



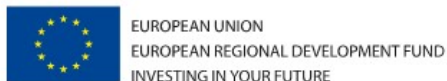
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Central European Institute of Technology
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History of electron microscopy

C9940 3-Dimensional Transmission Electron Microscopy
S1007 Doing structural biology with the electron microscope

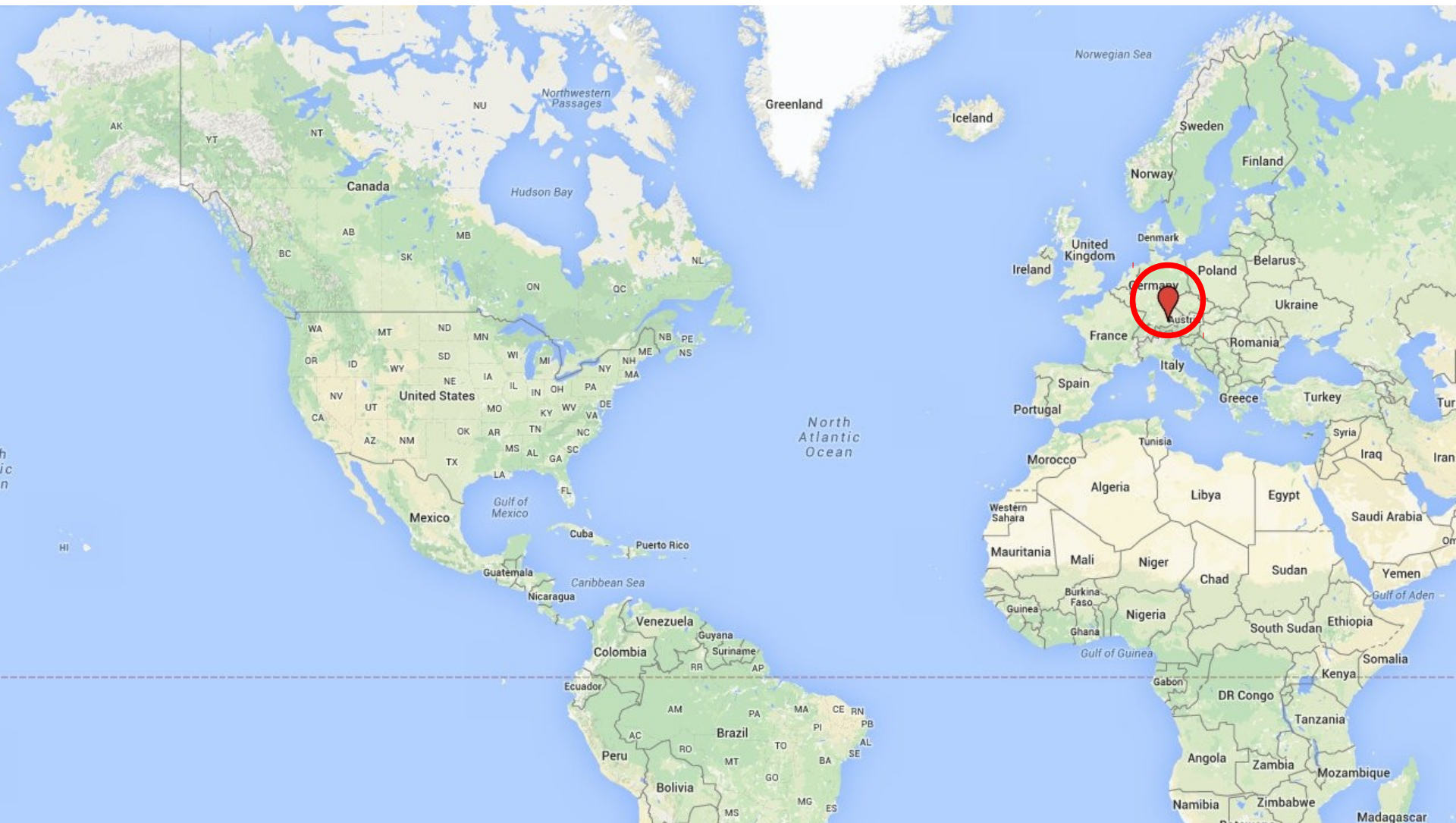
February 16, 2015



Syllabus

Week	Date	Instructor	Topic
1	02/16	D. Nemecek & T. Shaikh	Introduction/Tour/History
2	02/23	D. Nemecek & T. Shaikh	Electron Optics
3	03/02	D. Nemecek	Specimen preparation
4	03/09	T. Shaikh	Image analysis I
5	03/16	T. Shaikh	Image analysis II
6	03/23	T. Shaikh	3D reconstruction
7	03/30	T. Shaikh	Single-particle reconstruction (Easter)
8	04/13	D. Nemecek	Tomography I
9	04/20	D. Nemecek	Tomography II
10	04/27	D. Nemecek	Visualization/Segmentation
11	05/04	D. Nemecek	Hybrid methods
12	05/11	T. Shaikh	Computer practicals
13	05/18	D. Nemecek & T. Shaikh	Journal club

Munich: Ernst Ruska & Otto Scherzer



Ernst Ruska: timeline

1930 1940 1950 1960 1970 1980 1990 2000 2010

Milestones:

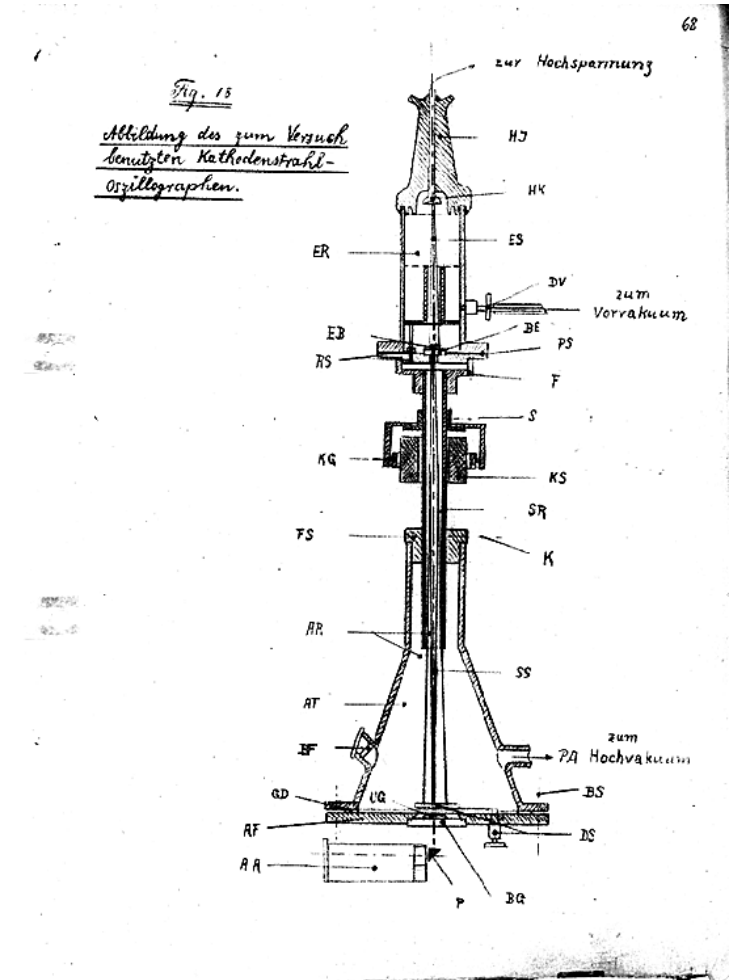
- ◆ 1931: Electron lens
 - magnification: 400X
- ◆ 1933: First electron microscope
 - mag: 7000X (vs. LM: 2000X)
- ◆ 1933: Completed Ph.D. (!)
- ◆ 1939: First commercial EM (Siemens)
 - mag: 100,000X
- ◆ 1952: Helmut Ruska (brother) moves from Siemens to Albany
- ◆ 1986: Nobel Prize in Physics

Ernst Ruska



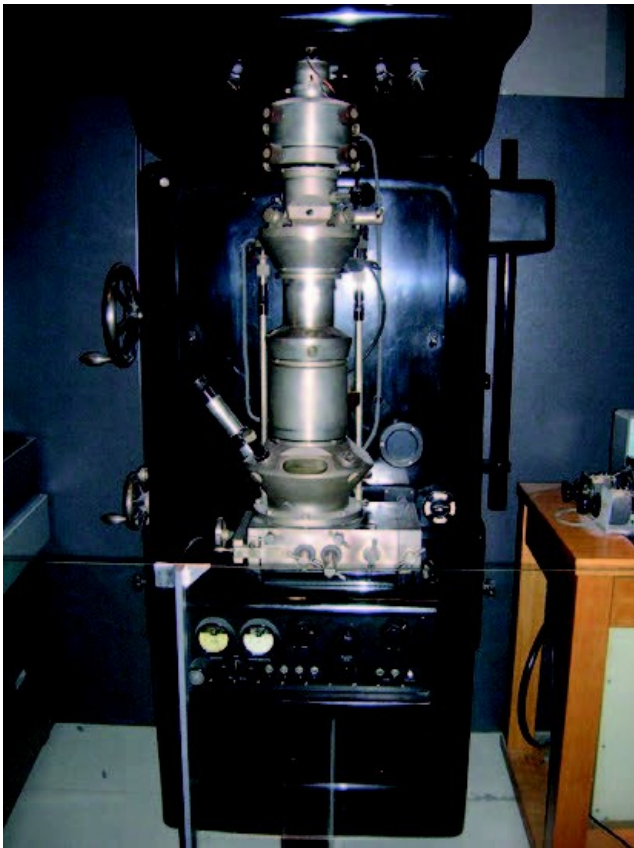
<http://www.biografiasyvidas.com>

Sketch from 1929



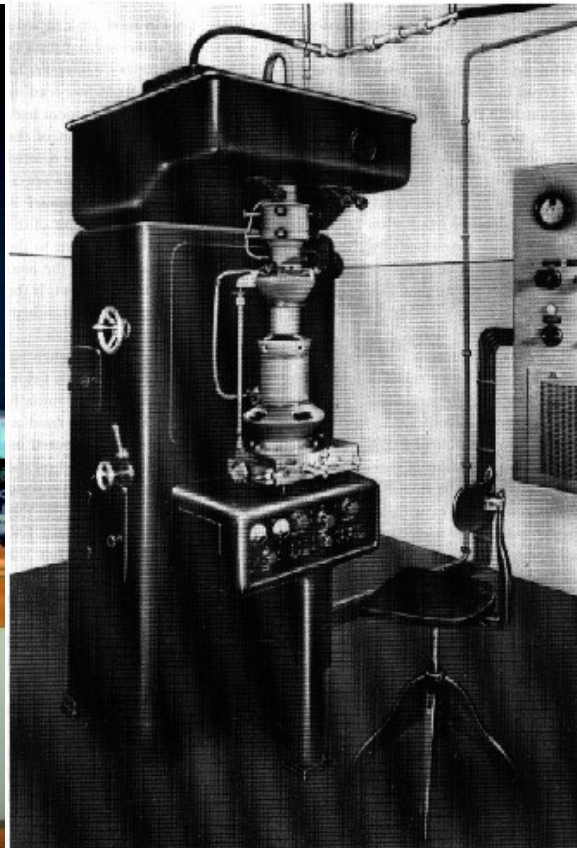
<http://ernst.ruska.de>

Replica of first electron microscope



<http://www.bluesci.org>

First commercial Siemens microscope



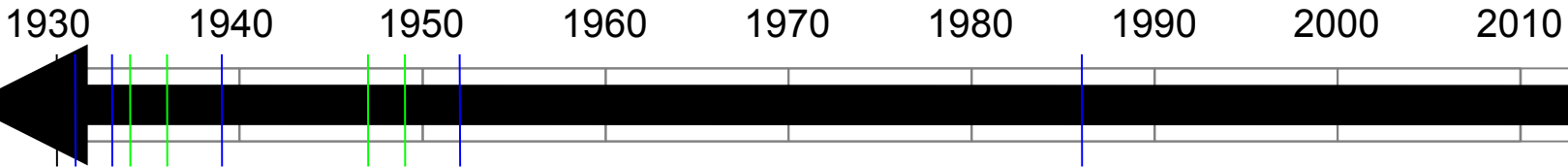
<http://ernst.ruska.de>

Helmut Ruska (standing)
next to Siemens-20
at Wadsworth Center in Albany



<http://www.wadsworth.org>

Otto Scherzer: timeline



Milestones:

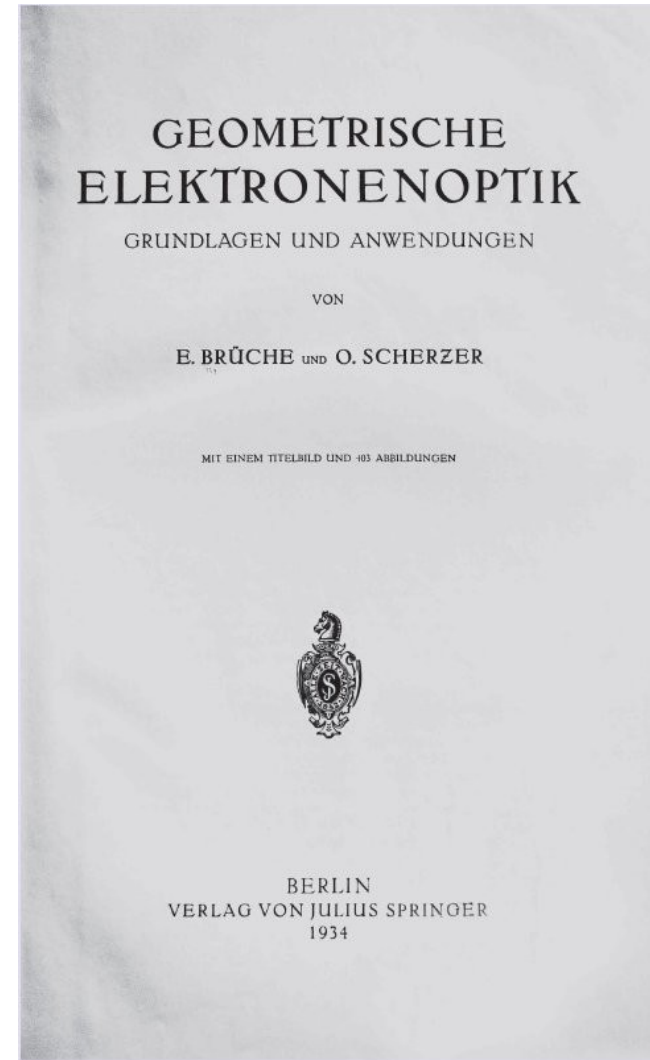
- ◆ 1934: First comprehensive book on electron optics
- ◆ 1936: Spherical aberration → resolution 50-100X the wavelength
- ◆ 1947-1951: Devised correction schemes for aberration correction
- ◆ 1949:
 - “Can atoms be visible in the electron microscope?”
 - “Scherzer focus”
- ◆ Scherzer → Harald Rose (Wadsworth, Darmstadt) → Max Haider

Otto Scherzer



<http://www.microscopy.org>

First book on electron optics



<http://www.microscopy.org>

Scherzer (1949) Physikalische Blätter & Scherzer (1949) Journal of Applied Physics

“Can atoms be visible in the electron microscope?”

PHYSIKALISCHE BLÄTTER

1949 Heft 10.11 Seite 460 — 463

Prof. O. Scherzer

Können Atome im Elektronen-Mikroskop sichtbar werden?

... des Auflösungsvermögens für möglich. Es ist also anzunehmen, daß die weitere Entwicklung des Elektronen-Mikroskops eines Tages nicht nur die schweren Jod-Atome des Moleküls, das wir unseren Betrachtungen zu Grunde gelegt haben, sichtbar machen wird, sondern auch die leichten Kohlenstoffatome und damit die Struktur von Molekülen, die weniger übersichtlich gebaut sind.

<http://www.microscopy.org>

“Scherzer focus”

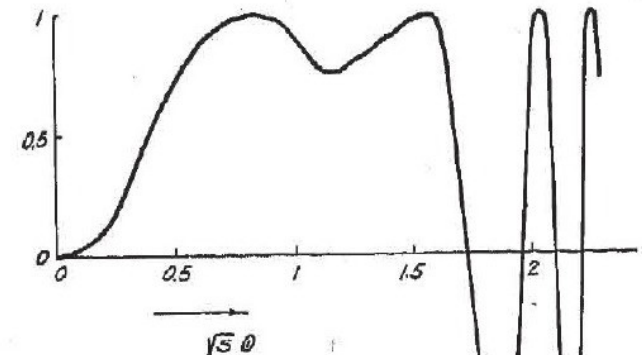
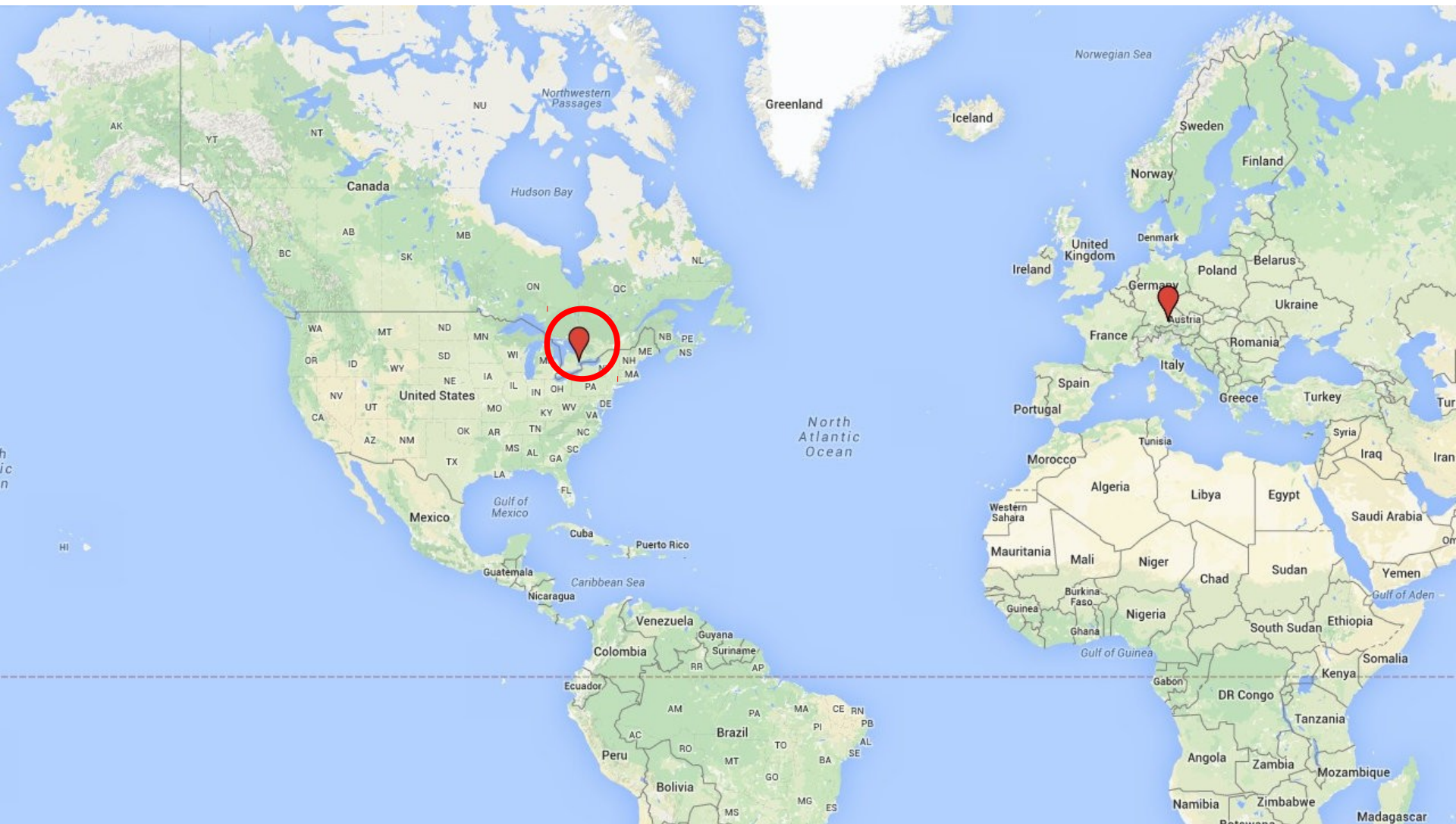


FIG. 4. The function $\sin(3s^2 - s^4)$, describing the phase shift in case of optimum contrast.

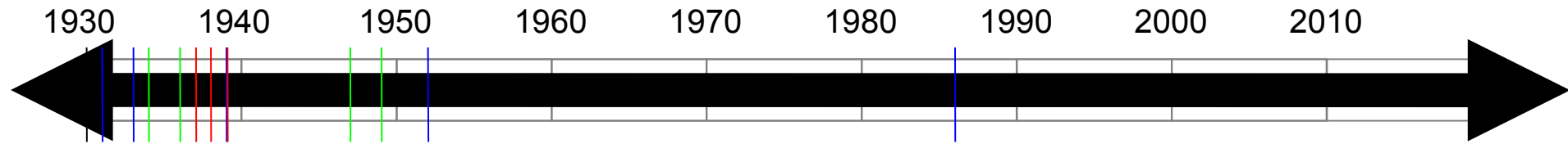
VOLUME 20, JANUARY, 1949

<http://www.microscopy.org>

Toronto group: E.F. Burton, James Hillier, etc.



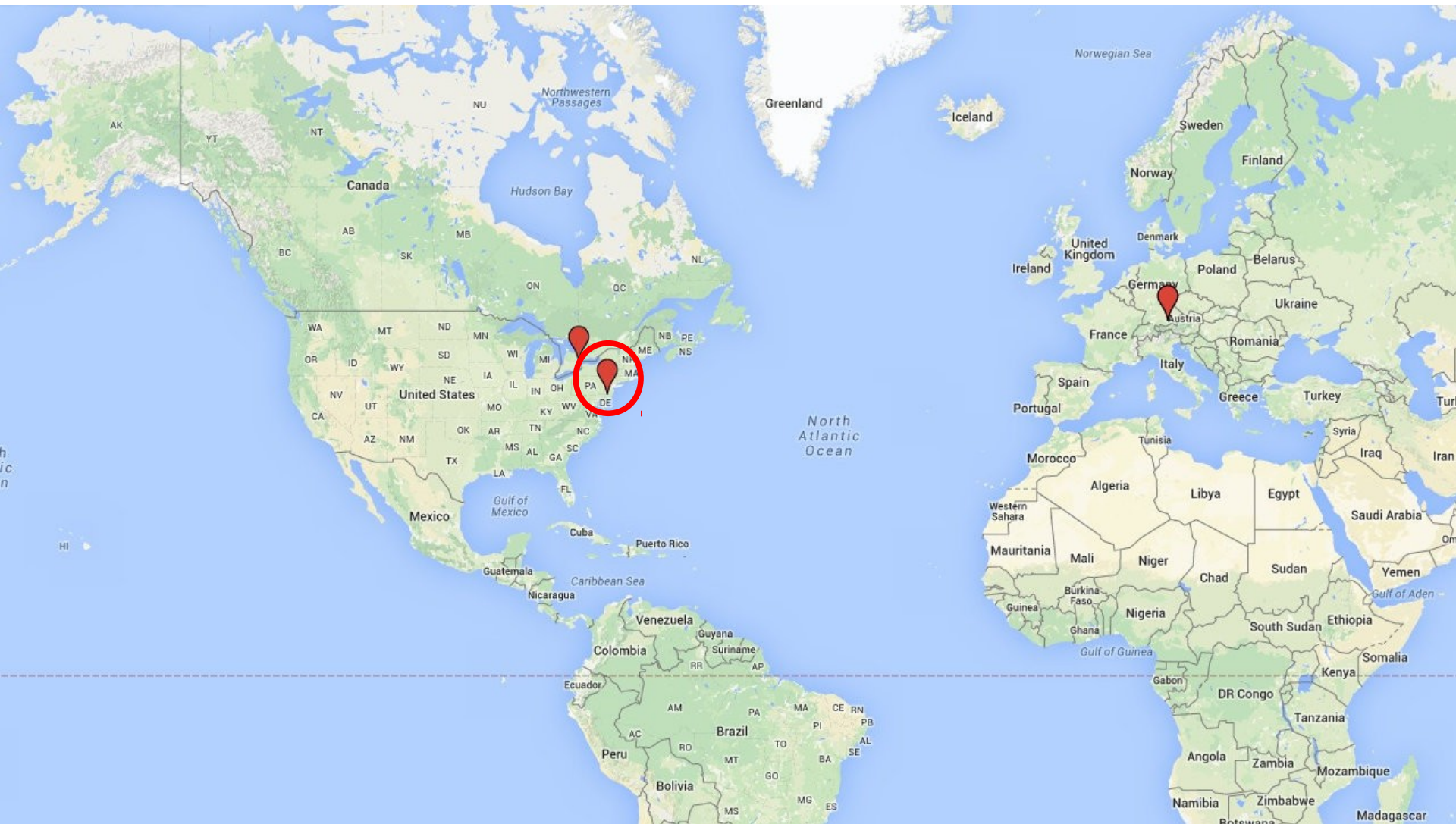
Toronto group: timeline



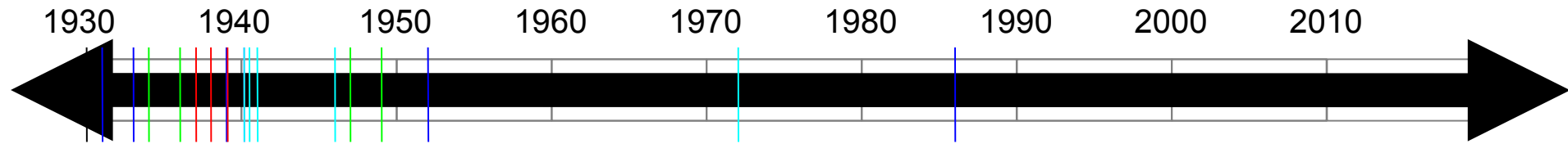
Milestones:

- ◆ 1937: Grad students James Hillier, Albert Prebus designed microscope over Christmas break
- ◆ 1938: First images
- ◆ 1939: E.F. Burton et al.
 - introduced airlock system
 - reduced specimen prep to 300nm thickness
 - resolution: 60Å, specimen limited
 - maximum mag: 180,000X

Radio Corporation of America (RCA)



James Hillier: timeline



Milestones:

- ◆ 1940 Feb
 - started at RCA
 - enlisted by Vladimir Dworykin (cathode ray tube)
- ◆ 1940 Jul 4: Commercial EM, Model B (EMB)
- ◆ 1941: 300kV, for dealing with thick specimens
- ◆ 1947: first stigmator
 - stigmators were iron screws tapped into the pole piece
 - resolution → 1nm
- ◆ 1973 (at VP of RCA): first videodisc

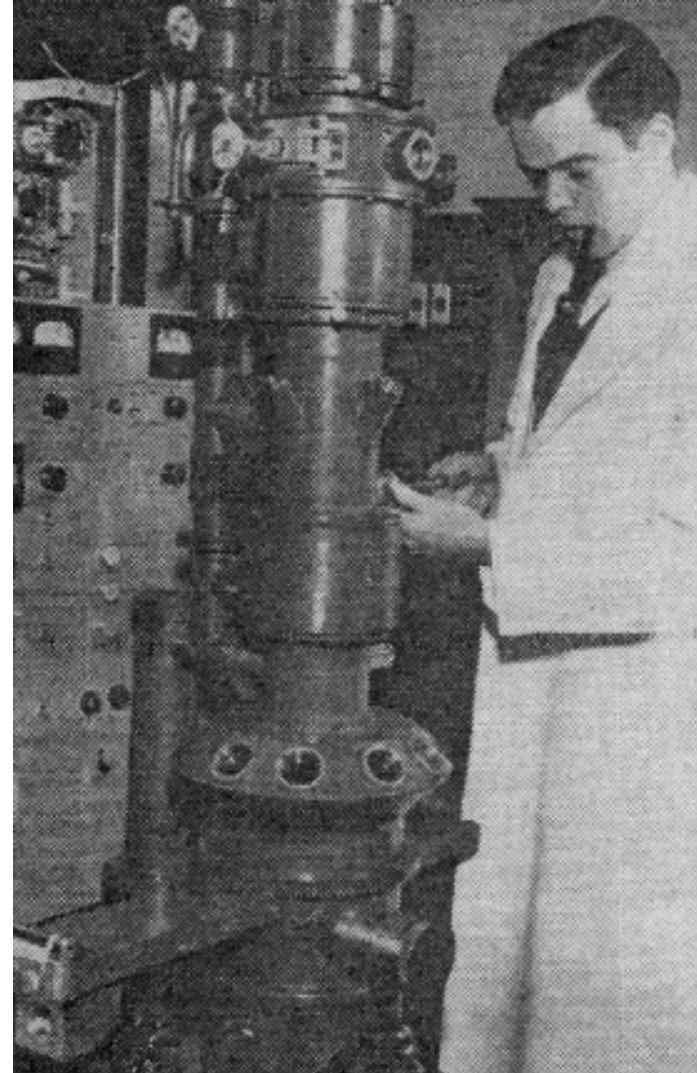
James Hillier

With Albert Prebus



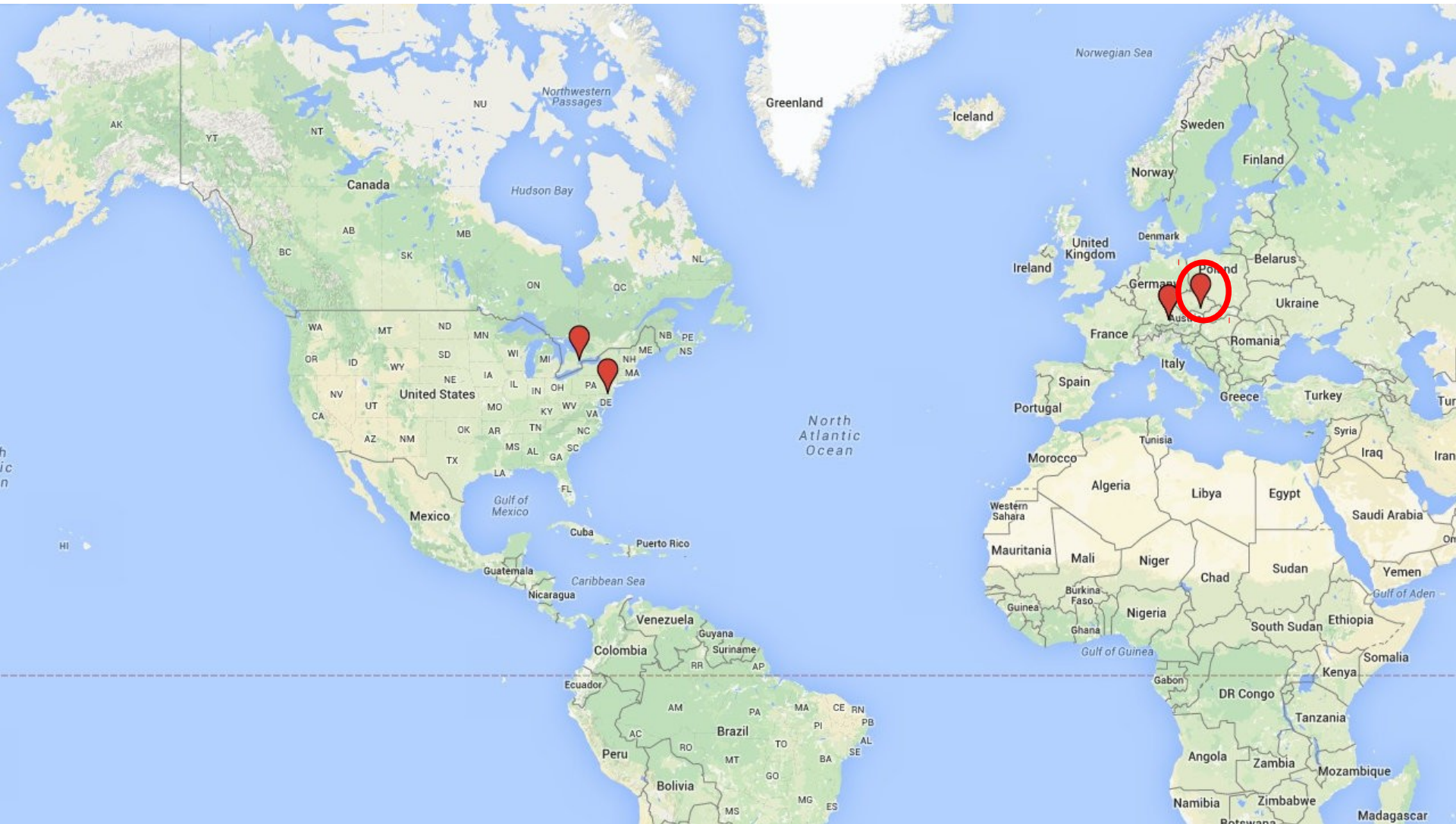
<http://www.museevirtuel.ca>

At RCA Model B, 1940

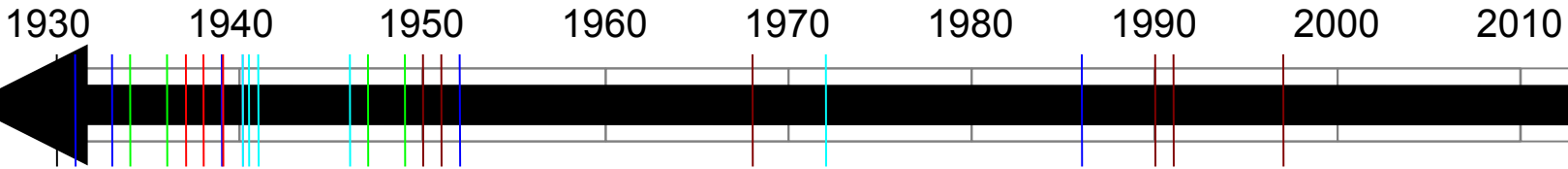


<http://www.rfcafe.com>

Electron microscopy in the Czech Republic



Electron microscopy in the Czech Republic

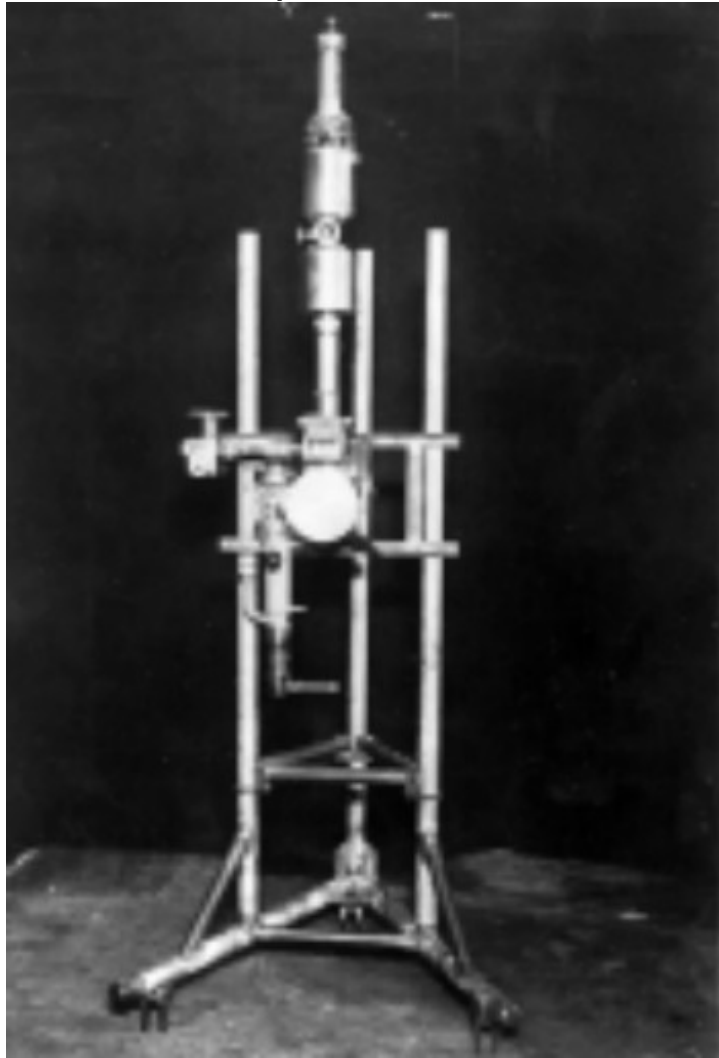


Milestones:

- ◆ 1950: Ales Blaha: “Tripod” at the Institute of Theoretical and Experimentation Electrotechnology of the Technical University
- ◆ 1951: Tesla BS241
 - first Czech commercial microscope
 - 50kV
 - resolution: 2nm
- ◆ 1968: First ultrahigh vacuum system (Institute of Scientific Instruments)
- ◆ 1990: Delong Instruments founded
- ◆ 1991: TESCAN founded
- ◆ 1997: FEI builds factory in Brno

Electron microscopy in the Czech Republic

“Tripod,” 1950



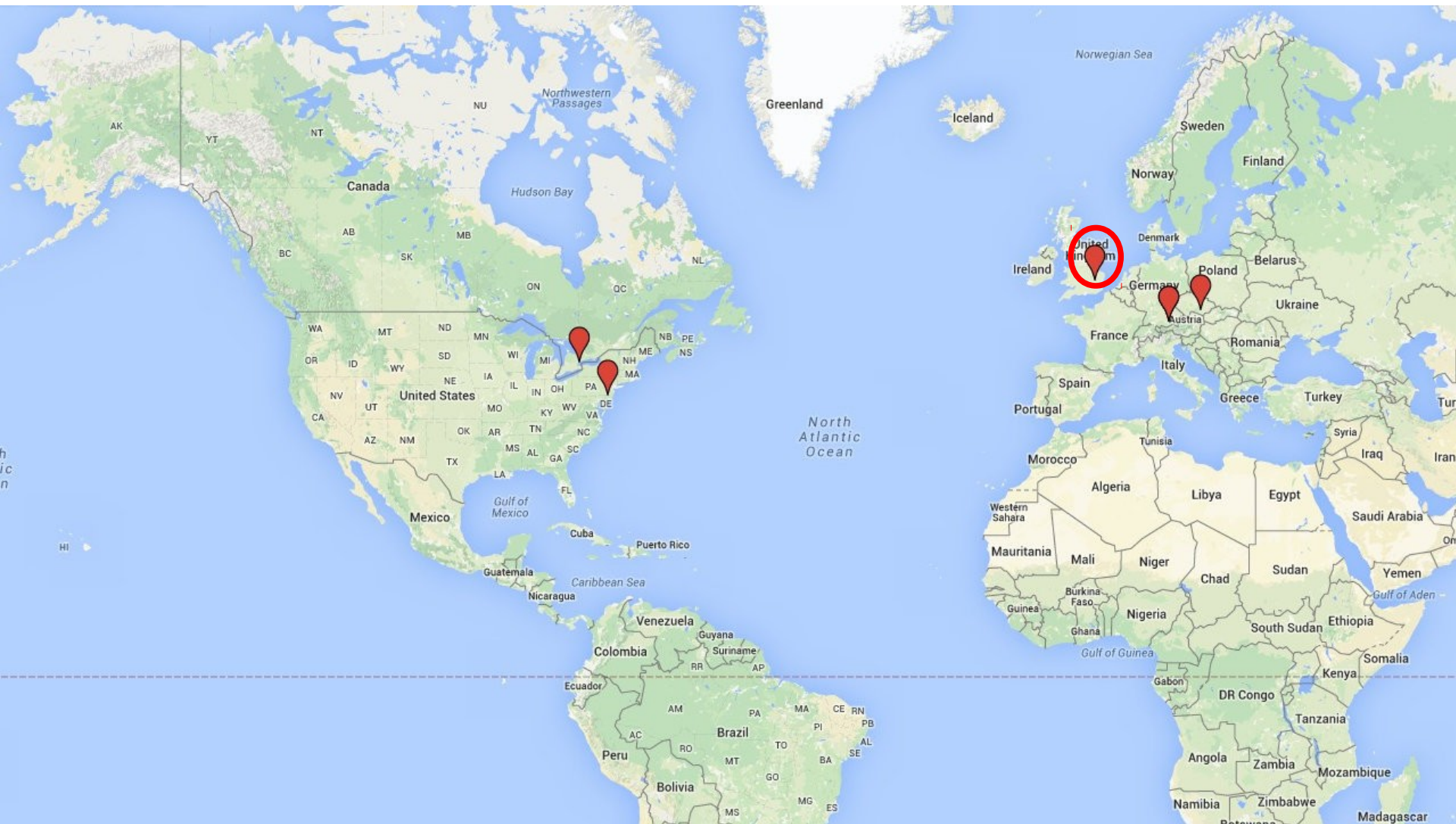
<http://www.isibrno.cz>

First high-vacuum system, 1961

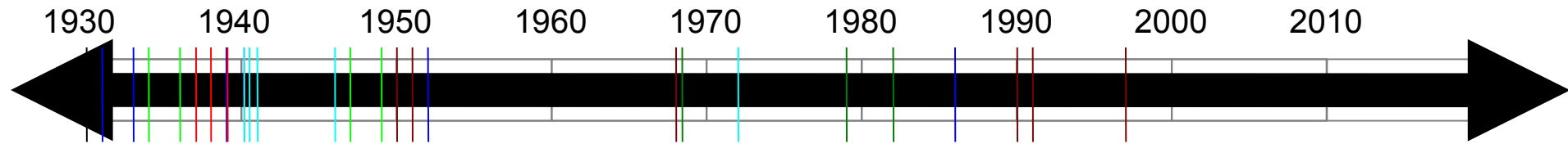


<http://www.isibrno.cz>

Medical Research Council (MRC), Cambridge



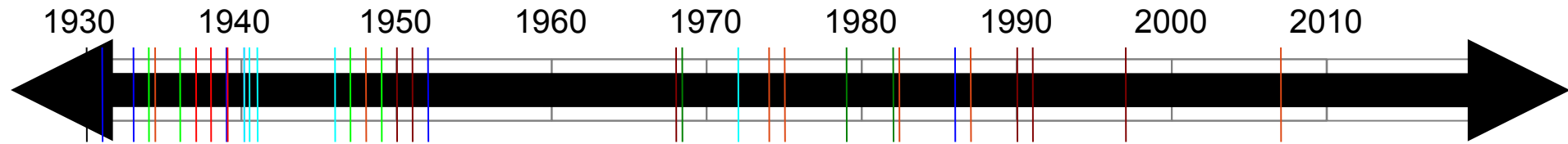
Aaron Klug: timeline



Milestones:

- ◆ 1968: DeRosier & Klug – first 3d EM reconstruction
- ◆ 1979: Cormack & Hounsfield receive Nobel Prize in Physiology for CAT scans
- ◆ 1982: Nobel Prize in Chemistry

Other notable events



Milestones:

- ◆ 1934: Ladislav L. Marton takes the first image of biological specimen
- ◆ 1937: Manfred von Ardenne (CRT) develops SEM
- ◆ 1948: Dennis Gabor develops electron holography (Nobel Prize in Physics, 1971)
- ◆ 1974: Ken Taylor & Bob Glaeser – electron crystallography of frozen hydrated specimens
- ◆ 1975: Richard Henderson – subnanometer electron crystallography
- ◆ 1982: Jacques Dubochet – modern cryo techniques
- ◆ 1987: Joachim Frank determines 3D reconstruction of an asymmetric specimen (50S ribosome)
- ◆ 2007: Direct Electron develops first commercial direct electron detector

Thank you for your attention



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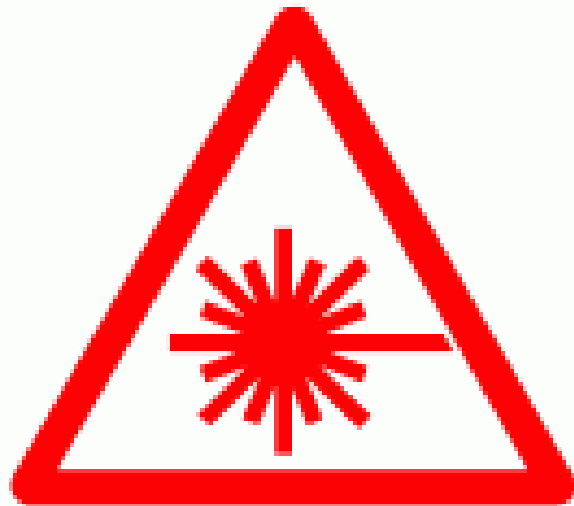
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DANGER



**DO NOT
LOOK INTO
LASER WITH
REMAINING
EYE**