



Avicenna Alliance

Association for Predictive Medicine

Enabling the Medical Digital Twin by advanced mesh morphing and high fidelity patient-specific simulations



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In silico?



Moving the boundaries of in-silico cardiovascular analysis



Agenda

- ► Who are we?
 - ► rbfLAB @University of Rome Tor Vergata
 - ► RBF Morph
- An overview on Digital Twin
- Medical Digital Twin in EC funded Research

Advanced mesh morphing by RBF

- ► MeDiTATe
- Copernicus
- DITAID



- Parametric airways
- ► ROM and SSM
- Conclusions



Who are we? rbfLAB

Department of Enterprise Engineering. Research team **rbfLAB**, Machine Design Group, involved in national and international research projects.













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- rbfLAB focus is on:
 - Structural and fluid dynamic shape optimization (automotive, nautical, aerospace, biomedical).
 - Static and dynamic fluid structure interaction.
 - Advanced use of RBF (image analysis of deformations, flow fields interpolation).
 - Large-scale high-fidelity numerical simulations of flows in complex geometric configurations.
 - Reduced Order Models and Digital Twins.

Who are we? RBF Morph

- RBF Morph is an ISV, pioneer and world-leading provider of numerical morphing techniques and CAE solutions. Inception in 2008 as on-demand solution for a Formula 1 top team
- Start Up founded at the beginning of 2016 to grow the business of the advanced mesh morphing software RBF Morph
- Software line composed by RBF Morph Fluids, Standalone RBF Morph, RBF Morph Structures.
- Technical Partner of ANSYS Inc. since 2009 (OEM since 2012)
- Scale Up stage expanding the market and the offer



- RBF Morph makes the CAE model parametric
- Shape parameters are driven by an orchestrator
- Shape parameters can be used to generate snapshots for real time Digital Twins (ROM/AI)







Who are we?

- Partnership between University of Rome "Tor Vergata" and RBF Morph: academic and industrial synergy
- Multi-sectoral CAE analysts, focused on high fidelity multi-physics problems
- Cutting edge technologies, academic research driven by industrial needs
- Privileged position: clear idea of the direction taken by industry, deep knowledge of the technologies available now and in the next future



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Digital Twin yesterday-today-tomorrow

- Digital Twins are nothing new. Today we talk about DT a lot. But we have experience of DT daily use. ABS / ESP in our car. The Prius Hybrid (year 2004)!
- The governing equations of the physics of the twin were previously written by hand and then embedded in the electronics. Software components made up of great skills (for example vehicle dynamics). Telemetry and racing strategies in Formula 1. Advanced control systems on board the products.

Energy Monitor OUTSIDE TEMP 72'F



Matlab Simulink





Digital Twin yesterday-today-tomorrow

- System integration according to standards (an example are the FMU defined according to the FMI protocol *functional mockup interface*)
- ► Generic purpose IIoT platforms are available
- Twinning of industrial assets intended for the optimization of service, performance and maintenance
- ► GE Predix

"Digital twin eliminates the guesswork when determining the best way to service critical physical assets—from engines to power turbines. Easy access to this unique combination of deep knowledge and intelligence about your assets paves the road to optimization and business transformation."

Colin Parris, Vice President GE Software Research





Digital Twin yesterday-today-tomorrow

- Integration of high fidelity CAE (FEA, CFD, FSI) and system simulation ones (Modelica)
- Combination of AI, Machine Learning and numerical simulation (ROM)
- Hybrid twins combining historic Big Data (when available) with synthetic Big Data by simulation – data fusion
- ANSYS Twin Builder







Digital Twin



- A digital twin is a digital copy of an existing and working physical asset.
- It's connected with the actual state of the asset, remembers its history
- It allows to evaluate more about the current status of the asset.
 Can be used to forecast its evolution



Functional Mock-Up Interface



Avicenna Alliance Webinar



Digital Twin Consortium

dig	ital	twi	n.
-	CONS	ORTIU	M

Founding Members



WORKING GROUPS - INITIATIVES - RE	INITIATIVES - RESOURCES -		
Aerospace & Defense	Definition of a Digital Twin		
FinTech	Global Ecosystem Expansion		
Healthcare & Life Sciences	Glossary of Digital Twins		
Infrastructure	Member Digital Marketplace		
Manufacturing	Open Source		
Natural Resources	Security & Trustworthiness		
Security & Trustworthiness	Use Case Reference Library		
Technology, Terminology & Taxonomy (3T)	Value-Innovation-Platform (VIP)		

https://www.digitaltwinconsortium.org/glossary/glossary.html



Medical Digital Twin

- ► Human body is a very important **physical asset**!
- Medical engineering combines in silico approach with the in vivo and in vitro ones
- CFD simulation of cardiovascular systems, structural simulations of stress acting on prostheses and on tissues, aerodynamic simulation of airways.



- Patient digital twin (Medical Digital Twin) aims at an easy adoption of in silico results in the medical environment (translation).
- Numerical simulation requires high performance computing (HPC) to have real time usage compression methods (ROM, PCA) are key enablers to adopt digital twin in real time
- Medical digital twin requires the fusion of image data and digital images (interactive visualization), the definition of biomarkers and the presentation of the results with tools and language that can be easily understood by the medical staff.
- https://www.avicenna-alliance.com/



Avicenna Alliance Association for Predictive Medicine



Examples of Medical Digital Twin

- Aneurysms prevention and treatment (MeDiTATe project -The Medical Digital twin for aneurysm prevention and treatment)
- Shunting according to the mBTS (FF4EuroHPC project experiment - Cloud-Based HPC Platform to Support Systemic-Pulmonary Shunting Procedures)
- Patient specific airways treatment (FF4EuroHPC project experiment - Digital-Twin for Airflow and Drug Delivery in Human Airways)
- Patient specific spine surgery (Spinner Project -SPINe: Numerical and Experimental Repair strategies)





THE MEDICAL DIGITAL TWIN FOR ANEURYSM PREVENTION AND TREATMENT



Consortium





Research Tracks

- 1. High fidelity **CAE multi-physics** simulation with RBF mesh morphing (FEM, CFD, FSI, inverse FEM).
- 2. Real time interaction with the Digital Twin by **Augmented Reality**, Haptic Devices and **ROM**.
- 3. HPC tools, including GPUs, and cloud-based paradigms for **fast and automated CAE processing** of clinical databases.



- 4. Big Data management for population of patients imaging data and high fidelity CAE twins.
- 5. Additive Manufacturing of **physical mock-up** for surgical planning and training.



Early Stage Researchers https://meditate-project.eu/early-stage-reserachers/





Individual Research Projects

https://meditate-project.eu/phd-projects/





The Anatomy and the Clinical Problem



The **criterion** to perform **ascending aortic aneurysm surgery** is currently based only on the evaluation of the ascending aorta **diameter**.







[1] Leonard N.Girardi, MD, Operative Techniques in Thoracic and Cardiovascular Surgery



Digital Twin and Real Time Simulation

Creating a workflow to go from images to simulation results in a few seconds





Endovascular Abdominal Aneurysm Repair





Endovascular Abdominal Aneurysm Repair





FF4EuroHPC



InSilicoTrials

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Copernicus

Cloud-based HPC platform to support systemicpulmonary shunting procedures

Fondazione Monasterio la ricerca che cura RIA CINECA



This project has received funding from the European High-Performance Computing Joint Undertaking Joint Undertaking (JU) under grant agreement No 951745. The JU receives support from the European Union's Horizon 2020 research and innovation programme and Germany, Italy, Slovenia, France, Spain.



The Problem

- Congenital heart diseases (CHDs) account for nearly one-third of all congenital birth defects and 7th cause of death in children younger than 1 year in 2017.
- Without the ability to alter the prevalence of CHD, interventions and resources must be focused to **improve survival** and **quality of life**.
- The Modified Blalock Taussig Shunt (mBTS) is a common palliative operation on cyanotic heart diseases, but it is associated with significant mortality (~7,2%).





Experiment Approach & Expected Outcome

- The Copernicus application aims to provide an interactive Medical Digital Twin (MDT) of the patientspecific district to support the surgery planning of mBTS under critical conditions.
- The procedure was designed considering advanced numerical means with the objective to deploy MDT within ~48hh.



Proposed solution

J J J EuroHPC



Proposed solution

Available POM:	Views. Parts J CutPlane0
Available ROM.	
⊻ velocity	velocity
	Velocity Magnitude (m/s)
Delete Bename	1.74
and a second sec	1.59
ROM Information	
Name : velocity	1.31
Parameters: 12	1.16
Learning Snapshots : 120	1.02
Modes: 18	0.873
Version : 2022R1	0.729
	0.584
Export to Twin builder	0.44
	0.296
Evaluate Roms	0.151
Parameter Value	
di 1 vol	





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Delft University of Technology



DiTAiD - A digital twin for airflow and inhaled drug delivery in human airways

The digital twin

- The developed digital twin can:
 - Provide similar results compared to CFD simulations
 - ✓ Keeping a good level of detail
 - Provide patient specific results within minutes compared to weeks
- The digital twin is created by combining a large number of CFD simulations (snapshots) using Reduced Order Modelling (ROM) techniques

From lung scan to medical use



Lung geometry definition

Base geometry is obtained from literature

- ✓ Constructed from several high-resolution CT scans of 47 year old healthy volunteer
- ✓ The base geometry has been studied in multiple experimental and numerical studies
- ✓ Includes up to the 4th generation (note, human lungs go up to 23 generations)
- Identify relevant input parameters for the digital twin
 - ✓ Shape
 - ✓ Flow
 - ✓ Particle

Z. Zhang, C. Kleinstreuer and S. Hyun, "Size-change and deposition of conventional and composite cigarette smoke particles during inhalation in a subject-specific airway model," *Journal of Aerosal Science*, vol. 46, pp. 34-52, 2012.
S. Kenjereš and J. L. Tjin, "Numerical simulations of targeted delivery of magnetic drug aerosols in the human upper and central respiratory system: a validation study," *Royal Society Open Science*, vol. 4, no. 12, p. 170873, 2017.



Identify shape parameters



- Potentially a huge amount of shape parameters!
- Amount of input parameters is limited by assuming:
 - ✓ Circularity is kept constant
 - ✓ Only considered angle is the branching angle
 - ✓ Diameter follows a fixed ratio6 of h=0.79
- Mouth-throat part: 3 parameters
- Lower airways: 23 parameters
 - ✓ Generation 0 (trachea): 1L, 1D, 1A
 - ✓ Generation 1: 2L, 2A
 - ✓ Generation 2: 4L, 4A
 - ✓ Generation 3: 8L



T. Van de Moortele et al.; "Morphological and functional properties of the conducting human airways investigated by in vivo computed tomography and in vitro MRI"



	Diameter Length [mm]		Branching	
Generation	[mm]	Left	Right	angle [deg]
0 (Trachea)	15 - 20	100 -	- 120	80 - 95
1		51 - 57	24 - 28	75 - 90
2		12 - 16	15 - 28	65 - 95
3		7 - 10	7 - 10	55 - 70

Identify flow & particle parameters

Physical parameters: 3 parameter

- ✓ Flow rate varies between 15 L/min and 120 L/min
- \checkmark Particle size varies between 0.1 µm and 10 µm
- Particle injection rate varies between 0 m/s and 10 m/s

26 shape parameters and 3 physical parameter

29 input parameters in total



Parametric study

- Design Of Experiments (DOE) table is generated:
 - \checkmark For the 29 input parameters
 - ✓ Using the Latin Hypercube Sampling for optimal spacing
 - ✓ Creating 1000 design points
- Fluent settings validated in literature
 - ✓ Steady state
 - ✓ RANS, transitional SST (4eq)
 - \checkmark Particles are one-way coupled



Results: Velocity



Results: Particle deposition





Results: interactive model













- Radial Basis Functions (RBF) were introduced as interpolators of scattered data in sixties. Usually the interpolation is comprised of:
 - A sum of weighted radial interactions
 - A polynomial correction
- ▶ RBF are commonly used to interpolate a scalar function defined in a multi-dimensional space ($\mathbb{R}^n \to \mathbb{R}$)

$$s(\mathbf{x}) = \sum_{i=1}^{N} \gamma_i \cdot \varphi(||\mathbf{x} - \mathbf{x}_{k_i}||) + h(\mathbf{x})$$

Source points
Evaluation point Polynomial
Radial interaction function
Weights of sources
Scalar function at evaluation point













- The weights of the RBF are computed using regression/interpolation:
 - From scalar values at source points
 - From scalar values at fit points
- ► RBF fit (known as RBF training):
 - Solving a linear system (interpolation)
 - ► Using Least Squares





RBF with global support

- ► Far field interactions
- Dense system of equations to be solved

RBF with compact support

- Local interactions
- Sparse systems of equations to be solved

RBF with global support	arphi(r)		
Spline type (R _n)	r^n , n odd		
Thin plate spline (TPS _n)	$r^n \log(r)$, n even		
Multiquadric (MQ)	$\sqrt{1+r^2}$		
Inverse multiquadric (IMQ)	$\frac{1}{\sqrt{1+r^2}}$		
Inverse quadratic (IQ)	$\frac{1}{1+r^2}$		
Gaussian (GS)	e^{-r^2}		
RBF with compact support	$\varphi(r) = f(\xi), \xi \le 1, \xi = \frac{r}{R_{sup}}$		
Wendland C ^o (CO)	$(1-\xi)^2$		
Wendland C ² (C2)	$(1-\xi)^4(4\xi+1)$		
Wendland C ⁴ (C4)	$(1-\xi)^6 \left(\frac{35}{3}\xi^2 + 6\xi + 1\right)$		

 $\varphi(r) = r$









- Scalar Function values g_{si} known at sources x_{si}
- Orthogonality condition
- ► Linear polynomial

$$s(\boldsymbol{x_{s_i}}) = g_{s_i}, 1 \le i \le N$$

$$\sum_{i=1}^{N} \gamma_i p(\boldsymbol{x}_{\boldsymbol{s}_i}) = 0$$

$$h(\boldsymbol{x}) = \beta_1 + \beta_2 x + \beta_3 y + \beta_4 z$$

$$\sum_{i=1}^{N} \gamma_i = \sum_{i=1}^{N} \gamma_i x_{k_i} = \sum_{i=1}^{N} \gamma_i y_{k_i} = \sum_{i=1}^{N} \gamma_i z_{k_i} = 0$$



- Linear system to be solved for the computation of unknown coefficients
- System matrix
 - Constraint matrix P_s
 - Interpolation matrix **M**

$$M_{ij} = \varphi\left(\left\| \boldsymbol{x_{s_i}} - \boldsymbol{x_{s_j}} \right\|\right), 1 \le i \le N, 1 \le j \le N$$

Ρ



Radial Basis Functions for mesh morphing

- Radial Basis Functions (RBF) can be used to drive mesh morphing (smoothing) from a list of source points and their displacements.
 - Surface shape changes (exact nodes control)
 - ► Volume mesh smoothing.
- RBF are recognized to be one of the best mathematical tool for mesh morphing.

$$\begin{cases} s_{x}(\boldsymbol{x}) = \sum_{i=1}^{N} \gamma_{i}^{x} \varphi(\|\boldsymbol{x} - \boldsymbol{x}_{s_{i}}\|) + \beta_{1}^{x} + \beta_{2}^{x} \boldsymbol{x} + \beta_{3}^{x} \boldsymbol{y} + \beta_{4}^{x} \boldsymbol{z} \\ s_{y}(\boldsymbol{x}) = \sum_{i=1}^{N} \gamma_{i}^{y} \varphi(\|\boldsymbol{x} - \boldsymbol{x}_{s_{i}}\|) + \beta_{1}^{y} + \beta_{2}^{y} \boldsymbol{x} + \beta_{3}^{y} \boldsymbol{y} + \beta_{4}^{y} \boldsymbol{z} \\ s_{z}(\boldsymbol{x}) = \sum_{i=1}^{N} \gamma_{i}^{z} \varphi(\|\boldsymbol{x} - \boldsymbol{x}_{s_{i}}\|) + \beta_{1}^{z} + \beta_{2}^{z} \boldsymbol{x} + \beta_{3}^{z} \boldsymbol{y} + \beta_{4}^{z} \boldsymbol{z} \end{cases}$$



- ► Surface segmentation
- Hierarchical tree structure
- Full automatic morphing via Python script
- Stand Alone RBF Morph API
- Final volume morphing on the baseline CFD model (could be a different mesh)





• Offset to control the diameter





Rotation and translation to control shape and lenghts





Mesh statistics for explored shapes



REAL-TIME SIMULATION



REDUCED ORDER MODELING



 \checkmark

 \checkmark



- Considering 26 shape parameters.
- Based on grid transformations using radial basis function (RBF) mesh morphing.
- Executed on both surface and volume meshes.
- Correctly validated.

- Combining 26 shape parameters + 3 physical parameters.
- Implemented for parameters of clinical interest:
 - Accretion rate
 - Pressure
 - Turbulent kinetic energy
 - Velocity
 - Wall shear stress
- *Partially* validated.

 \checkmark

 \checkmark

 \checkmark

MODEL ORDER REDUCTION



ROM ERRORS

(1) The Reduction Relative error represents the mean error projection of the vectors used to calculate the r modes (SVD).

 $\|M-M_r\|$

|M|

Reduction Relative error

$$\frac{\sum_{i=r+1}^{n}\sigma_i^2}{\sum_{i=1}^{n}\sigma_i^2} \qquad (1)$$

The number of shape modes used should be selected according to (1)

In other words, it is the error that is made in using a small number r of modal components.

(2) The other error is the ROM relative error which is the difference between the high-fidelity snapshot X_{ref} and the ROM-built snapshot X_{ROM} .

ROM relative error =
$$\frac{||X_{ref} - X_{ROM}|}{||X_{ref}||}$$

ROM validation should be performed on the excluded snapshots using (2)

The ROM relative error therefore also takes projection errors into account.

GEOMETRIC REDUCED ORDER MODEL(s)

If 200 snapshots are used: 1 hour of calculation for the building.

The leave-one-out (LOO) cross-validation demonstrates that ROM is able to correctly represent new unseen shapes.



960 snapshots are used: 12 hours of calculation for the building.





Conclusions



- Medical Digital Twins are feasible today!
- The In Silico path, i.e. MDT driven by high fidelity simulations, is ready and requires
 - Patient specific data (from images)
 - State of the art multi-physics simulation
 - Reduced order models and advanced mesh morphing
- ► A clear **business model** is required
 - Public funds are today the major resource
 - Certification is complex
- We are moving in the right direction and there is mainstream focus on Medical Digital Twins







Next steps? New RBF Morph Stand Alone



- ► To be released in 2024
- ► Read in STL, STEP
- Unity OpenCascade
- Solver independent process that supports many mesh formats
- Scriptable via python



Next steps? AR/VR







Thank you!

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TOR VERSITÀ DEGLI STUDI DI ROMA

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