children with Cancer UK

Web version: www.electric-fields.com
Leukaemia:

<table>
<thead>
<tr>
<th>Report</th>
<th>Number of independent studies</th>
<th>Positives</th>
<th>Significant positives</th>
</tr>
</thead>
<tbody>
<tr>
<td>IARC 2002</td>
<td>33</td>
<td>23.5</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>(p&lt;0.001)</td>
<td>(p&lt;0.01)</td>
<td></td>
</tr>
<tr>
<td>California 2002</td>
<td>43</td>
<td>32</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>(p&lt;0.001)</td>
<td>(p&lt;10^-12)</td>
<td></td>
</tr>
</tbody>
</table>

There were no significant-negative results in either IARC or CHD list.

Results for adult brain cancer gave a similar, but less clear, message.

"Aggregating all the studies suggests that results for childhood leukemia are not stronger numerically than those for adult leukemia. CDHS did not note the number of significant-positives, but noted the meta-analytic summary and the number of positives, forming a view about the strength of these findings.

IARC shows no evidence of considering the aggregation of results other than subjectively. It considered individual studies but this led to a tendency to fragment and dismiss evidence that is inherently highly significant."
A selected extract from the 2012 Bioinitiative report
Potential energy of magnetic particle in the Earth’s field
- Compare this with the thermal energy $kT$

$U = -\mu \cdot B$ where $\mu = v M$

$U =$ potential energy of dipole magnet in field $B$
$\mu =$ magnetic moment
$v =$ particle volume; $r =$ radius
$M =$ 4.8 x 10$^{-5}$ J T$^{-1}$ m$^{-3}$
$k =$ Boltzmann’s constant, 1.3807 x 10$^{-23}$ J K$^{-1}$, and $T =$ the absolute temperature.

The energy required to rotate the particle 180° is 2U, compare this to the thermal energy $kT$ at 300° K.

But the sensitivity is magnified with arrays & clusters of iron-based minerals

Magnetite can readily transduce a 0.4 muT 50 Hz field
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?

Turtles
- Kloc et al. 1996 Reported that turtles with magnets on their shells when released well away from their nesting sites were initially confused.
- However, they eventually found their way back to their nesting sites.

Pigeons
- 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.

Now a common question that physicists ask is how can a field of 0.4 μT (at ELF frequency) make any difference alongside the existing DC field from the Earth?

The results of these studies show that turtles and pigeons respond changing magnetic fields and are not disturbed by a static (DC) field.
Static MFs alter circadian rhythms via cryptochromes


Study: Drosophila melanogaster. 23-29 flies per group: mean circadian period under blue light 25.8 ± 0.14 h.

Methods:
(i) Wild type flies exposed 0 and 300 µT, red light; then 0, 150, 300, 500 µT, blue light plus:
(ii) FAD impaired (cryb)
(iii) Mutants lacking CRY (cryOUT)
(iv) Clock-gene promoter/CRY over-expressed (tim-Gal4/uas-cry) flies

Findings:
(i) No MF effect under red light. Under blue light circadian rhythm lengthened >0.5 h at 300 µT and (i) cryb: no MF effect; (ii) cryOUT: no MF effect and (iii) tim-Gal4/uas-cry: at 300 µT, 2 h period lengthening and most flies arrhythmic.

What about effects in humans?

Wever 1979. In a long series of experiments, human volunteers were exposed for several weeks to 10 Hz square wave electric fields of only 2.5 V/m. The 24 h circadian rhythm was disrupted. Volunteers were immediately entrained to the external signal. Effect lasted for a few days, indicating E-fields acting as zeitgebers.

FAD = flavin-adenine dinucleotide

Here I talk through the significance that cryptochromes control circadian rhythm


FAD = flavin-adenine dinucleotide
Light, cryptochrome expression and reduced plasma melatonin

- Jaundiced neonates treated by blue light exposure with the eyes covered*

- Expression of circadian genes: Bmal1 and Cry1 in peripheral blood mononuclear cells and reduction in plasma melatonin

- Reduction in plasma melatonin usually interpreted as reduced production in the pineal gland

- Could indicate increased consumption in quenching free radicals in the bloodstream

- Could it be that the blue light also creates radical pairs in the cryptochromes, so that plasma melatonin was consumed in quenching these radicals?

- If so, could environmental MFs exacerbate this effect – resulting in increased radical damage to blood cells?

*Zhejiang Children's Hospital. 24 h exposure to 5,500–7,200 lux from 12 x 20 W fluorescent light bulbs
Circadian rhythms & melatonin* disruption and cancer risk  
- could potentially explain many of the EMF health effects

- Stevens (1987) proposed that exposure to light-at-night and EMF may increase breast cancer risk, by melatonin disruption

- Night-shift workers have ~50% increased risk of breast cancer

- IARC 98 (2010) night-shift work 2A Probable Carcinogen

Melatonin produced in the pineal gland at night when light levels fall below ~200 lux
*Broad-spectrum, ubiquitously-acting antioxidant and anti-cancer agent, highly protective of oxidative damage to the human haemopoietic system

Richard G. Stevens 2012 Hypothesis: Does electric light stimulate cancer development in children?  
Cancer Epidemiology Biomarkers & Prevention, doi:10.1158/1055-9965.EPI-12-0015

The adverse health effects associated with ELF MF exposure could all potentially be explained by circadian rhythm disruption

Melatonin is a broad-spectrum, ubiquitously-acting antioxidant and anti-cancer agent. Which also reduces growth of human myeloid leukemia cells and whose disruption by light-at-night is associated with increased cancer risk.
Some MF effects in vitro

1. At high fields - 1 mT 50 Hz:
   Enhance cell proliferation and DNA damage in HL-60 human leukaemia cells (Wolf et al. 2005 Biochim Biophys Acta 1743 :120-9)

2. At environmentally relevant fields:
   Stress response induced in HL-60 cells (10 μT, 50 Hz: Tokalov & Gutzeit 2004. Environ. Res. 94:145–51)
   A gene–environment analysis in 123 childhood ALL patients revealed an association between DNA repair enzymes and average MF exposure of 0.18 μT.
   - Yang et al. 2008 Leuk Lymphoma 49:2344–50 – Shanghai School of Medicine
Epidemiological Studies show a doubling of Childhood Leukaemia risk associated with average 0.3/0.4 μT, 50/60 Hz magnetic field exposure – and links with other adverse health outcomes too…

Is the magnetic field association with childhood leukaemia causal?
Some MF effects \textit{in vitro}

1. At high fields - 1 mT 50 Hz:  
   - Release of reactive oxygen intermediates in human cord blood-derived monocytes \cite{Lupke2004}  
   - Enhance cell proliferation and DNA damage in HL-60 human leukaemia cells \cite{Wolf2005}  

2. At environmentally relevant fields:  
   - Stress response induced in HL-60 cells (10 \(\mu\)T, 50 Hz; Tokalov & Gutzeit 2004. Environ. Res. 94:145–51)  
   - A gene–environment analysis in 123 childhood ALL patients revealed an association between DNA repair enzymes and average MF exposure of 0.18 \(\mu\)T. \cite{Yang2008}  
   - Shanghai School of Medicine
An evidence-based possible cause of childhood leukaemia should in any reasonable interpretation for the public mean an adverse effect. People don’t want to expose their children to an evidence-based possible cause of childhood leukaemia, even if there isn’t not a fully proven cause.

Further down the web page, this paragraph (which is given in quotes in the article) is blatant spin by the well used but crude technique of saying what was NOT said but hiding what WAS said:

"National and international health and scientific agencies have reviewed more than 30 years of research into electromagnetic fields. None of these agencies has concluded that exposure to electromagnetic fields from power lines or other electrical source is a cause of any long-term adverse effects on human, plant or animal health."

They did of course conclude on the basis of evidence that the exposure was a possible cause.
1 μm Magnetite particles encapsulated in polystyrene dramatically decreased the time for 50% haemolysis of UV irradiated human erythrocytes. 


Hypothesised childhood leukaemia arose from SP magnetite particles in blood which transduced/amplified 50 Hz fields, creating free radicals by the RPM.

The RPM may act due to the MF around magnetite particles — increasing the lifetime of free radicals

Erythrocytes

1 μm magnetite particles (1 per 4 erythrocytes)

Surrounding MF

surface: ~200 mT
1 mm away: ~0.5 mT
5 mm away: ~0.1 mT

Binhi 2008 (IJRB 84:569-79): - Hypothesised childhood leukaemia arose from SP magnetite particles in blood which transduced/amplified 50 Hz fields, creating free radicals by the RPM.
A second mechanism of low level MF detection

- Low intensity MFs can increase the lifetime of free radical pairs making them potentially more available to cause biological damage.

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.

Radical pairs created by - created by light absorption, excitation and electron transfer.

Typical timescale of ~1 μs.

This is known as the Radical Pair Mechanism, RPM.
As an introduction to the RPM this slide goes back to basics

On the left we see the familiar Zeeman effect. If you put an electron in a static magnetic field, it will align its spin vector either up or down with respect to the field direction.

This energy difference between these states may be represented by a photon of energy $h\nu$ where $h$ is Planck's Constant and $\nu$ is the photon frequency. A spectroscopic transition can be induced between these energy states by applying radiation at the correct frequency. At 50 $\mu$T, $\nu = 1.4$ MHz.

I am showing this to point out that the energy difference is $\sim10^{-7}$ of the thermal energy $kT$. i.e. the phenomenon is not only well below $kT$, but is has nothing to do with classical energies, rather we are talking about the quantum-mechanical interaction of the magnetic field with the electron spin.

On the right is the classical physics model of this, taken from NMR & MRI, that the electron is precessing about the magnetic field at frequency $\nu$, 1.4 MHz, the so-called Larmor frequency. I will be using this model in a moment.
Here I talk through how RP mixing occurs, using the precession model
continued:

The field vector, B has two components: (i) due to high-abundance magnetic nuclei e.g. 1H 14N, and (ii) due to the Earth’s field.

For a compass, maximum sensitivity occurs when the Earth’s field has little influence on precession on radical 1, but is the only influence on radical 2.

The precession is governed by hyperfine interaction with the proton in the nucleus, consisting of an isotropic S-wave, or S-orbital interaction, and an anisotropic dipole interaction.
I’ve slipped this slide in here to point out models of the actual RP pathways in cryptochrome

FAD = flavin-adenine dinucleotide
Low fields open up new S-T mixing pathways increasing the rate of S-T conversion.

**Examples of RPM in chemical systems:**

- Scaiano et al 1997: Photoreduction of benzophenone by 1,4-cyclohexadiene;
- Mohtat et al 1998: Radical pair derived from hydrogen abstraction of triplet benzophenone;
- Streiner & Ulrich 1989: Table 6 (Molecular crystals): e.g. Naphthalene, 1,4-dibromonaphthalene, anthracene; Table 5: e.g.s of photochemical reactions in the gas phase;
- Brocklehurst & McLauchlan 1996: benzaldehyde (PhCHO, Ph = C6H5) in tetrachloromethane; RPs created from UV irradiation of the condensed ring aromatic hydrocarbon pyrene (Py) in solution with 1,3-dicyanobenzene (DCB);
- Vink & Woodward (2004): Radical recombination reaction occurring after the photodecomposition of 2-hydroxy-4¢-(2-hydroxyethoxy)-2-methylpropiophenone (R-HP);

**References:**