

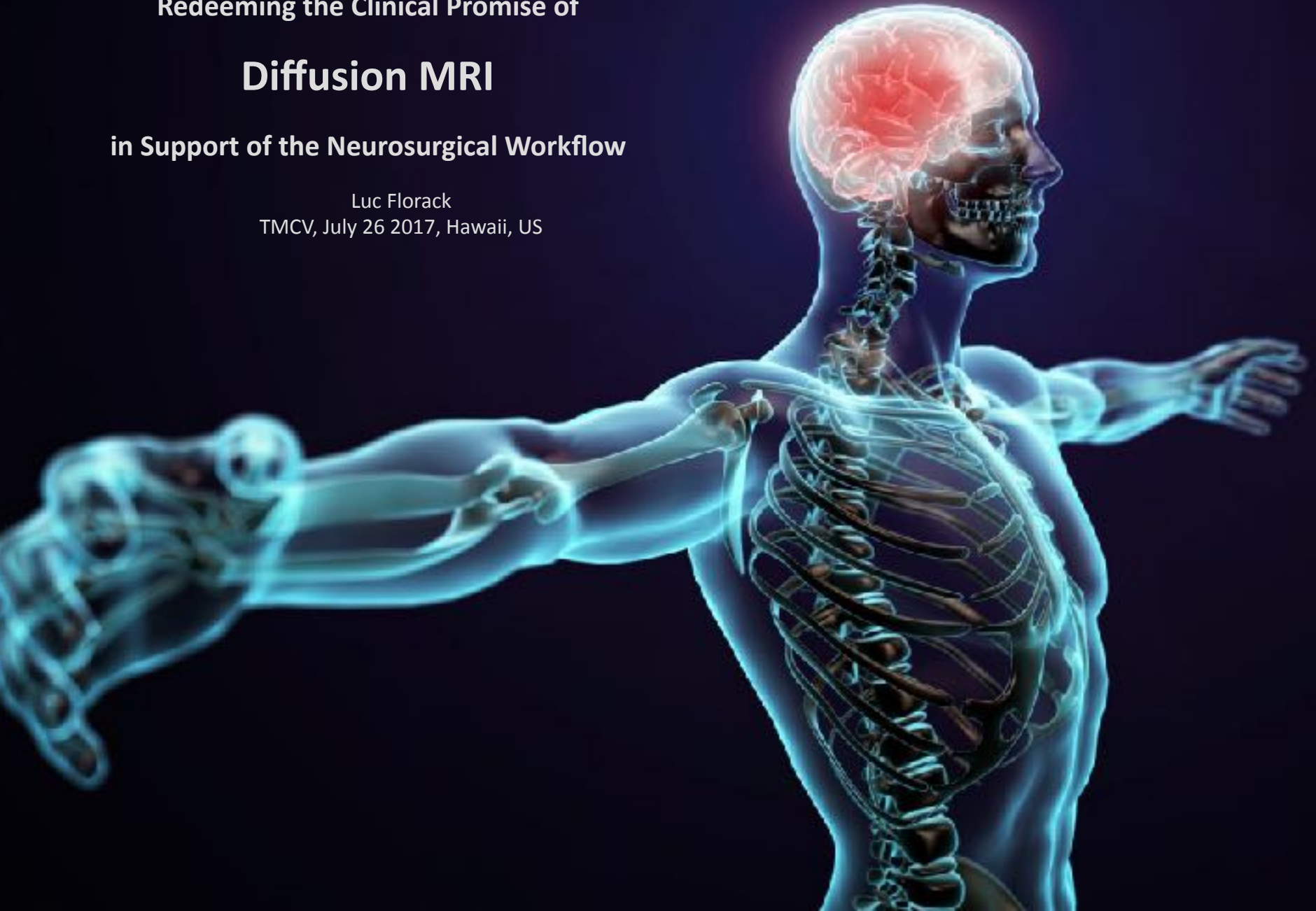
Redeeming the Clinical Promise of

Diffusion MRI

in Support of the Neurosurgical Workflow

Luc Florack

TMCV, July 26 2017, Hawaii, US



Economic Cost of Brain Disorders in Europe 2010:
€ 798 billion ...

European Journal of Neurology 2012, 19: 155–162



(N)MRI scanner

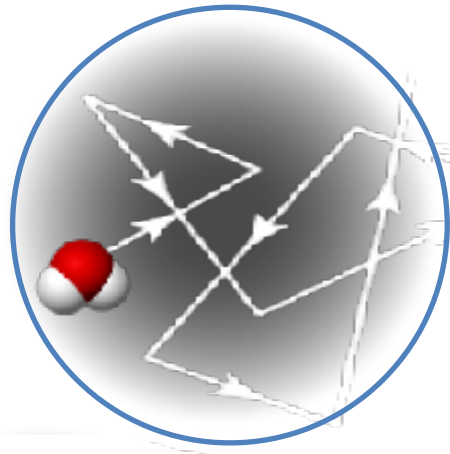




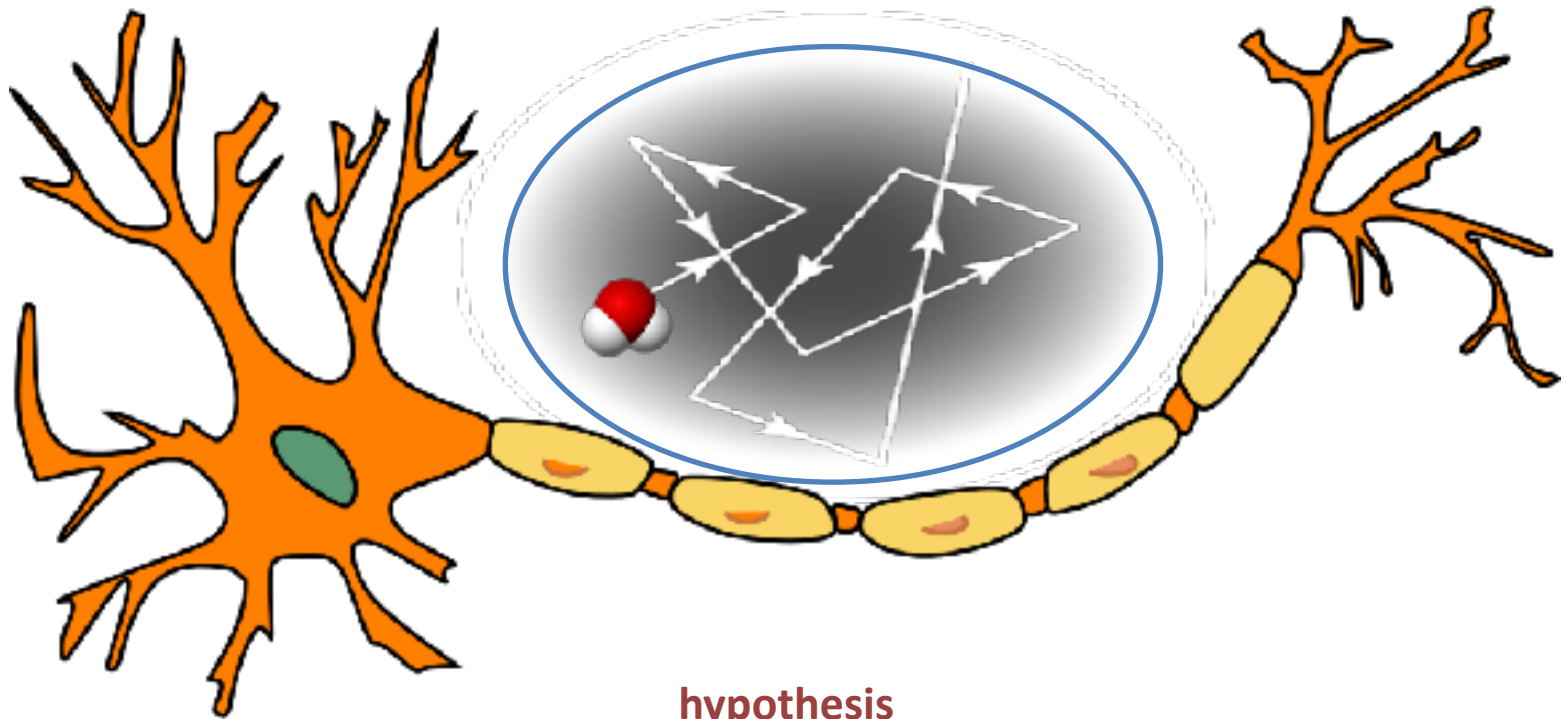
“everything must be made as simple as possible, but not one bit simpler”

attributed to Albert Einstein

operational model: brain = **constrained** water



operational model: brain = constrained water

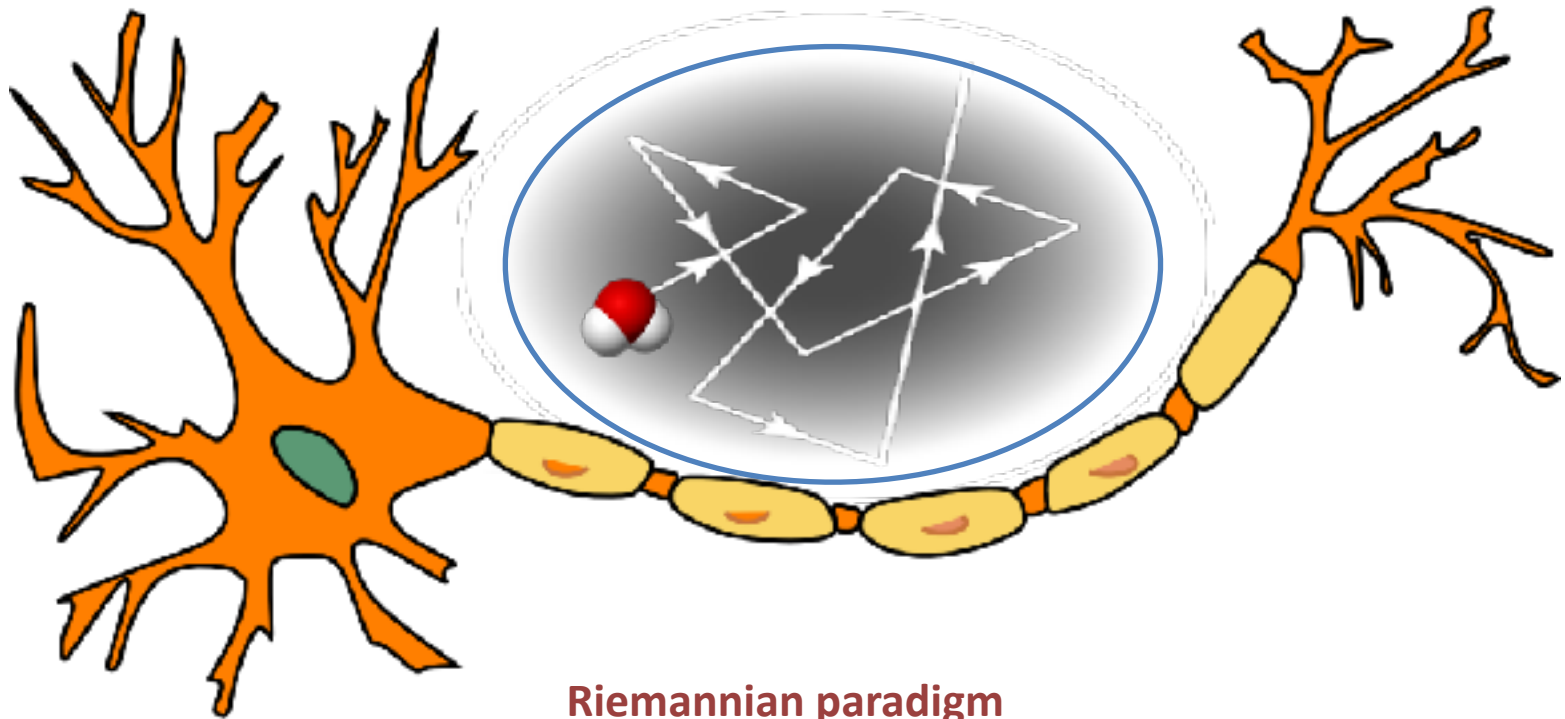


hypothesis

tissue microstructure imparts non-random barriers to water diffusion

C. Beaulieu, NMR Biomed. 2002, vol. 15, nr. 7-8, DOI: 10.1002/nbm.782

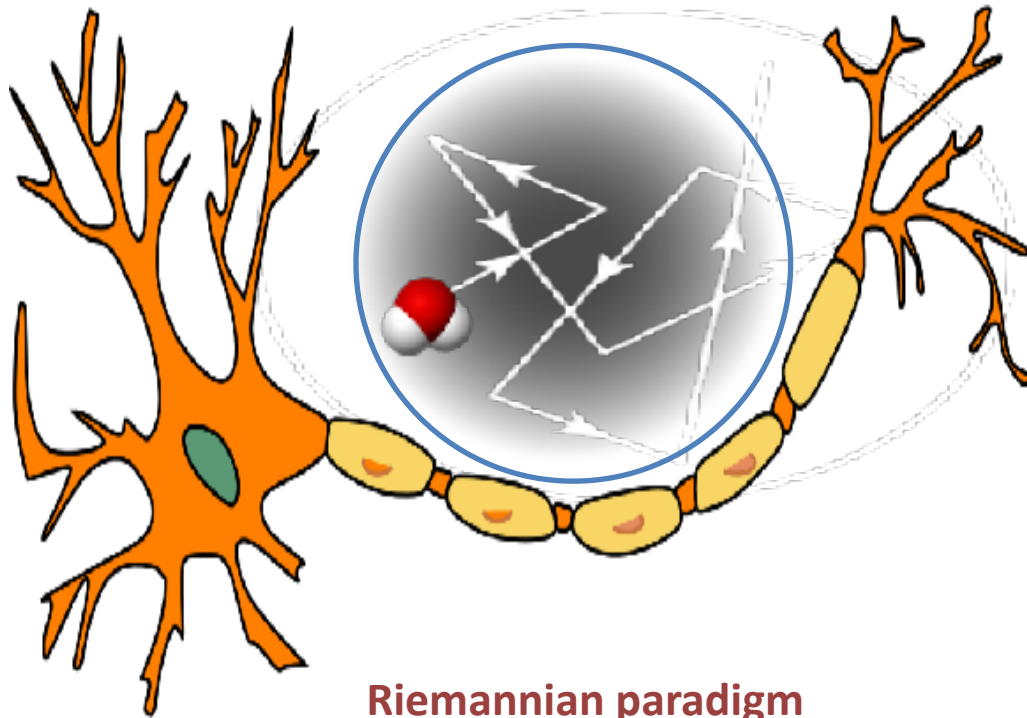
operational model: brain = constrained water



Riemannian paradigm

extrinsic diffusion on Euclidean space \approx intrinsic geometry of a Riemannian space

operational model: brain = constrained water

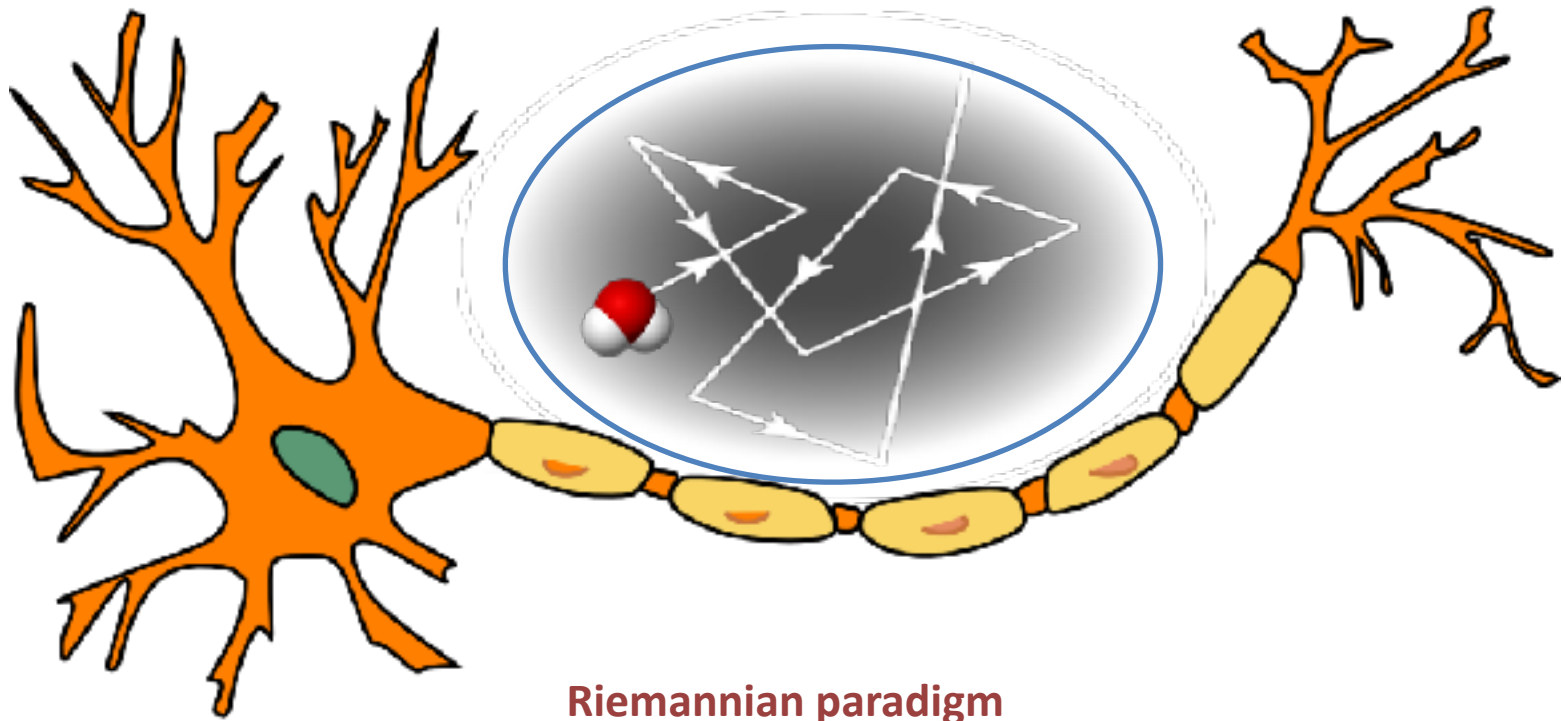


Riemannian paradigm



extrinsic diffusion on Euclidean space \approx intrinsic geometry of a Riemannian space

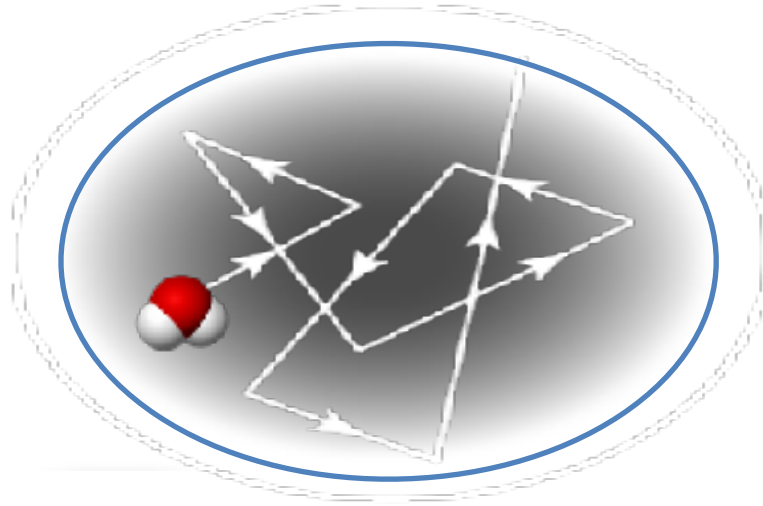
operational model: brain = constrained water



Riemannian paradigm

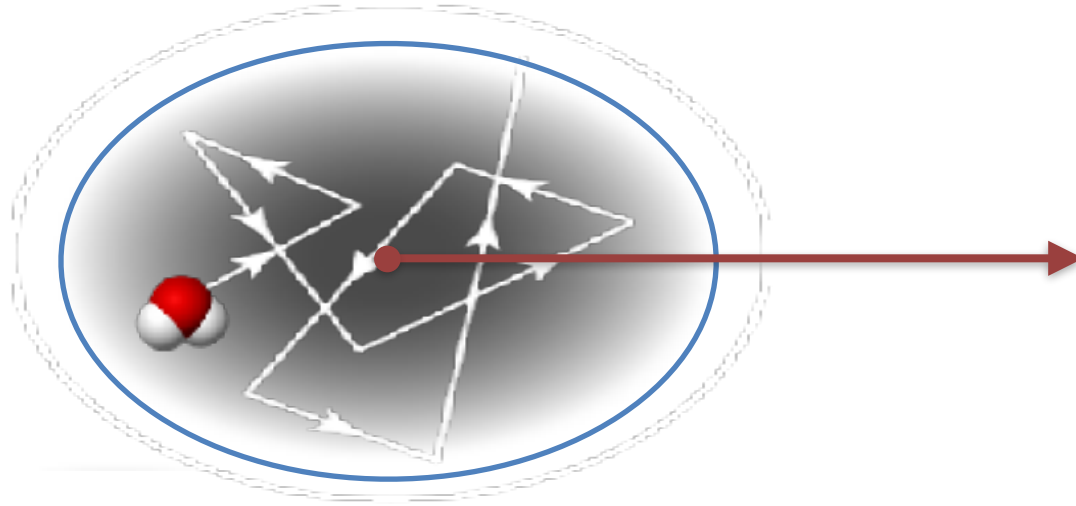
extrinsic diffusion on Euclidean space \approx intrinsic geometry of a Riemannian space

local gauge figure
Riemann geometry

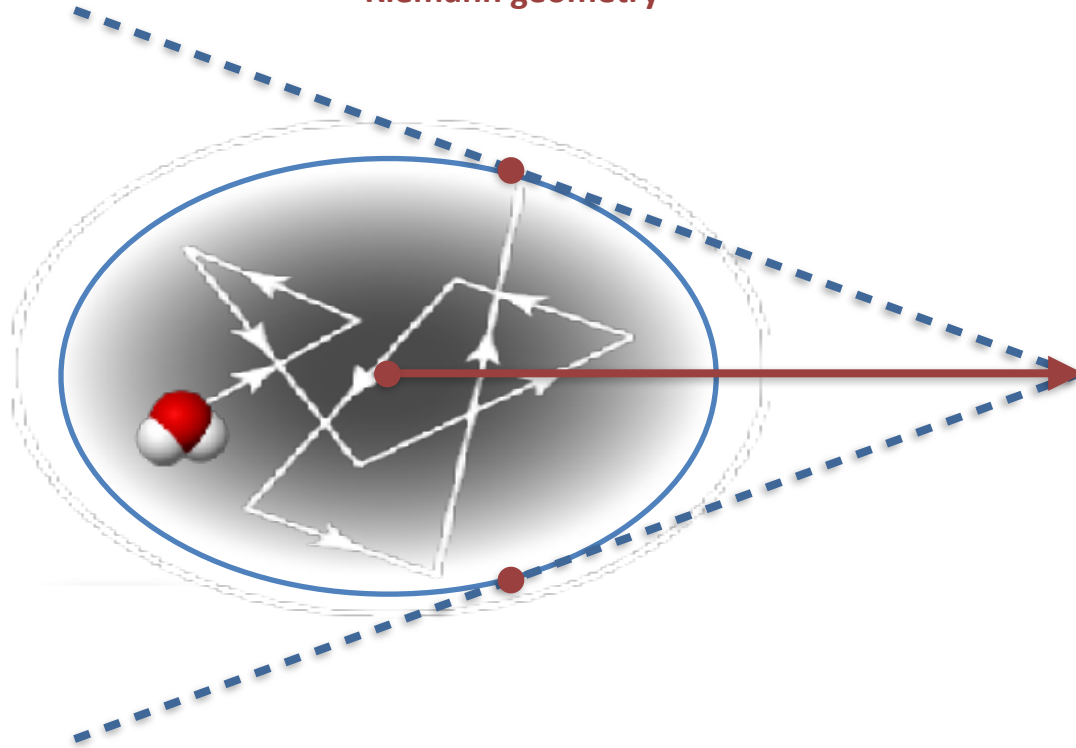


gauge figure = unit sphere = indicatrix = Riemannian metric = inner product

local gauge figure
Riemann geometry

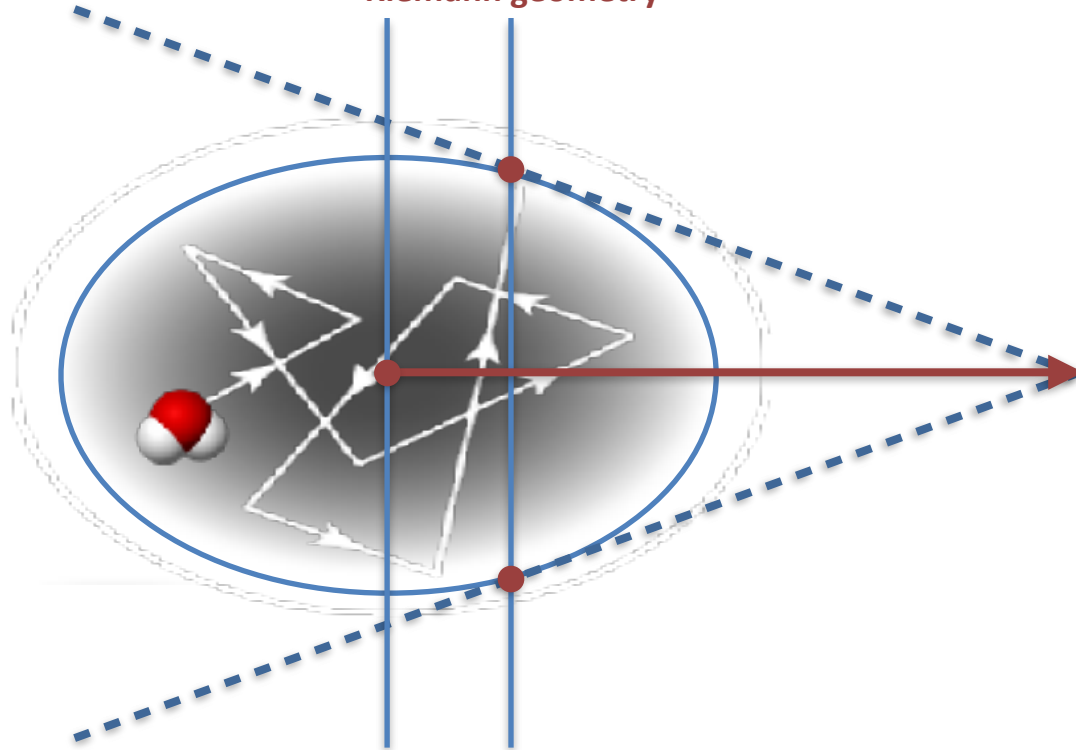


local gauge figure
Riemann geometry



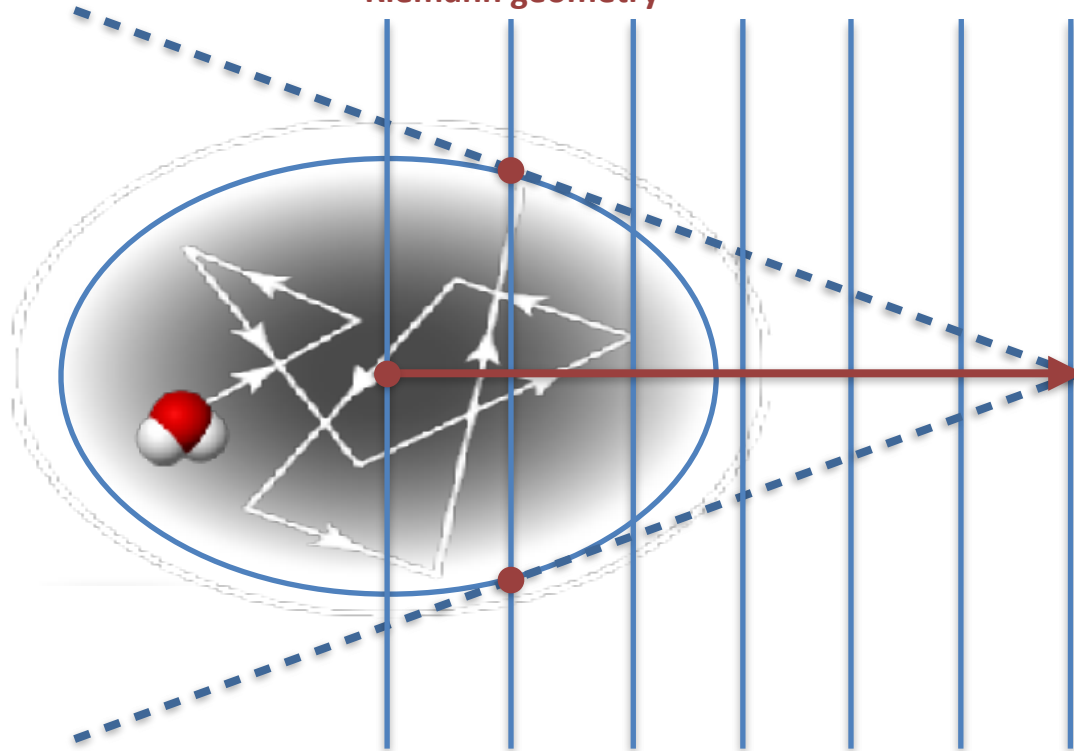
local gauge figure

Riemann geometry



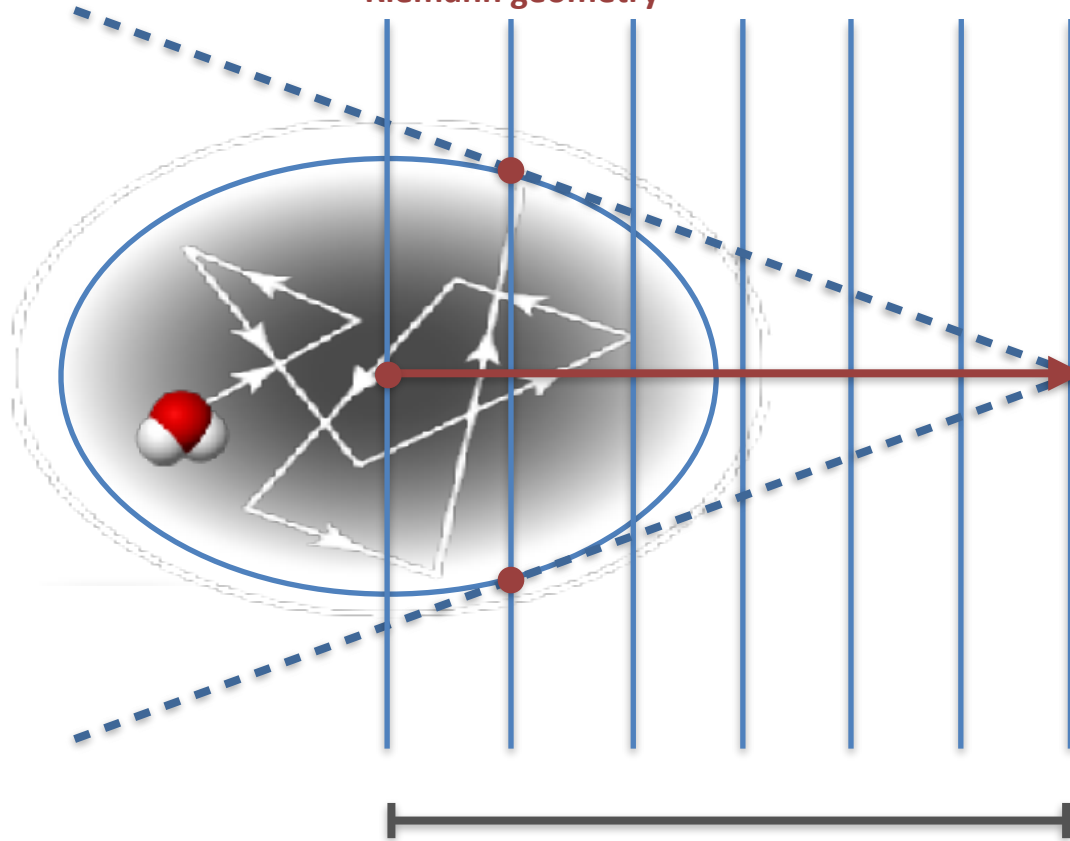
local gauge figure

Riemann geometry



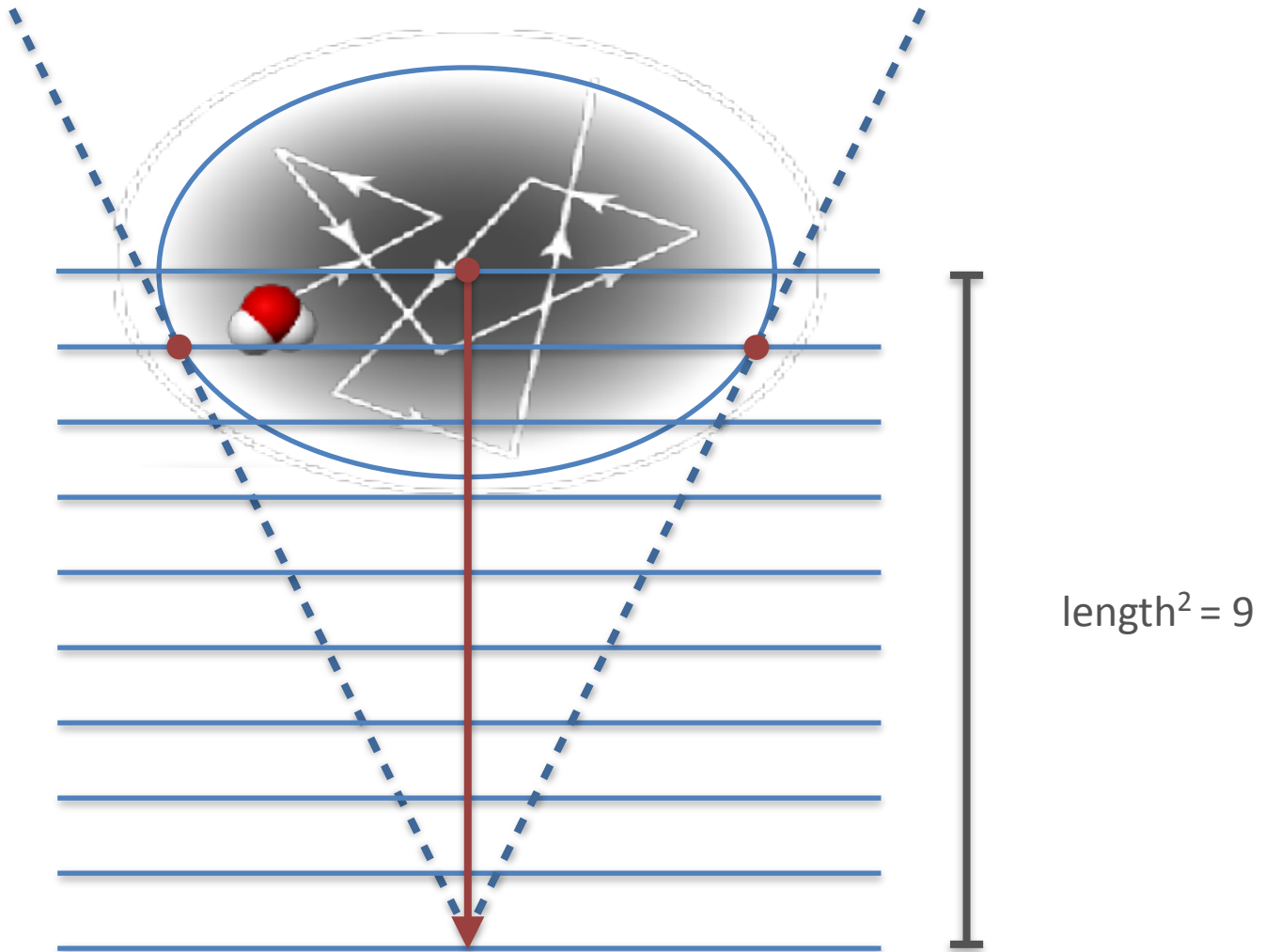
local gauge figure

Riemann geometry

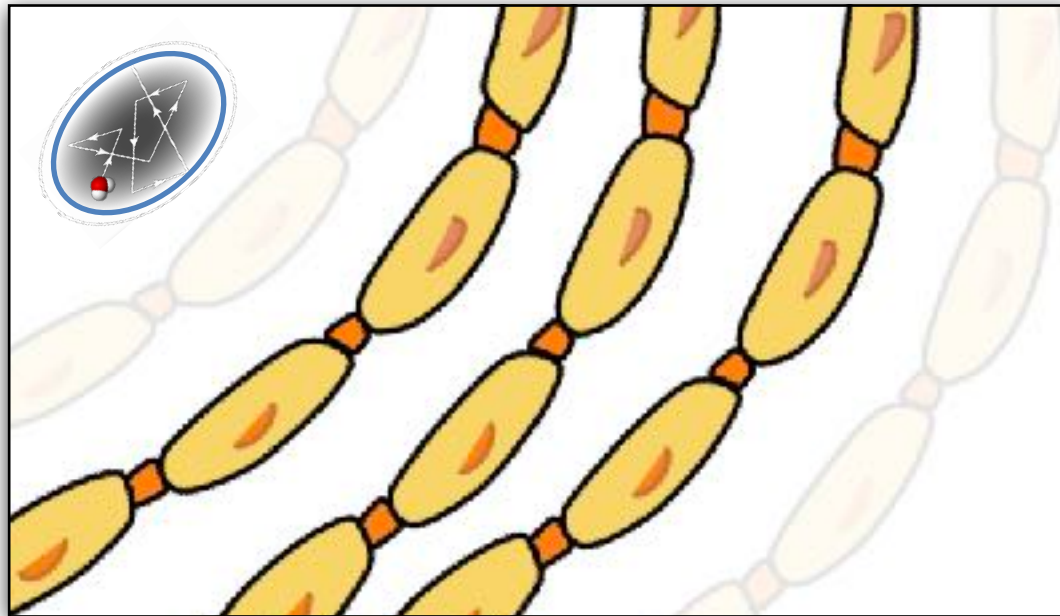


$$\text{length}^2 = 6$$

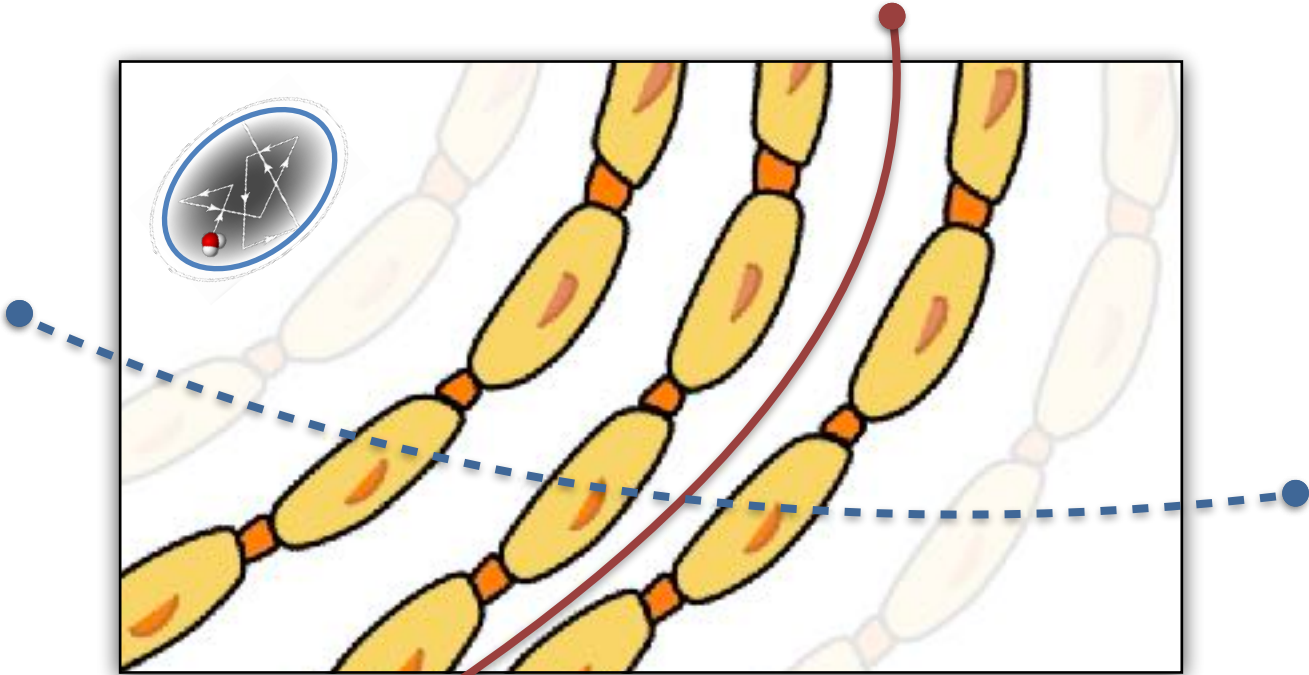
local gauge figure
Riemann geometry



geodesic tractography



geodesic tractography



Riemannian length : Euclidean length

'short' geodesic



$5.0 : 6.0 < 1$

'long' geodesic



$7.5 : 6.0 > 1$

Diffusion Tensor Imaging

versus

local gauge figure



Diffusion Tensor Imaging

physics pipeline

physics in a nutshell:

nuclear spin quantization → Zeeman splitting → Boltzmann statistics → magnetization → Bloch-Torrey equation → DTI

mathematics in a nutshell:

DTI → local gauge figure → geodesic tractography

Diffusion Tensor Imaging

physics pipeline

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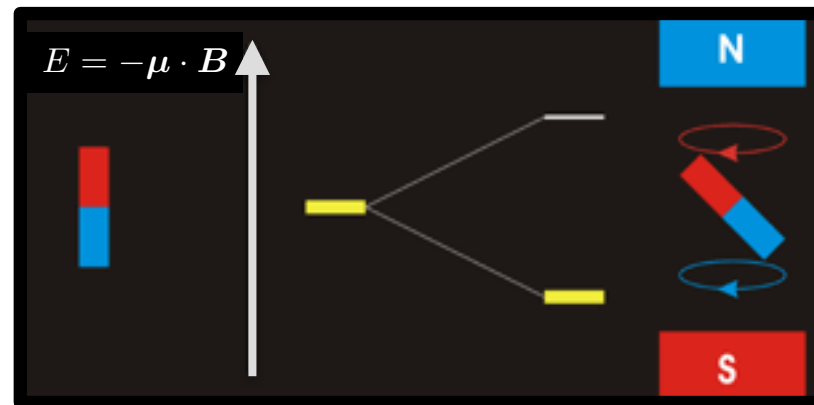
physics in a nutshell:

nuclear spin quantization → Zeeman splitting → Boltzmann statistics → magnetization → Bloch-Torrey equation → **DTI**

mathematics in a nutshell:

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nuclear spin quantization → Zeeman splitting



$$E_{\downarrow} = +\frac{1}{2}\gamma\hbar B_z$$

$$E_{\uparrow} = -\frac{1}{2}\gamma\hbar B_z$$

$$\Delta E = \gamma\hbar B_z = \hbar\omega_{\text{Larmor}}$$

Boltzmann statistics → magnetization
(typical clinical 3T MRI scanner)

$$\frac{N_{\uparrow}}{N_{\downarrow}} = \exp \left[\frac{\Delta E}{KT} \right] \approx 1 + \frac{\gamma \hbar B_z}{KT}$$

$$\frac{N_{\uparrow} - N_{\downarrow}}{N_{\uparrow} + N_{\downarrow}} \approx \frac{\gamma \hbar B_z}{2KT} \approx 10^{-5}$$

'low sensitivity modality'

$$M_z = \frac{N_{\uparrow} - N_{\downarrow}}{N_{\uparrow} + N_{\downarrow}} M_{\max} \approx (N_{\uparrow} + N_{\downarrow}) \frac{\gamma^2 \hbar^2 B_z}{4KT}$$

'big x small = measurable'



Bloch-Torrey equation → DTI

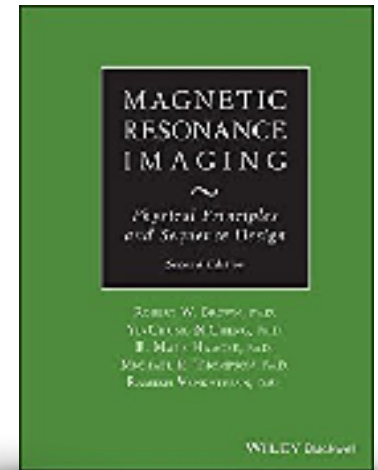
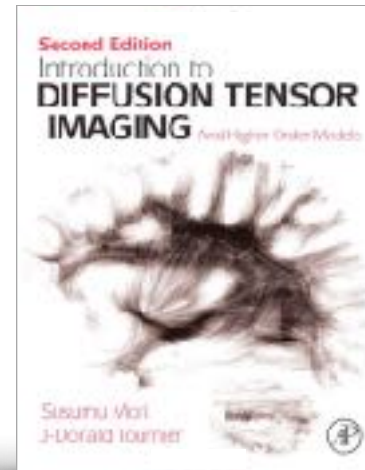
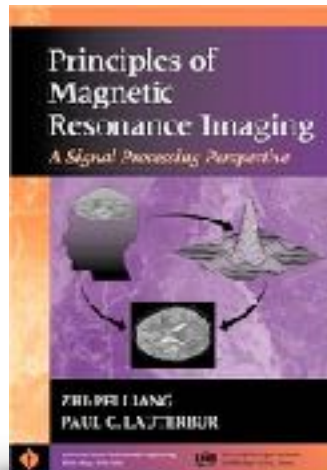
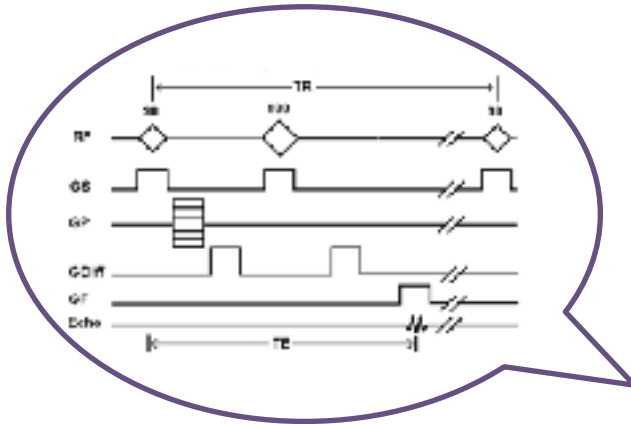
Bloch-Torrey / Stejskal-Tanner / Basser-Mattiello-Le Bihan:
Gaussian signal attenuation in q-space

$$\frac{\partial M_{\perp}}{\partial t} = -i\gamma(M_{\perp}B_{\parallel} - M_{\parallel}B_{\perp}) - \frac{M_{\perp}}{T_2} + \nabla \cdot \mathbf{D} \nabla M_{\perp}$$

$$S(x, q, \tau) = S_0(x) \exp(-\tau q \cdot \mathbf{D}(x) q)$$

$$\mathbf{D}(x) = -\frac{1}{\tau} \nabla_q^2 \ln \frac{S(x, q, \tau)}{S_0(x)}$$

Bloch-Torrey equation \rightarrow DTI further reading



geodesic tractography

mathematics pipeline

physics in a nutshell:

nuclear spin quantization → Zeeman splitting → Boltzmann statistics → magnetization → Bloch-Torrey equation → DTI

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DTI → local gauge figure → geodesic tractography

geodesic tractography

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DTI → local gauge figure → geodesic tractography

DTI → local gauge figure

DTI signal model: $S(x, q, \tau) = S_0(x) e^{-\tau q^T D(x) q}$

Riemann metric: $G(\xi, \xi) |_x = \xi^T G(x) \xi$

Lenglet et al. / O'Donnell et al.: $G(x) \doteq D^{\text{inv}}(x)$

Fuster et al.: $G(x) \doteq D^{\text{adj}}(x)$

local gauge figure → tractography

$$G(v, v) = \|v\|^2$$

Riemann metric: lengths & angles

$$\nabla_{\dot{x}} \dot{x} = 0$$

Levi-Civita connection: parallel transport

$$\ddot{x}^i + \sum_{jk} \Gamma_{jk}^i(x) \dot{x}^j \dot{x}^k = 0$$

Christoffel symbols: “pseudo-forces” (relative to local coordinate frames)

local gauge figure → tractography

$$G(v, v) = \|v\|^2$$

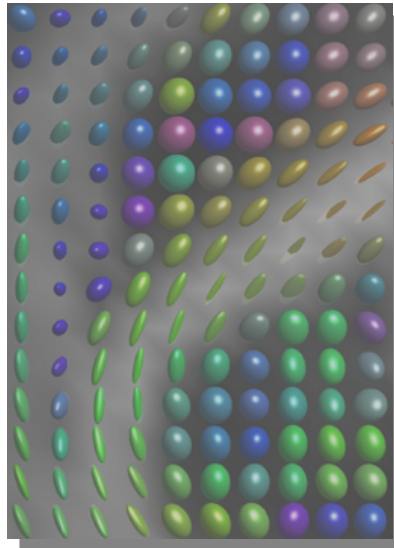
$$\nabla_{\dot{x}} \dot{x} = 0$$

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local gauge figure → tractography

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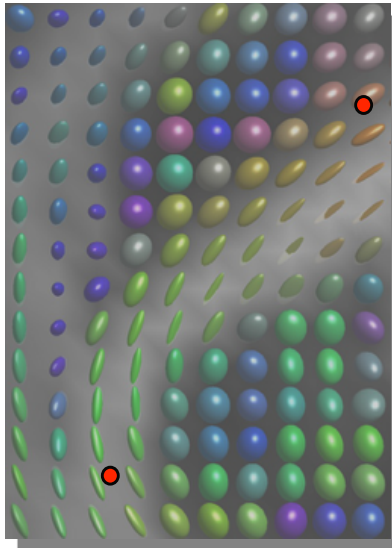
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local gauge figure → tractography

$$G(v, v) = \|v\|^2$$

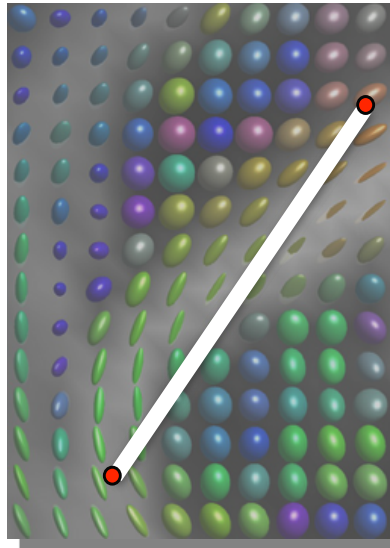
$$\nabla_{\dot{x}} \dot{x} = 0$$

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Riemann metric: lengths & angles

Levi-Civita connection: parallel transport

Christoffel symbols: “pseudo-forces” (relative to local coordinate frames)



Euclidean geodesic

local gauge figure → tractography

$$G(v, v) = \|v\|^2$$

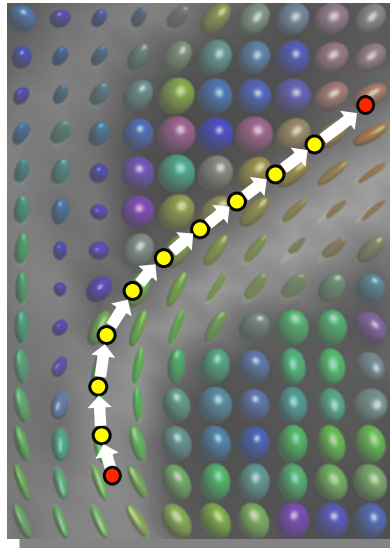
$$\nabla_{\dot{x}} \dot{x} = 0$$

$$\ddot{x}^i + \sum_{jk} \Gamma_{jk}^i(x) \dot{x}^j \dot{x}^k = 0$$

Riemann metric: lengths & angles

Levi-Civita connection: parallel transport

Christoffel symbols: “pseudo-forces” (relative to local coordinate frames)



Riemannian geodesic

Riemann-DTI paradigm:

- neural fiber bundles correspond to relatively short geodesics in a Riemannian 'brain space'
- the Riemannian structure can be inferred from DTI



Riemann-DTI paradigm

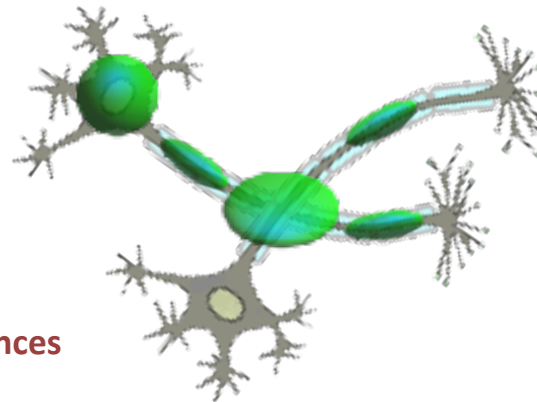
pros & cons

geodesic completeness
=
redundant connections



pro: pixels \rightarrow geodesic congruences

ellipsoidal gauge figure
=
poor angular resolution



con: destructive interference of orientation preferences

beyond the Riemann-DTI paradigm a paradigm shift

specific model (DTI):

$$S(x, q, \tau) = S_0(x) \exp(-D(x, q, \tau))$$

with

$$D(x, q, \tau) = \tau q^T D(x) q$$

6 d.o.f.'s per point sample
↓
6 d.o.f.'s of local gauge figure



generic model (HARDI):

$$S(x, q, \tau) = \sum_{k=0}^{\infty} S^{i_1 \dots i_k}(x, \tau) \phi_{i_1 \dots i_k}(q)$$

or

$$D(x, q, \tau) = \sum_{k=0}^{\infty} D^{i_1 \dots i_k}(x, \tau) \psi_{i_1 \dots i_k}(q)$$

∞ d.o.f.'s per point sample



beyond the Riemann-DTI paradigm
a paradigm shift

DTI

C

HARDI

beyond the Riemann-DTI paradigm
a paradigm shift

DTI

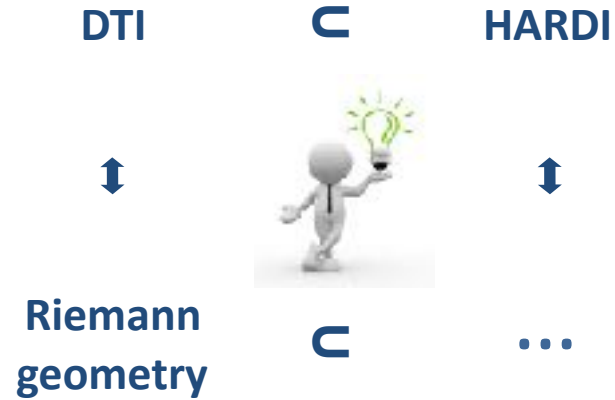
C

HARDI



**Riemann
geometry**

beyond the Riemann-DTI paradigm
a paradigm shift

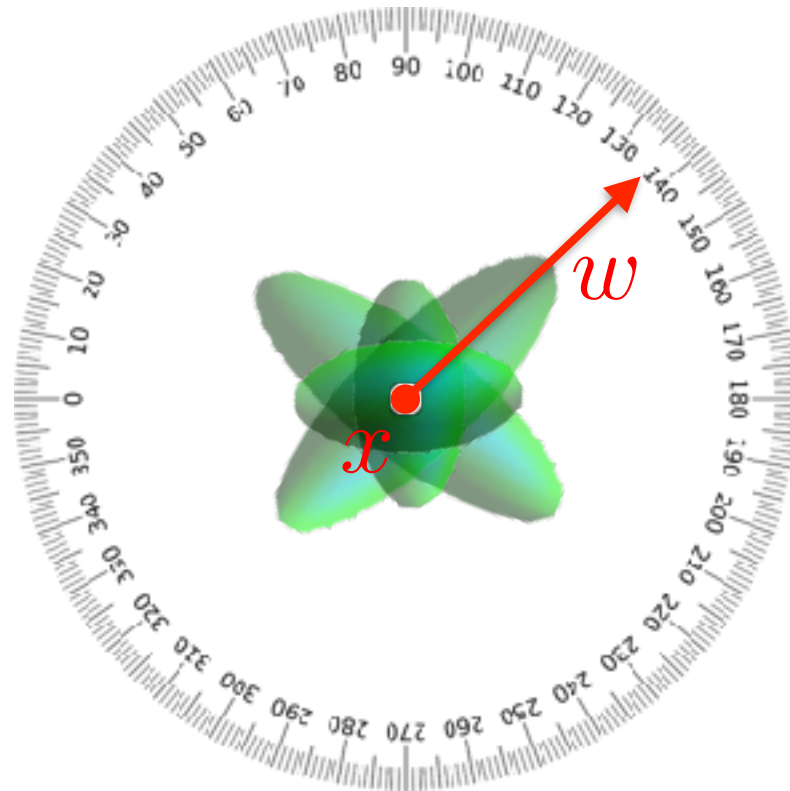


beyond the Riemann-DTI paradigm
a paradigm shift



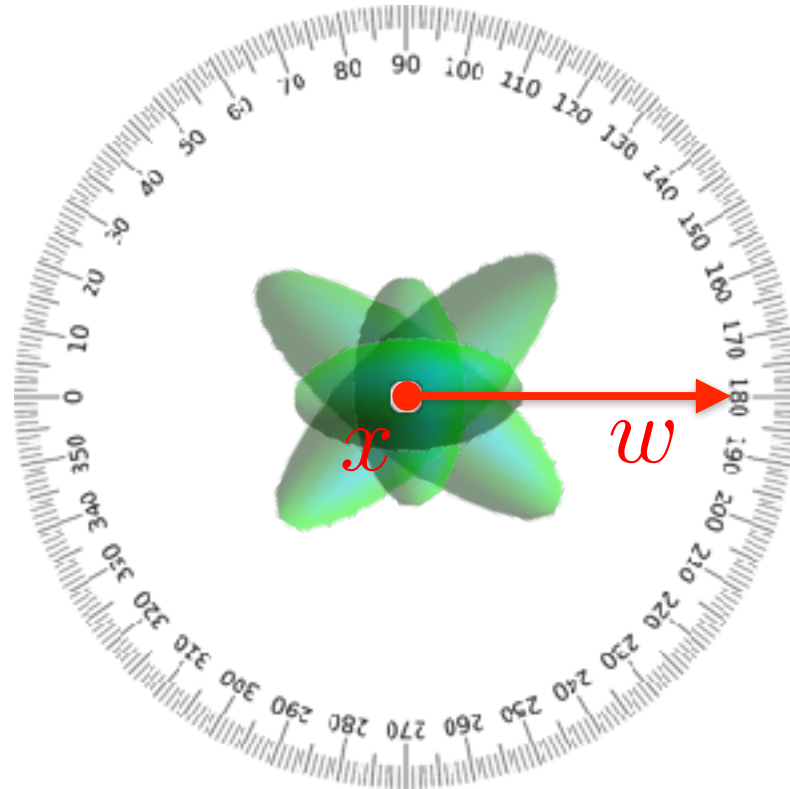
Finsler geometry

heuristics



Finsler geometry

heuristics



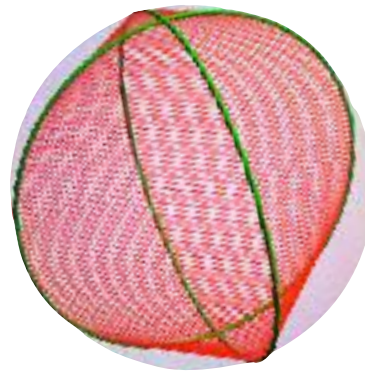
osculating indicatrices

base manifold: $x \in \mathbb{R}^3 \rightarrow (x, w) \in \mathbb{R}^3 \times \mathbb{S}^2$ (sphere bundle)

base manifold: $x \in \mathbb{R}^3 \rightarrow (x, \xi) \in \mathbb{R}^3 \times \mathbb{TR}^3 \setminus \{0\}$ (slit tangent bundle)

Finsler geometry

heuristics



family of osculating indicatrices
↓
single (convex) indicatrix

gauge figure = unit sphere = indicatrix = Finsler metric \neq inner product

Finsler geometry axiomatics

HV-splitting

connections

2.3 Connections in Riemann-Finsler Geometry

There is no "obvious" connection prescription for parallel transport on a Riemann-Finsler manifold. The Boreard, Cartan, Chern-Rund and Hashiguchi connection may all be considered "natural" extensions of the Levi-Civita connection in Riemannian geometry. For instance, the (torsion-free) Chern-Rund connection is defined by²

$$\overset{\mathcal{C}}{\nabla}_X Y = \frac{\partial Y^i}{\partial x^j} X^j + \frac{\partial g_{ij}}{\partial x^k} X^k Y^i - \frac{\partial g_{ij}}{\partial x^i} X^k Y^j, \quad (19)$$

and is expressed in terms of the "classical" Christoffel symbols of Riemannian geometry by formally replacing the Riemannian metric $g_{ij}(x)$ by the Riemann-Finsler metric $g_{ij}(x, \dot{x})$, Eq. (5), and spatial derivatives by horizontal vectors

$$\frac{\partial}{\partial x^i} \stackrel{\mathcal{C}}{\leftarrow} \frac{\partial}{\partial x^i} - N_i^j(x, \dot{x}) \frac{\partial}{\partial \dot{x}^j}. \quad (20)$$

The coefficients $N_i^j(x, \dot{x})$ define the so-called *covariant connection* [36]:

$$N_i^j(x, \dot{x}) = \gamma_{ij}^k(x, \dot{x}) \dot{x}^k - C_{ij}^k(x, \dot{x}) \dot{x}^k \dot{x}^i \dot{x}^j, \quad (21)$$

in which the formal Christoffel symbols of the second kind are introduced as

$$\gamma_{ij}^k(x, \dot{x}) = \frac{1}{2} g^{kl}(x, \dot{x}) \left(\frac{\partial g_{li}(x, \dot{x})}{\partial x^j} + \frac{\partial g_{lj}(x, \dot{x})}{\partial x^i} - \frac{\partial g_{ij}(x, \dot{x})}{\partial x^k} \right). \quad (22)$$

Note that in the Riemannian limit, both Eq. (19) as well as Eq. (22) simplify to

$$F_{ij}^k(x) = \frac{1}{2} g^{kl}(x) \left(\frac{\partial g_{li}(x)}{\partial x^j} + \frac{\partial g_{lj}(x)}{\partial x^i} - \frac{\partial g_{ij}(x)}{\partial x^k} \right), \quad (23)$$

These are the standard Christoffel symbols of the second kind defining the torsion-free Levi-Civita connection in Riemannian geometry. A comparison reveals that³

$$\overset{\mathcal{C}}{\nabla}_X Y = \overset{\mathcal{R}}{\nabla}_X Y + C_{ij}^k(x, \dot{x}) \dot{x}^k Y^i - C_{ij}^k(x, \dot{x}) \dot{x}^k X^i Y^j + C_{ij}^k(x, \dot{x}) \dot{x}^k X^i Y^j, \quad (24)$$

in which indices have been lowered with the help of the Riemann-Finsler metric tensor:

$$F_{ij}(x, \dot{x}) = g_{ij}(x, \dot{x}) \dot{x}^k \dot{x}^l \delta_{kl} = g_{ij}(x, \dot{x}) \dot{x}^k \dot{x}^l \delta_{kl}, \quad (25)$$

and in which the *quadratic coefficients* are defined as⁴

$$C_{ij}^k(x, \dot{x}) = \frac{\partial g_{ij}(x, \dot{x})}{\partial \dot{x}^k} - \frac{1}{2} g^{kl}(x, \dot{x}) \dot{x}^l \dot{x}^m \frac{\partial g_{lm}(x, \dot{x})}{\partial \dot{x}^i} - \frac{1}{2} g^{kl}(x, \dot{x}) \dot{x}^l \dot{x}^m \frac{\partial g_{lm}(x, \dot{x})}{\partial \dot{x}^j} + \frac{1}{2} g^{kl}(x, \dot{x}) \dot{x}^l \dot{x}^m \frac{\partial g_{lm}(x, \dot{x})}{\partial \dot{x}^k}, \quad (26)$$

$$C_{ij}^k(x, \dot{x}) = \gamma_{ij}^k(x, \dot{x}) \dot{x}^l \dot{x}^m \delta_{lm}, \quad (27)$$

recall Eq. (21).

²Cartan in [37] Rand defines these symbols as $\overset{\mathcal{C}}{\nabla}_X Y$.

³Cartan in [37] Rand defines these symbols as $F_{ij}^k(x, \dot{x})$.

⁴Cartan in [37] Rand defines these symbols as $\gamma_{ij}^k(x, \dot{x}) \dot{x}^l \dot{x}^m \delta_{lm}$.

2.4 Horizontal-Vertical Splitting

The heuristic coupling of position and orientation is formalized in terms of the so-called horizontal and vertical basis vectors, recall Eq. (20).

$$\frac{\delta}{\delta x^i} \stackrel{\text{def}}{=} \frac{\partial}{\partial x^i} - N_i^j(x, \dot{x}) \frac{\partial}{\partial \dot{x}^j} \quad \text{and} \quad \frac{\partial}{\partial \dot{x}^i}. \quad (28)$$

These constitute a basis for the horizontal and vertical tangent bundles over the slit tangent bundle:

$$\mathcal{H}_{(x,\dot{x})}^* \text{TM} = \text{span} \left\{ \frac{\delta}{\delta x^i} \Big|_{(x,\dot{x})} \right\} \quad \text{and} \quad \mathcal{V}_{(x,\dot{x})}^* \text{TM} = \text{span} \left\{ \frac{\partial}{\partial \dot{x}^i} \Big|_{(x,\dot{x})} \right\}. \quad (29)$$

Their direct sum yields the complete tangent bundle

$$\text{TTM}_{(0)} = \mathcal{H}^* \text{TM} \oplus \mathcal{V}^* \text{TM} \quad (30)$$

pointwise. By the same token one considers the horizontal and vertical basis covectors,

$$dx^i \quad \text{and} \quad \delta \dot{x}^i \stackrel{\text{def}}{=} d\dot{x}^i + N_i^j(x, \dot{x}) dx^j, \quad (31)$$

yielding the corresponding horizontal and vertical cotangent bundles:

$$\mathcal{H}_{(x,\dot{x})}^* \text{TM} = \text{span} \left\{ dx^i \Big|_{(x,\dot{x})} \right\} \quad \text{and} \quad \mathcal{V}_{(x,\dot{x})}^* \text{TM} = \text{span} \left\{ \delta \dot{x}^i \Big|_{(x,\dot{x})} \right\}. \quad (32)$$

such that

$$\text{T}^* \text{TM}_{(0)} = \mathcal{H}^* \text{TM} \oplus \mathcal{V}^* \text{TM} \quad (33)$$

pointwise.

The above vectors and covectors satisfy the following duality relations:

$$dx^i \left(\frac{\delta}{\delta x^j} \right) = \delta^i_j \left(\frac{\partial}{\partial \dot{x}^i} \right) = \delta^i_j \quad \text{and} \quad dx^i \left(\frac{\partial}{\partial \dot{x}^i} \right) = \delta \dot{x}^i \left(\frac{\delta}{\delta x^i} \right) = 0. \quad (34)$$

Incorporating a natural scaling so as to ensure zero-homogeneity with respect to \dot{x} (so that it indeed represents orientation rather than "velocity") we conclude that

$$\text{TTM}_{(0)} = \text{span} \left\{ \frac{\delta}{\delta x^i}, F(x, \dot{x}) \frac{\partial}{\partial \dot{x}^i} \right\}, \quad (35)$$

and similarly

$$\text{T}^* \text{TM}_{(0)} = \text{span} \left\{ dx^i, \frac{\delta \dot{x}^i}{F(x, \dot{x})} \right\}. \quad (36)$$

The so-called *Sasaki metric* furnishes the slit tangent bundle with a natural Riemannian metric:

$$g(x, \dot{x}) = g_{ij}(x, \dot{x}) dx^i \otimes dx^j + g_{ij}(x, \dot{x}) \frac{\delta \dot{x}^i}{F(x, \dot{x})} \otimes \frac{\delta \dot{x}^j}{F(x, \dot{x})}. \quad (37)$$

Cartan tensor

Finsler geometry

axiomatics

Finsler metric: $F^2(x, \xi) = g_{ij}(x, \xi) \xi^i \xi^j \Leftrightarrow g_{ij}(x, \xi) = \frac{1}{2} \partial_{\xi^i} \partial_{\xi^j} F^2(x, \xi)$

Riemannian limit: $F^2(x, \xi) = g_{ij}(x) \xi^i \xi^j \Leftrightarrow g_{ij}(x) = \frac{1}{2} \partial_{\xi^i} \partial_{\xi^j} F^2(x, \xi)$

distance: $d(x_1, x_2) = \inf \left\{ \int_{\gamma} F(\gamma(t), \dot{\gamma}(t)) dt \mid \gamma \in C^1([t_1, t_2], \mathbb{R}^3), \gamma(t_1) = x_1, \gamma(t_2) = x_2 \right\}$

Cartan tensor: $C_{ijk}(x, \xi) = \frac{1}{2} \partial_{\xi^k} g_{ij}(x, \xi) = \frac{1}{4} \partial_{\xi^i \xi^j \xi^k} F^2(x, \xi)$

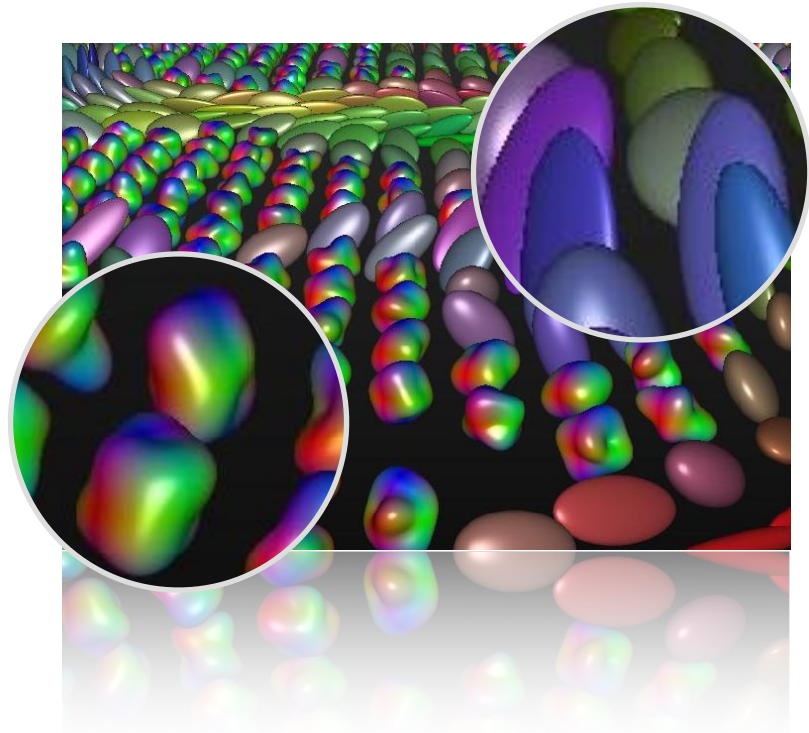
Riemannian limit: $C_{ijk}(x, \xi) = 0$ (Deicke's Theorem)

Finsler geometry

axiomatics

Deicke's Theorem:

Space is Riemannian iff the Cartan tensor vanishes.



Finsler-DTI paradigm

geodesic tractography

DTI ~ Riemannian geometry (inner product norm):

$$F^*(x, q) = \sqrt{q^T \mathbf{D}(x) q}$$

$$F(x, y) = \sqrt{y^T \mathbf{D}^{\text{inv}}(x) y}$$



HARDI ~ Finslerian geometry (generalized norm):

$$F^*(x, \lambda q) = |\lambda| F^*(x, q)$$

$$F(x, \lambda y) = |\lambda| F(x, y)$$



Finsler-DTI paradigm

geodesic tractography

$$G_v(v, v) = \|v\|_F^2$$

Finsler metric: lengths

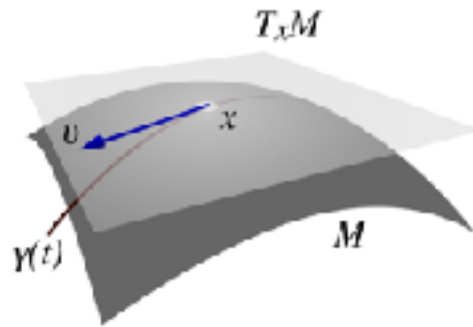
$$\nabla_{\dot{x}} \dot{x} = 0$$

Chern-Rund (or other) connection: parallel transport

$$\ddot{x}^i + \sum_{jk} \Gamma_{jk}^i(x, \dot{x}) \dot{x}^j \dot{x}^k = 0 \quad \text{formal Christoffel symbols: "pseudo-forces"}$$

Finsler-DTI paradigm operationalization*

- neural fiber bundles correspond to relatively short geodesics in the 3-dimensional ‘horizontal part’ of a 5-dimensional ‘brain space’ furnished with a Finslerian structure
- this Finslerian structure can be inferred from diffusion MRI measurements
- the Finslerian dual metric can be interpreted as a ‘5-dimensional (3x3) DTI’ tensor
- Finsler geometry encompasses Riemannian geometry as a special case
- the Finsler metric admits ∞ d.o.f.’s per spatial point as opposed to 6 d.o.f.’s for the Riemannian limit
- the Finsler-DTI paradigm admits versatile dimensionality reduction in trade-off with acquisition time



* Tom Dela Haije, PhD thesis, May 16 2017, Eindhoven

Finsler-DTI paradigm summary



Finsler function:

$$F^*(x, \lambda q) = |\lambda| F^*(x, q)$$

$$F(x, \lambda y) = |\lambda| F(x, y)$$

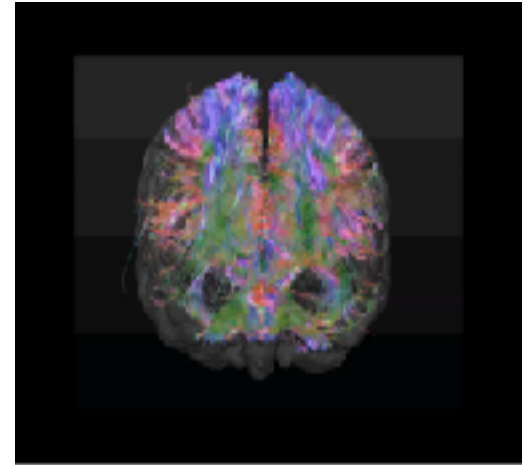
Finsler-DTI paradigm summary



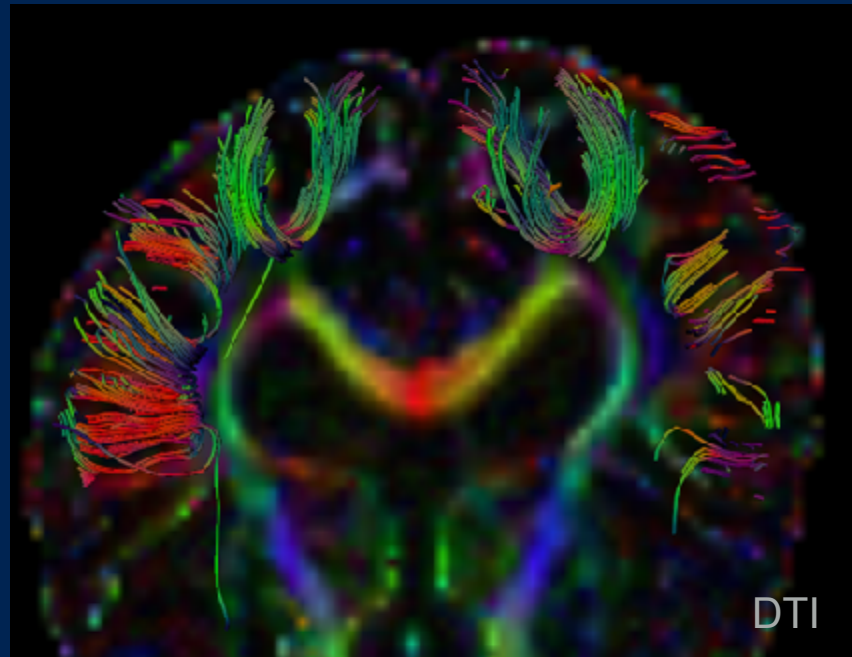
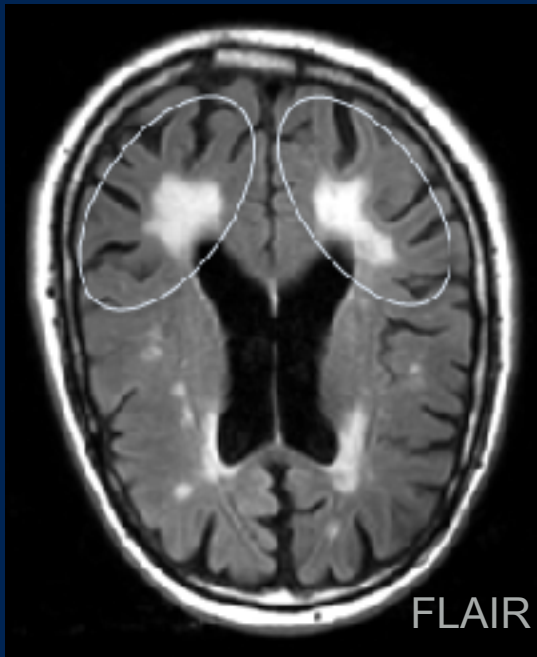
Finsler function:

$$F^*(x, \lambda q) = |\lambda| F^*(x, q)$$

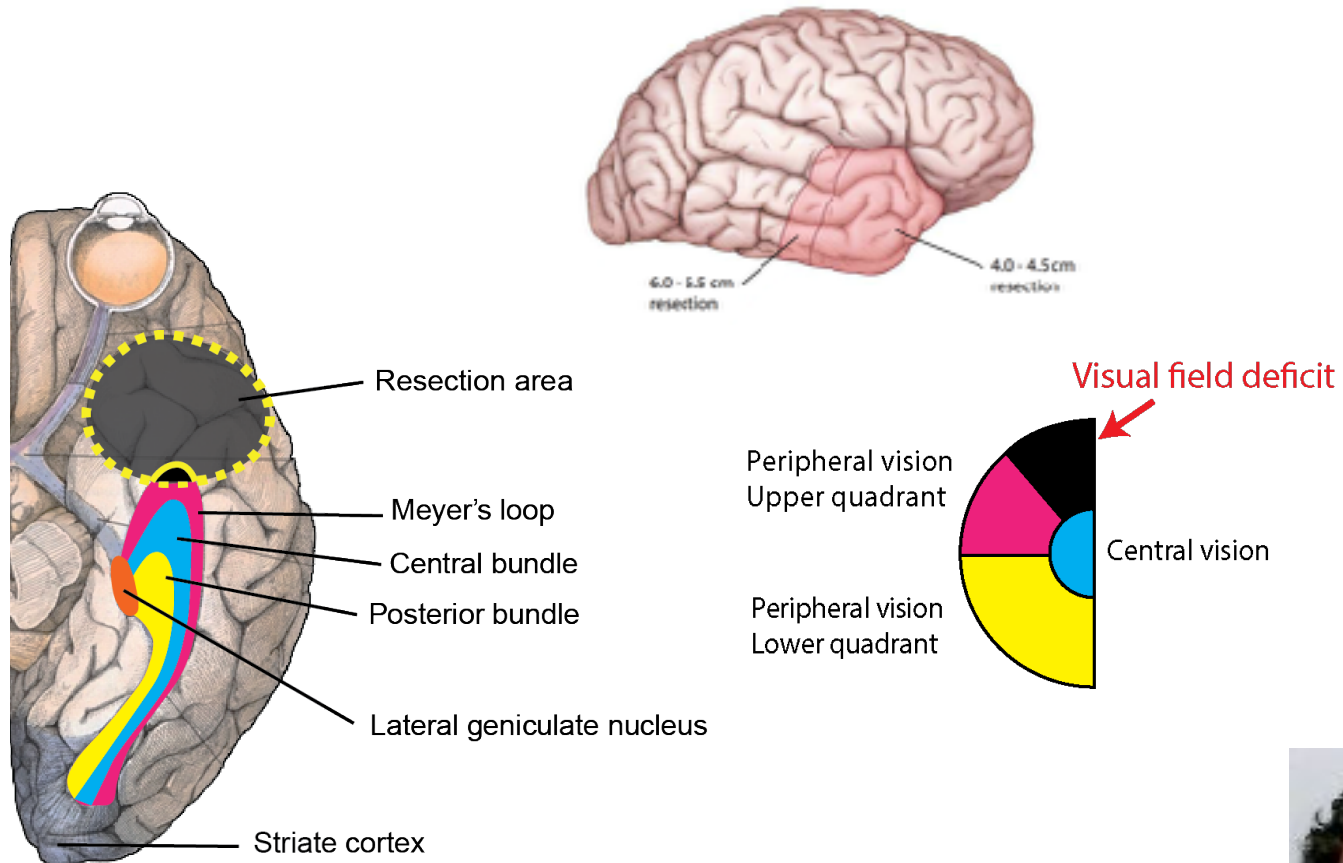
$$F(x, \lambda y) = |\lambda| F(x, y)$$



applications & outlook



applications & outlook

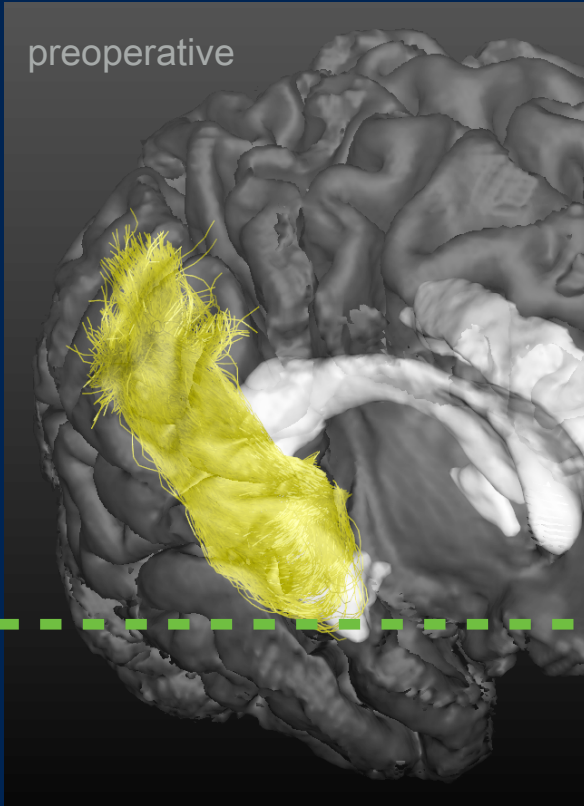


Stephan Meesters et al., electronic poster 3476, ISMRM 2017, Hawaii

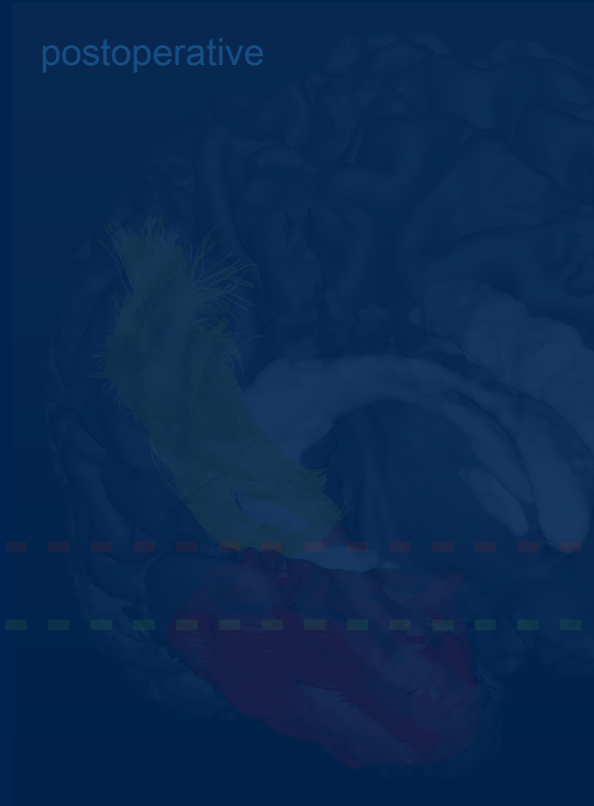


applications & outlook

preoperative

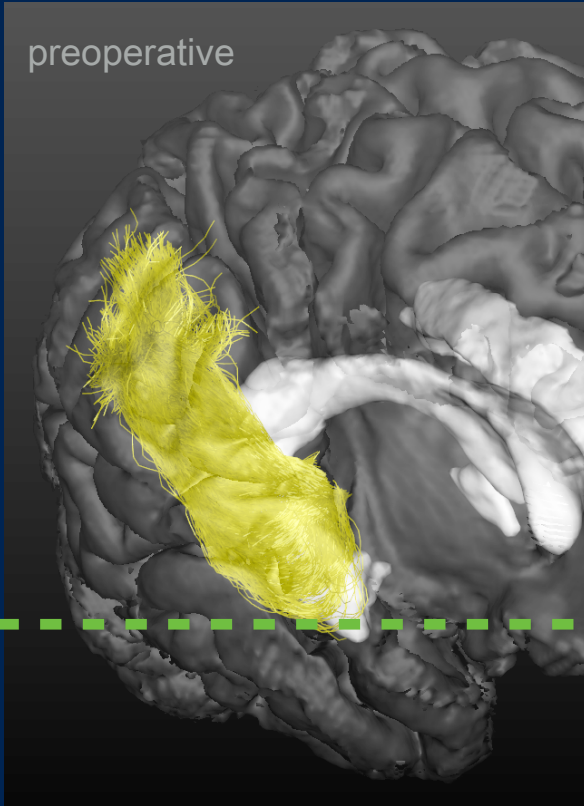


postoperative

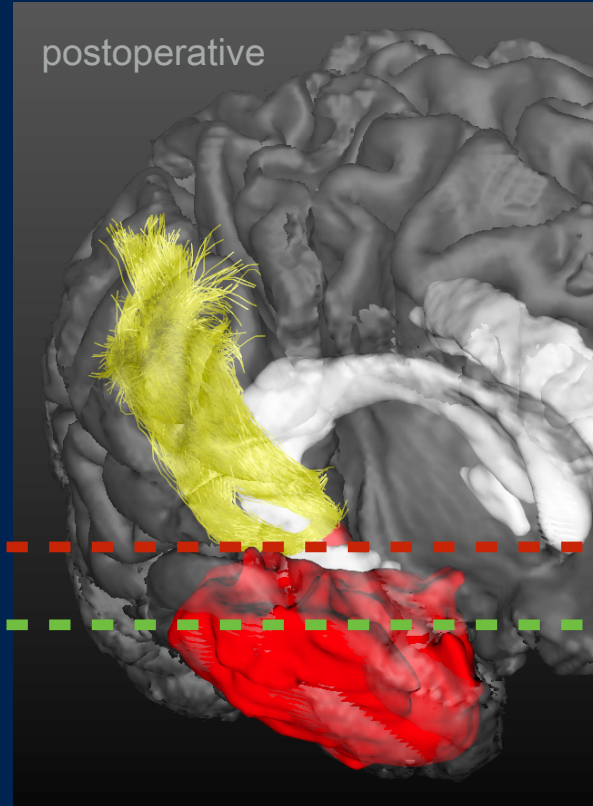


applications & outlook

preoperative

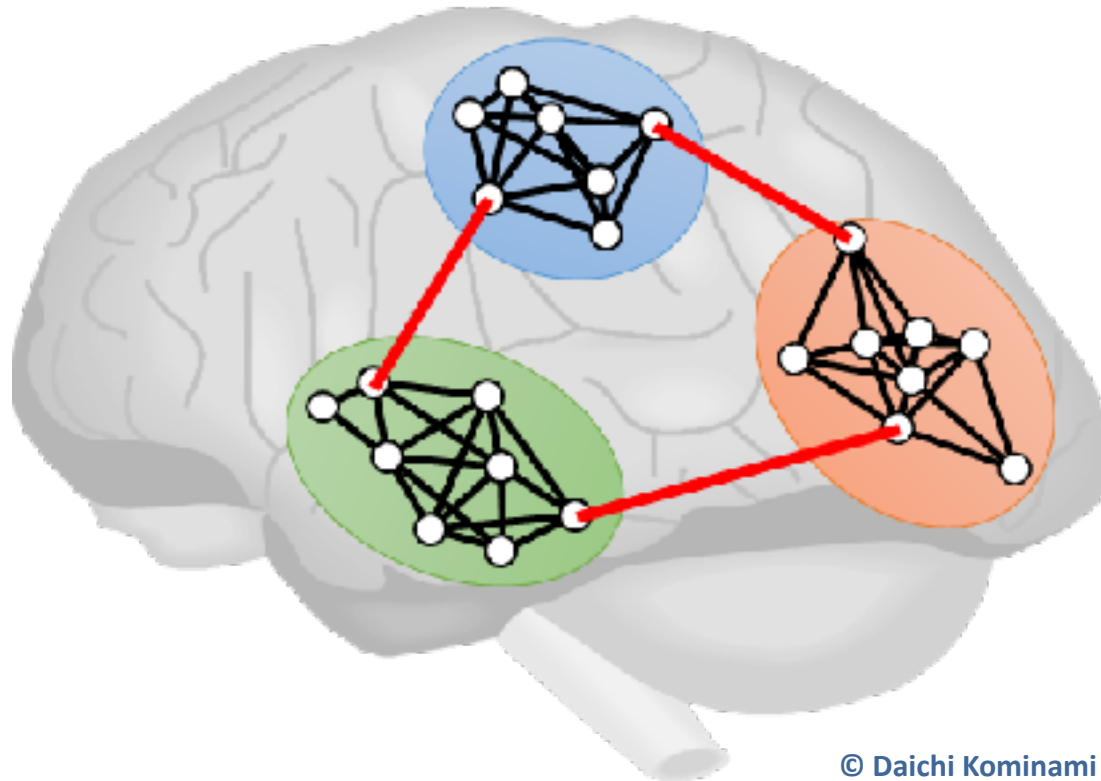


postoperative



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applications & outlook



© Daichi Kominami

conclusion

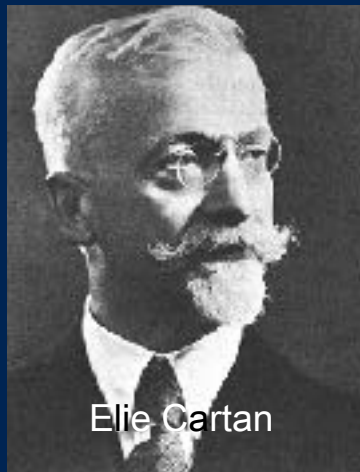
- Finsler geometry is a generic and potentially powerful framework for diffusion MRI beyond classical DTI
- this framework allows us to exploit a rich body of knowledge gained over more than a century by great scientists



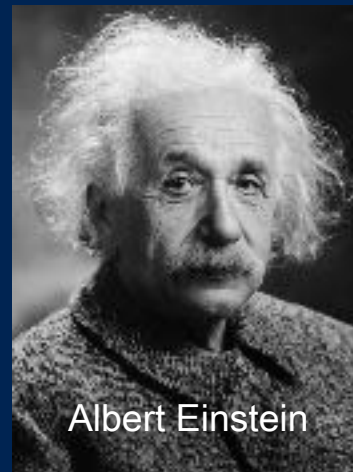
Bernhard Riemann



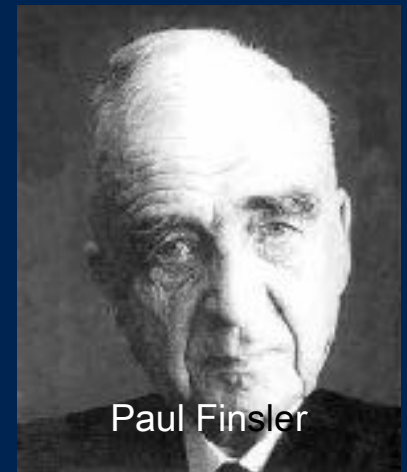
Sophus Lie



Elie Cartan



Albert Einstein



Paul Finsler



