# **Development of an analytical model to predict<br>
Self-folding of 4D bioprinted scaffolds<br>
Alessio Esposito<sup>1</sup>, Irene Chiesa<sup>1</sup>, Claudia Dell'Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br>** *Department of Information Engin* The partment of an analytical model to predict<br>
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Alessio Esposito<sup>1</sup>, Irene Chiesa<sup>1</sup>, Claudia Dell'Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup>

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alessio Esposito', Irene Chiesa', Claudia Dell'Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br> *Department of Information Engineer* **Development of an analytical model to**<br> **Self-folding of 4D bioprinted scaff**<br>
Alessio Esposito<sup>1</sup>, Irene Chiesa<sup>1</sup>, Claudia Dell'Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmel<br> *Department of Information Engineering and Research Ce* chosen because it can mimic several anatomical structures, such Control Control Control Control Control Control (Abstract—Four Dimensions of Three Dimensions of the supporties the appropriate models and approach which adds the fourth dimension "time" at the three appropriate modelling

Keywords-4D printing, bioprinting, modelling, neural stem cells.

**4** D printing is a fabrication technique that increases shape is linked to the evidence that capabilities and application of additive manufacturing have a hollow-cylinder like geom

(AM) adding time dependent shape changing. In general, a as trache, blood vessels and, in particular, the neural turbs, which has the blood vessels and the blood vessels and the particular, the neural turbs are the state of given the turbs are the particular in the constrained will be here modelled through human pluripotent stem cells.<br> *Caryords*—4D printing, bioprinting, modelling, neural stem<br>
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cells.<br>
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L. INTRODUCTION<br>
determinate a different gelatin is<br>  $\leftarrow$ *Keywords*—ID printing, bioprinting, modelling, neural stem<br>
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different gelatin and crossinic concernations that<br>
I. INTRODUCTION<br>
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different gelatin and crossitiver concentrations that<br>
determinate a different of equation of a distinction technique that increases to the folding of the structure prigation This leads<br>
denote the s 1. LITRODUCTION difference of expansion coefficient. This leads<br> **41** princing is a difference of the final system increases that find the final specific streates the tracheal of the section of a lability the section of a **D** primiting is a factor of the device is the folding of the structure ( $\frac{1}{4}$ .) In the anatomic combines in the device interest and angle is the column to control anominal particular and application of additive munif **4D** printing is a fabrication technique that increases shape is linked to the evidence that several anatom<br>
(AM) adding time dependent of additive manifacturing have a hollow-cylinder like geometry, as example<br>
(AM) addi given by shape memory hydrogels, which have been used to (AM) adding time dependent shape changing. In general, a vessels, nerves and traches. Additionally, this particular<br>
4D primed structure is defined as a 3D printed structure that movement is present in the neural ube form 4D principle structure is defined as a 3D principle structure that movement is present in the aenual the formation during<br>dcharges shape, function and properties because of a predefined compropries i§). The developmental changes shape, function and properties because of a predefined<br>
enchrypsgenesis [8]. The developmental process of neutral<br>
external simulates [1]. Active materials are at the base of 4D involves a series of coordinated mo external stimulus [1]. Active materials are at the base of 4D involves a series of coord<br>primting. They can change their properties in a predefined way embry<br>ogenesis, which reaching the properties that the application of shape changing. An example is the study of Hendrikson et al. after the application of an external sitmulus ( $e_g$ , variation of<br>mositure application of an external sitmulus ( $e_g$ , variation of<br>mositure and electromorphical energy in the produced based on the spatial arrangement of t moisture, pH, temperature and electromagnetic field). Thus, tube, the primordium of the entire central<br>by combining different materials in a specific spatial (CNS) (Fig. 1). Failure during neutral<br>distribution it is possi by combining different materials in a specific squalid (CNS) (Fig.1). Failure during neural tions distinuition it is possible to achieve the desired change of the constrained particular and the stretch that constrained pa distribution it is possible to achieve the desired change of the defects, main cause of sever neurodevelopmental particular stretching in the spatial arangement of in human [9]. Here, the 4D bioptimed self-folding the sma

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Sension Sposito<sup>1</sup>, Irene Chiesa<sup>1</sup>, Claudia Dell'Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br>** *Department of Information Engine* prince cell growth and differentiation. In this work, we<br>developed to predict the shape changing of planar bilayer<br>developed an analytical model to predict, in space, the movement structures that turn in tubular ones (i.e Development of an analytical model to predict<br>
self-folding of 4D bioprinted scaffolds<br>
self-folding and the movement of hybronical changes and Research Center Enrico Plaggio, University of Pisa, haty<br>
logarithment of hyb **Development of an analytical model to predict<br>
self-folding of 4D bioprinted scaffolds<br>
self-folding to the charactery, Marco Onorati, Carmelo De Maria<br>** *Charmactery, Marco Hanga Bearath Cramelo De Maria<br>
Department of H* **Development of an analytical model to predict<br>
self-folding of 4D bioprinted scaffolds<br>
self-folding to the specific shape change change changes and the specific shape of the specific shape change changes and the specifi** as trachea, blood vessels and, in particular, the neural tube, which<br>lines at lower concentration, that were 4D printed on top of the will be here modelled through human pluripotent stem cells.<br>casted gelatin film. Dipping these structures in a water-based Esposito<sup>1</sup>, Irene Chiesa<sup>1</sup>, Claudia Dell'Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De<br> *arment of Information Engineering and Research Center Enrico Piaggio. University of Pisa, 1<br>
<sup>2</sup>Unit of Cell and Developmental Biology, D* D printing is a fabrication technique that increases shape is linked to the evidence that several anatomical parts **Abstract—Controlled through line as a standard structure in the structure is defined as a standard properties of the structure in the s** external stimulus [1]. Active materials are at the base of 4D involves a series of coordinated morphological events during approach which adds the fourth dimensions "fine the three incomparison consults in a colling to the stage change in a properties in a properties in a properties incolling of the shape change in specific ture change tis ha spaint dimensions of Three-Dimensional (3D) printing, A 4D responsible printed object can change its shape and function in these shape, matrix predict from Figure and properties and interior an appropriate stimulus (stimu moisture, pH, temperature and electromagnetic field). Thus, tube, the primordium of the entire central nervous system an appropriate simulus. All printing finds application in tissue and propriate the several particle of the several variables that are entangled in the principal propriate of the principal process particle of the system pr engineering and the finder distribution. Letecht, the change in shape of  $\sim$ the desired change of the change of the change of the control of the state of t structure of the mean intervention of a different mean in the spatial are the state of the state of the structure of th However the system with the measure and the measure with the system and the prediction of the system of the s decreased an analytical material pattern and pattern specific since the specific state in a specific state of the perform of pattern with the perform is a state of the specific shape that the specific pattern with the spec one. This meetifie shape change correct to averidable the specific shape may be the specific shape than the specific shape that a set application of the set application of the set application of the application of the appl debate heat painties everal anatomical structures such cases because the content of the veral of the stationary and the stationary and the because of the method of the station of the station of the station of the station o <sup>1</sup><br> **ytical model to predict**<br> **ioprinted scaffolds**<br>
Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br> *h Center Enrico Piaggio, University of Pisa, Italy*<br> *arment of Biology, University of Pisa, Italy*<br>
adhesion [6]. Al appropriate modelling of the shape changing phenomenon. A model is needed to predict the final geometry once the initial **ytical model to predict**<br> **ioprinted scaffolds**<br> **ioprinted scaffolds**<br> **Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br>** *h Center Enrico Piaggio, University of Pisa, Italy***<br>** *athesion* **[6]. All these applications are on** due to the several variables that are entangled in the 4D <sup>1</sup><br> **ytical model to predict**<br> **ioprinted scaffolds**<br> **Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br>** *An Center Enrico Piaggio, University of Pisa, Italy***<br>** *athreent of Biology, University of Pisa, Italy***<br>
adhesion [6]** <sup>1</sup><br> **ytical model to predict**<br> **ioprinted scaffolds**<br> **amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br>** *h Center Enrico Piaggio, University of Pisa, Italy***<br>** *arment of Biology, University of Pisa, Italy***<br>** *adhesion* **[6]. ytical model to predict**<br> **ioprinted scaffolds**<br> **structures**<br> **i** Center Enrico Piaggio, University of Pisa, Italy<br>  $h$  Center Enrico Piaggio, University of Pisa, Italy<br>  $h$  Center Enrico Piaggio, University of Pisa, It **ytical model to predict**<br> **ioprinted scaffolds**<br> **Amico**<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br> *h Center Enrico Piaggio, University of Pisa, Italy*<br> *athenent of Biology, University of Pisa, Italy*<br>
adhesion [6]. All are homogeneous films of gelatin (fabricated by solvent casting, using an applicator) at high concentration with parallel **ytical model to predict**<br> **ioprinted scaffolds**<br> **Samico**<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br> *h Center Enrico Piaggio, University of Pisa, Italy*<br> *athenent of Biology, University of Pisa, Italy*<br>
adhesion [6]. A **COPY CONTROM SET ASSET CONTROM SET AS A SET AND A MARGE SCALL A MODE POSTABLE A MORE FURNIC AND A MORE FURNIC AND A MORE FURNIC AND A MORE AND A MORE AND A MORE AND A MORE AND A Suppression (6). All these applications ar** solution, the two layers absorb water differently, due to the **1ODTIINTECI SCATTOIIGS**<br>
Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br> *h Center Enrico Piaggio, University of Pisa, Italy*<br> *artment of Biology, University of Pisa, Italy*<br>
artment of Biology, University of Pisa, Ita **Amico<sup>2</sup>**, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br>
Ancientrico Piaggio, University of Pisa, Italy<br>
artment of Biology, University of Pisa, Italy<br>
artment of Biology, University of Pisa, Italy<br>
adhesion [6]. All these appl Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br>*h Center Enrico Piaggio, University of Pisa, Italy*<br>*turnent of Biology, University of Pisa, Italy*<br>adhesion [6]. All these applications are only possible with an<br>model is Amico<sup>2</sup>, Marco Onorati<sup>2</sup>, Carmelo De Maria<sup>1</sup><br>*h Center Enrico Piaggio, University of Pisa, Italy*<br>*tartment of Biology, University of Pisa, Italy*<br>*athesion* [6]. All these applications are only possible with an<br>approp have a hollow-cylinder like geometry, as examples: blood vessels, nerves and trachea. Additionally, this particular movement is present in the neural tube formation during *Emeral of* (3. All these applications are only possible with an adprooming (1. All these applications are only possible with an appropriate modelling of the shape changing phenomenon. A model is needed to predict the fin adhesion [6]. All these applications are only possible with an appropriate modelling of the shape changing phenomenon. A model is needed to predict the final geometry once the initial shape, material properties and intensi appropriate modelling of the shape changing phenomenon. A model is needed to predict the final geometry once the initial shape, material properties and intensity of stimulus are known, shape, material properties and inten riched is needed to predict the final geometry once the initial shore, material properties and intensity of stimulus are known, shape, material properties and intensity of stimulus are known, due to the several variables shape, material properties and intensity of stimulus are known,<br>due to the several variables that are entangled in the 4D<br>primiting process [7]. In this study, an analytical model is<br>developed to predict the shape changin due to the several variables that are entangled in the 4D<br>printing process [7]. In this study, an analytical model is<br>developed to predict the shape changing of planar bilayer<br>structures that turn in tubular ones (*i.e.*, printing process [7]. In this study, an analytical model is<br>developed to predict the shape changing of planar bitlayer<br>structures that turn in tubular ones (i.e., self-folding) after<br>immersion in a water solution. More in developed to predict the shape changing of planar bilayer<br>structures that turn in tubular ones (i.e., self-folding) after<br>tructures in the more involution. More in detail, these structures<br>immersion in a water solution. Mo structures that turn in tubular ones  $(i.e., \text{ self-folding})$  after<br>immersion in a water solution. More in detail, these structures<br>are homogeneous films of gelatin (fabricated by solvent<br>casting, using an applicator) at high concent usability in a biological environment. Fig. 1: a) Neurulation process [10]. b) Folding of produced mental in the current in the common diversion of the film the conversion of the film proposensis, which result in the conversion of the film proposensis, which re



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II. MATERIAL AND METHODS<br>
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A. *Geometry definition and known models* torques are in equili<br>
The geometry to be modelled, can be schematized as a<br>
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The geometry to be modelled, can be schematized as a<br>
parallelepiped with a series of smaller parallelepipeds on its<br>
top (Fig.2).



II. MATERIAL AND METHODS<br>
Since no external forces are present, internal force<br>
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(Fig.2).<br>
(Fig.2).<br>
The most used analysis to predict the bending<br> II. MATERIAL AND METHODS<br>
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torques are in equilibrium (Fig.1 and Fig.2).<br>
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A. *Geometry definition and known models*<br>
torques are in equilibrium (Eq.1 and Eq.2):<br>
The geometry to be modelled, can be schematized as a<br>  $P_1' + P_1'' = P_2 = P$  (1)<br>  $\frac{P_1}{P_2P_3}$ .<br>
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torques are in equilibrium (Eq.1 and Eq.2):<br>
The geometry to be modelled, can be schematized as a<br>
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Since no external forces are present, internal for<br>
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odelled, can be schematized as a<br>  $P_1' + P_1'' = P_2 = P$  (1)<br>  $\frac{P_1}{P_1} + \frac{P_2}{P_2$ 11. MATENIAL AND METHODS<br>
4. Geometry definition and known models<br>  $F_4$  and Eq.2).<br>
The geometry to be modelled, can be schematized as a<br>
parallelepiped with a series of smaller parallelepipeds on its<br>
from geometry to A. Geometry definition and known models<br>
The geometry to be modelled, can be schematized as a<br>
paralleleipped with a series of smaller paralleleippeds on its<br>  $P_1' + P_1'' = P_2 = P$ <br>  $\downarrow$ <br>  $\uparrow$  ( $\uparrow$  if  $\uparrow$  if  $\uparrow$  if  $\$ geometric parameters (e.g., moment of inertia of section,  $\mu$ <br>thickness of layers, number and dimension of printed lines), The geometric be modelled, can be schematized as a<br>parallelepiped with a series of smaller parallelepipeds on its<br>top (Fig.2).<br>
Fig.2: Five of modelled geometry<br>
Thig.3: Geometrical parameter and acting force<br>
of a bilaye parallelepped with a sense of smaller paralleleppeds on its<br>
coefficient).<br>
Fig.2: For of modelled geometry<br>
Fig.2: Geometrical parameter and acting force on the strict<br>
of the higher structure is the Timeshenko developed Fig.2: View of modelled geometry<br>
In literature, the most used analysis to predict the bending<br>
In literature is the Timoshenko's model [11]. In 1925<br>
Timoshenko developed a model that can predict the bending<br>
dimension, Fig. 2: Here of model and physical power is the filmer the lines of the starting power of the starting force on the simulation of principal and bigger strating force on the simulation of a bigger starting in the particula Fig. 2: Fine of modelled geometry<br>
Fig. 3: Geometrical parameter and acting force on the structure, before an<br>
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of developed a model t Fig. 2: Plev of modella geometry<br>
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are the most used anomalous to predict the bending<br>
structure is the Timoshenko's model [11]. In 1925<br>
Structure is the Timoshenko's model [11]. In 1925<br> *Fig.2: Floor of modelled geonetry*<br> *Fig.3: Gromerical parameter and acting force on the structure is the Timoshniko is predict the bending of the stange change change.<br>
transition-the base tased analysis to predict the* are, the most used and yest increase the benchming<br>structure is the Timoshenko's model [11]. In 1925<br>
of developed a model then are predict the radius of<br>
of developed a model then are section to the Fig. 1 and Fig. 2 onl structure is the Timoshenko's model [11]. In 1925<br>
structure is the best and Eq.2 and Eq.2 only two lines of<br>
or developed a model that can predict the radius of<br>
or a bimedal beam once known the section<br>
In the Eq.1 and of developed a model that can precise the readulos of the bending the proper and Fig. 2 only two lines of material 1 are mechanical and physical properties of the used considered. More in general, since we have N printed a bunefit be earn once known the sector<br>
and Fig.1 and Fig.2 only two lines of more and the temperature difference. The model is the Eq.1 and Fig.2 only two lines of method only for beams and in consequence limited to one

need to be done.

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With these hypotheses we can assume that the printed lines Substituting Eq.7 in Eq.6 we obtain Eq.8: create a preferential direction for shape change and this direction in the next sections, the same steps<br>
direction is the same of Fig. Fb to be a constructed one geometry<br>
of Fig. Pb to be<br>
direction in the radius of eurotic ones. In the same steps of Fig. Fig. P<sub>2</sub> = P<sub>2</sub> + P<sub></sub> of Timoshenko's analysis have been applied to the geometry<br>of Fig. b to obtain the radius of curvature as function of<br>geometric parameters (e.g., moment of inertia of section,<br>the  $P * \frac{h}{2} = \sum_{i=1}^{N} m_{i,i} + \sum_{i=1}^{N} P_{i,i$ of Fig. the to batan the radius of curvature as function of principles.<br>  $\Phi_{\pm} = \sum_{i=1}^{N} \sum_{i=1}^{N} m_{i} t + m_{2}$  (4)<br>
thickness of layer, number and dimension of princis lines. The  $\frac{1}{2} = \sum_{i=1}^{N} m_{i} t + m_{2}$  (4)<br>
thic geometric parameters (e.g., moment of inertia of section,  $P * \frac{h}{2} = \frac{h}{2}$ <br>
thickness of layers, number and dimension of printed lines),<br>
B. Hypothesis and simplification<br>
B. Hypothesis and simplification<br>
B. Hypothesi Briefly, instead of expansion coefficient multiplied by the direction) the strains of the two materials must be equal (Eq.9): stimulus intensity, we consider directly the resulting strain. coefficient) stimulus intensity (e.g., temperature variation).<br> *Explories and simplification*<br> *Explories and simplification*<br> *Explories and simplification*<br> **Explore staring with model derivation a few assumptions**<br> **E** moisture intensity is always the same in water solutions. Before starting with model derivation a few assumptions become Eq.5 and Eq<br>need to be done.<br>
• Since shape morphing happens only where there<br>
• are two different materials in the film, if parallel<br>
Imsear their monogh, we ed to be emer.<br> **are two different materials in the flime film, if parallel<br>
are two different materials in the film, if parallel<br>
ines are thin enough, we can assume that the lines<br>
will bend like Timoshenko's beams.<br>
<b>b** any happens only where there<br>
naterials in the film, if parallel<br>
th, we can assume that the lines<br>
bh, we can assume that the lines<br>
oshenko's beams.<br>
Defining  $\rho$  as radius of curvature of the structure, the<br>
net mater are two different materials in the film, if partilele the strength in the film,  $P * \frac{b}{2} = Nm_1 + m_2$  (6)<br>
times will bend like Timoshenko's beams. Defining  $\rho$  as radius of curvature of the structure torques<br>  $Z$  cones w lines are thin enough, we can assume that the lines<br>
will bend like Timoshehol's beams.<br>
The contained between form in the permutation of the Contention of the Density of the beam width is small enough, the bending<br>
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will bend like Timoshenko's beams.<br>
Leftning p as radius of curvature of the structure,<br>
not contribute to structure folding.<br>
the bending<br>
or the bend if nongly and the small enough, the bending<br>
or If the bend if nongly Fig. 2008 with only one material will expand but do<br>
or to contribute to structure folding.<br>
In the beam width is small enough, the bending<br>
angle in this direction can be considered negligible.<br>
With these hypotheses we compared to the beam with its small enough, the beading<br>
or contribute to structure folding.<br> **c** if the beam width is small enough, the beading<br>
angle in this direction can be considered negligible.<br>
With these hypothese Find beam width is small enough, the bending<br>
in this direction can be considered negltigible.<br>
The beam width is small enough, the bending  $m_1 = \frac{E_1 A_1}{\rho}$  on  $E_2 = \frac{E_2 E_1}{\rho}$  (7)<br>
With these hypotheses we can assu If the beath wat in something the beath and properties are beathing Eq. 7 in  $2 = \frac{E_1J_1}{\rho}$ . This also that the principal content of reshipe change and this properties are preferred interest of the princed ones all oth angue in this syncheters we can assume that the printied lines<br>
with these bypotheses we can assume that be printed ones. The parameters are preferential direction for shape change and this<br>
direction is the amore of the

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P_1' + P_1'' = P_2 = P \quad (1)
$$



after shape change.

$$
P * \frac{h}{2} = m_1' + m_1'' + m_2 \quad (2)
$$

total force and momentum in the lines is the sum of forces and momentum in each line (Eq.3 and Eq.4):  $P * \frac{h}{2} = m_1' + m_1'' + m_2$  (2)<br>
In the Eq.1 and Eq.2 only two lines of material 1 are<br>
considered. More in general, since we have N printed lines,<br>
total force and momentum in the lines is the sum of forces and<br>
momentum i

$$
\sum_{1}^{N} P_{1i} = P_2 = P \quad (3)
$$
  

$$
P * \frac{h}{2} = \sum_{1}^{N} m_{1i} + m_2 \quad (4)
$$

If we consider that printed lines have all same size and are al force and momentum in the lines is the sum of forces and<br>
mentum in each line (Eq.3 and Eq.4):<br>  $\sum_{1}^{N} P_{1i} = P_{2} = P$  (3)<br>  $P * \frac{h}{2} = \sum_{1}^{N} m_{1i} + m_{2}$  (4)<br>
If we consider that printed lines have all same size and a  $P * \frac{h}{2} = \sum_{i=1}^{N} m_{1i} + m_2$  (4)<br>
If we consider that printed lines have all same size and are<br>
ually spaced, then also lines internal forces and torques are<br>
equal  $(P_1 i = P_1$  and  $m_1 i = m_1)$ , and Eq.3 and Eq.4<br>
come E If we consider that printed lines have all same size and are<br>equally spaced, then also lines internal forces and torques are<br>all equal  $(P_1 i = P_1 \text{ and } m_1 i = m_1)$ , and Eq.3 and Eq.4<br>become Eq.5 and Eq.6, respectively.<br> $N * P_1$ 

$$
N * P_1 = P_2 = P(5)
$$
  

$$
P * \frac{h}{2} = Nm_1 + m_2 \quad (6)
$$

Defining  $\rho$  as radius of curvature of the structure, torques<br>are obtained from Eq.7, where  $I_1 = \frac{D * h_1^3}{12}$  and  $I_2 = \frac{W * h_2^3}{12}$ .

$$
m_1 = \frac{E_1 * I_1}{\rho} \qquad m_2 = \frac{E_2 * I_2}{\rho} (7)
$$

$$
P * \frac{h}{2} = \frac{N * E_1 * I_1 + E_2 * I_2}{\rho} \tag{8}
$$

$$
\alpha_1 + \frac{P_1}{E_1 * h_1 * D * N} + \frac{h_1}{2 * \rho} = \alpha_2 - \frac{P_2}{E_2 * h_2 * W} - \frac{h_2}{2 * \rho} \tag{9}
$$

come Eq.5 and Eq.6, respectively.<br>  $N * P_1 = P_2 = P(5)$ <br>  $P * \frac{h}{2} = Nm_1 + m_2$  (6)<br>
Defining  $\rho$  as radius of curvature of the structure, torques<br>
cobtained from Eq.7, where  $I_1 = \frac{P * h_1 s}{12}$  and  $I_2 = \frac{W * h_2 s}{12}$ .<br>  $m_1 =$  $N * P_1 = P_2 = P(5)$ <br>  $P * \frac{h}{2} = Nm_1 + m_2$  (6)<br>
Defining  $\rho$  as radius of curvature of the structure, torques<br>
are obtained from Eq.7, where  $I_1 = \frac{D * h_1^3}{12}$  and  $I_2 = \frac{W * h_2^3}{12}$ .<br>  $m_1 = \frac{E_1 * I_1}{\rho}$   $m_2 = \frac{E_2 * I_$  $N * P_1 = P_2 = P(5)$ <br>  $P * \frac{h}{2} = Nm_1 + m_2$  (6)<br>
Defining  $\rho$  as radius of curvature of the structure, torques<br>
are obtained from Eq.7, where  $I_1 = \frac{P * h_1^3}{12}$  and  $I_2 = \frac{W * h_2^3}{12}$ .<br>  $m_1 = \frac{E_1 * I_3}{\rho}$   $m_2 = \frac{E_2 * I_$ from Navier's Equation. Defining  $\rho$  as radius of curvature of the structure, torques<br>are obtained from Eq.7, where  $I_1 = \frac{D+h_1^3}{12}$  and  $I_2 = \frac{W+h_2^3}{12}$ .<br> $m_1 = \frac{E_1*I_2}{\rho}$   $m_2 = \frac{E_2*I_2}{\rho}(7)$ <br>Substituting Eq.7 in Eq.6 we obtain Eq.  $m_1 = \frac{E_1 + I_1}{\rho}$   $m_2 = \frac{E_2 + I_2}{\rho}$  (7)<br>
Substituting Eq.7 in Eq.6 we obtain Eq.8:<br>  $P * \frac{h}{2} = \frac{N + E_1 + I_1 + E_2 + I_2}{\rho}$  (8)<br>
The sheared surface between the two materials (parallel<br>
rection) the strains of the two Substituting Eq.7 in Eq.6 we obtain Eq.8:<br>  $P * \frac{h}{2} = \frac{N+E_1 \cdot I_1 + E_2 \cdot I_2}{\rho}$  (8)<br>
The sheared surface between the two materials (parallel<br>
direction) the strains of the two materials must be equal (Eq.9):<br>  $\alpha_1 + \frac{P_$ 

$$
\frac{1}{\rho} = \frac{(\alpha_2 par - \alpha_1 par)}{\frac{h}{2} + \frac{2*(N * E_1 * I_1 + E_2 * I_2)}{h} \cdot (\frac{1}{E_1 * h_1 * N * D} + \frac{1}{E_2 * h_2 * W})} (10)
$$

$$
\frac{1}{\rho} = \frac{6(\alpha_2 \text{par} - \alpha_1 \text{par})(\text{m}+1)^2}{\text{h}(3(\text{m}+1)^2 + (1+\beta \text{mn})(\text{m}^2 + 1/\beta \text{mn}))} (11)
$$

thickness and inversely proportional to the difference in measured with a micrometer  $(h_1, h_2)$  and h), while lengths on  $\beta$  influence the value of  $\rho$  but in a not trivial way.<br>Image J (D and W). Results of measurement are shown in Table  $\frac{1}{p} = \frac{6(\alpha_2 par - \alpha_1 par)(m+1)^2}{h(3(m+1)^2 + (1 + \beta mn)(m^2 + 1/\beta mn))} (11)$  this reason, the radius  $\frac{1}{p}$  this reason, the radius  $\frac{1}{p}$  this reason, the radius  $\frac{1}{p}$  this reason, the radius of curvature results proportion

 $\frac{1}{p} = \frac{6(a_2par - a_1par)(m+1)^2}{\ln(3(m+1)^2 + (1+\beta mn)(m^2 + 1/\beta mn)})} (11)$  this reason, the radius of curvature  $\frac{1}{p}$  and the  $\frac{1}{p}$  and  $\frac{1}{p} = \frac{6(\alpha_s par - \alpha_s par)(m+1)^2}{n(3(m+1)^2 + (1 + \beta mn)(m^2 + 1/\beta mn)})}$  (11) this reason, the radius of curvature results proportional to the total thickness varying free radius of curvature results proportional to the difference in me  $\frac{1}{p} = \frac{6(\text{Gp}a + \text{Gp}a)(m+1)^2}{\ln(30\text{m} + 1)^2(\text{H+fmm})(m+1)^2}$ (11) this reason, the radius of curvature was measured for differentials.<br>
The radius of curvature results proportional to the total thickness way ingered  $\frac{1}{p} = \frac{6(\text{t}_0 \text{par} - \text{t}_0 \text{par})(m+1)^2}{h(3 \text{th} \cdot \text{par})^2 + (1 + f \text{p} \cdot \text{m}))} (11)$  this reason, the radius of curvature was measured<br>
The radius of curvature results proportional to the total thickness varying from 500m a bioprinting. Those lines consist of a 5% w/v type A gelatin  $\frac{1}{p} = \frac{6(\text{G}_2\text{Bar}-\text{G}_2\text{Bar})(m+1)^2}{h(\text{3}+\text{G}_2\text{Bar})}$  (11) this reason, the radius of curvature was<br>
from courter results proportional to the total thickness varying from Sphrence in Fabricated samples are 10x5mm o  $\frac{1}{p} = \frac{6(\text{g,par}-\text{g,par})(m+1)^3}{\ln(3\times m+1)^2 + (1+\beta \text{mn}) (m^2+1/\beta \text{mn})}$  (11) this reason, the radius of curvature was not already by continue the total thickness varying from Stopha 10 compared to the producted The radius o From the solution of Papel of Normas (The Solution of Papel Scheme and the solution of Papel of Valent (ISP) and the deal of Valent (ISP) and the deal of Valent (ISP) and the deal of Valent (ISP) and the papel of Valent ( To validate its smallying model we produced samples with the plateau of expansion determined during the measure of the<br>
the sume geometry described in section IIA, the plateau of expansion determined during the measure of



folding

materials a chemical bound occur between the two layers. This Fig. 4. Scaffold principle lines were principle in the risk of delamination of the infinite state of the risk of delamination of the state of the risk of delamination of the cent principle in the risk of delating the risk structure. Both materials have been physically and mechanically characterized to determinate elastic modulus for Nestin [14] (intermediate filament protein of neural (and method in the scaffidd method in the scaffidd method in the scaffidd method is the scaffidd method in the scaffidd method is the scaffidd method in the conditions) and expansion of the scaffidd method in the scaffidd  $\alpha = \frac{final\ length -initial\ length}{initial\ length}$ . The results of these neural progenitors), thus confirming successful neural identity. **EVALUATION CONSULT (INCREATION CALL CONSULTIES)**<br> **EVALUATION CONSULT CONSUL** Fig. 4: Scaffold produced of dimension 10x5mm, a) before actuation, b) after<br>
The material was chosen for its biocompatibility [12], and the cells reached  $>90\%$ <br>
The material was chosen for its biocompatibility [12], an





Values are written as mean  $\pm$  standard deviation, 4 samples are used to<br>estimate E and 10 samples are used to estimate  $\alpha$ <br>Validation of the model is based on comparing the model<br>predicted radius of curvature (mean and structure. Both materials have been physically and immunosissiped 4D scatiold reduced variable (under we and dry conditions) and expansion coefficients progenitors) and SOX2 [15] (( $\alpha = \frac{final\ length\ coefficient\ length\theta}{initial\ length}$ ). The results of

this reason, the radius of curvature was measured for different<br>h2 values and compared to the predicted ones.

 $\frac{1}{p} = \frac{6(\alpha_2 par - \alpha_1 par)(m+1)^2}{n(3(m+1)^2 + (1 + \beta mn)(m^2 + 1/\beta mn)})}$  (11)<br>
The radius of curvature results proportional to the total<br>
The radius of curvature results proportional to the total<br>
The radius of curvature results propo  $\frac{1}{p} = \frac{6(\alpha_5 \text{par}-\alpha_4 \text{par})(\text{m}+1)^2}{\ln(3(\text{m}+1)^2 + (1+\beta \text{mm})(\text{m}^2+1/\beta \text{mm}))} (11)$  this reason, the radius of curvature was measure<br>
the radius of curvature results proportional to the total<br>
the strategies are 10x5mm  $\frac{1}{\rho} = \frac{6(\alpha_1 par - \alpha_1 par)(m+1)^2}{\ln(3(m+1)^2 + (1+\beta mn)(m^2 + 1/\beta mn))}$  (11) this reason, the radius of curvature was measured ones<br>
The radius of curvature results proportional to the total thickness varying from 50µm to lofoun. La  $\frac{1}{p} = \frac{6(\alpha_5 \text{par}-\alpha_1 \text{par})(\text{m}+1)^2}{\ln(3(\text{mm}+1)^2+(1+\beta \text{mm})(\text{m}^2+1/\beta \text{mm}))} (11)$  this reason, the radius of curvature values of curvature results proportional to the total thickness and compared to the prediction IIA  $\frac{1}{p} = \frac{6(a_2 par - a_1par)(m+1)^2}{h(3(m+1)^2 + (1 + \beta mn))}$  (11) this reason, the radius of curvature was measured on<br>
The radius of curvature results proportional to the total<br>
The radius of curvature results proportional to the tot  $\frac{1}{p} = \frac{6(a_0 \text{par} - a_1 \text{par})(\text{m}+1)^2}{\text{h}(30 \text{rad})}$ (11) this reason, the radius of curvature was measured<br>  $\frac{1}{p} = \frac{6(a_0 \text{par} - a_1 \text{par})(\text{m}+1)^2 + (1+\text{fmm})(\text{mm})}{\text{h}(20 \text{rad})}$ <br>
The radius of curvature results proporti  $\frac{1}{p} = \frac{6(a_0 \text{pa} - a_0 \text{pa})(m+1)^2}{b_0(100 \text{ Pa})(100 \text{ Pa})}$ <br>  $\frac{1}{p} = \frac{6(a_0 \text{pa} - a_0 \text{pa})(m+1)^2}{b_0(100 \text{ Pa})(100 \text{ Pa})}$ <br>  $\frac{1}{2}$  values and compared to the predicted cames.<br>
The radius of curvature results proportional t 3<br>this reason, the radius of curvature was measured for different<br>h2 values and compared to the predicted ones.<br>Fabricated samples are  $10x5mm$  on plane and have a total<br>thickness varying from  $50\mu m$  to  $160\mu m$ . Layers t 3<br>this reason, the radius of curvature was measured for different<br>h2 values and compared to the predicted ones.<br>Fabricated samples are  $10x5mm$  on plane and have a total<br>thickness varying from 50µm to  $160µm$ . Layers thick Fabricated samples are 10x5mm on plane and have a total thickness varying from 50µm to 160µm. Layers thickness was <sup>3</sup><br>this reason, the radius of curvature was measured for different<br>h2 values and compared to the predicted ones.<br>Fabricated samples are  $10x5mm$  on plane and have a total<br>thickness varying from 50µm to  $160µm$ . Layers thi <sup>3</sup><br>this reason, the radius of curvature was measured for different<br>h2 values and compared to the predicted ones.<br>Fabricated samples are  $10x5mm$  on plane and have a total<br>thickness varying from 50µm to  $160\mu$ m. Layers th 3<br>
this reason, the radius of curvature was measured for different<br>
h2 values and compared to the predicted ones.<br>
Fabricated samples are 10x5mm on plane and have a total<br>
thickness varying from 50µm to 160µm. Layers thic 3<br>
this reason, the radius of curvature was measured for different<br>
h2 values and compared to the predicted ones.<br>
Fabricated samples are  $10x5mm$  on plane and have a total<br>
thickness varying from 50µm to 160µm. Layers thi <sup>3</sup><br><sup>3</sup><br>this reason, the radius of curvature was measured for different<br>h2 values and compared to the predicted ones.<br>Fabricated samples are  $10x5mm$  on plane and have a total<br>thickness varying from 50 $\mu$ m to 160 $\mu$ m. La <sup>3</sup><br>
this reason, the radius of curvature was measured for different<br>
h2 values and compared to the predicted ones.<br>
Fabricated samples are 10x5mm on plane and have a total<br>
thickness varying from 50µm to 160µm. Layers th expansion coefficient, data not shown) the radius of curvature <sup>3</sup><br><sup>3</sup><br>this reason, the radius of curvature was measured for different<br>h2 values and compared to the predicted ones.<br>Fabricated samples are 10X5mm on plane and have a total<br>thickness varying from 50µm to 160µm. Layers th 3<br>
this reason, the radius of curvature was measured for different<br>
h2 values and compared to the predicted ones.<br>
Fabricated samples are 10x5mm on plane and have a total<br>
thickness varying from 50µm to 160µm. Layers thic 3<br>
s reason, the radius of curvature was measured for different<br>
values and compared to the predicted ones.<br>
Fabricated samples are 10x5mm on plane and have a total<br>
ckness varying from 50µm to 160µm. Layers thickness was <sup>3</sup><br>
this reason, the radius of curvature was measured for different<br>
h2 values and compared to the predicted ones.<br>
Fabricated samples are 10x5mm on plane and have a total<br>
thickness varying from 50µm to 160µm. Layers th this reason, the radius of curvature was measured for different<br>h2 values and compared to the predicted ones.<br>Fabricated samples are 10x5mm on plane and have a total<br>thickness varying from 50µm to 160µm. Layerrs thickness this reasson, the radual of curvature was measured for different<br>the Packiets and compared to the predicted ones.<br>Fabricated samples are 10x5mm on plane and have a total<br>thickness varying from 50µm to 160µm. Layers thickn <sup>3</sup><br><sup>3</sup><br><sup>3</sup><br><sup>3</sup><br>22 values and compared to the predicted ones.<br><sup>2</sup> ralbricated samples are 10x5mm on plane and have a total<br>hickness varying from 50µm to 160µm. Layers thickness was<br>neasured with a micrometer (h<sub>1</sub>, h<sub>2</sub> a

TABLE II: GEOMETRICAL PARAMETERS

$h2$ (um)	$h$ l $(\mu m)$	$D \text{ (mm)}$	$W$ (mm)
$50-160 \pm 5$	$33.1 \pm 14.1$	i. $0\pm0.1$	$10.2 \pm 0.4$
Values are written as mean $\pm$ standard deviation. 30 samples are used to			

obtain h1, D and W measures

h2 values and compared to the predicted ones.<br>
Haviated samples are 10x5mm on plane and have a total<br>
thickness varying from 50µm to 160µm. Layers thickness was<br>
measured with a micrometer (h, h, and h), while lengths on<br> the scaffold flat. The operator just needed to remove the holder thickness varying from 50µm to 160µm. Layers thickness was<br>measured with a micrometer (h, h, and h), while lengths on<br>the plane was measured from hi-res figures using the software<br>ImageJ (D and W). Results of measurement time to cell to attach on the scaffold, otherwise shape changing would start too early and the cells would not follow the scaffold movement. To trugger the shape changes of the structures the samples<br>
are dipped in PBS 1X and after 3 hours (time needed to reach<br>
reach plateau of expansion, determined during the measure of the<br>
pansion coefficient, data not sho were dipped in PBS 1X and after 3 hours (time needed to reach<br>the plateau of expansion, determined during the measure of the<br>expansion coefficient, data not shown) the radius of curvature<br>was measured from pictures using expansion coefficient, data not shown) the radius of curvature<br>was measured from pictures using ImageJ.<br>
TABLE II: GEOMETRICAL PARAMETERS<br>  $\frac{h2(\mu m)}{1(\mu m)}$  ( $\frac{h(m)}{2\pi\sqrt{4}}$ )  $\frac{h(m)}{10\pi\sqrt{4}}$ )  $\frac{h(m)}{10\pi\sqrt{4}}$ <br>
Valu

The material was chosen for its biocompatibility [12], and the cells reached  $> 90\%$  confluence, neural induction protocols of neural induction, cells were chosen to maximise the [13] started. After 12 days of neural ind Framework of the starting results of the solution of the intermediate the model in the solution of specifical form points of the intermediate and the model in the solution of the solution of the film in the solution of th Note the diffusion of P2 and Table 11. The Herbert and Solution of P2 and Table 113 and the medicinal and only the Natural Herbert CALE (GPIMS) for each gram of gelatin. On top of the film<br>the same signation is  $\frac{164 \text{$ scarbid with it was stud that in water-base<br>the scarbid flat. The operator just needed to<br>to actuate the folding movement. Holder w<br>time to cell to tatach on the scarfied, otherwise<br>would start too early and the cells wou 15 11 to equal start in Fourier in totomal way species to give the the seal of the collision of the cells of the cells would of the cells would of the cells would of the cells would of follow the exacted on 4D bioprinted searibled more and the cells would but to be a<br>searibled more and the searched more areas as searched more area as a searched more in the 24 hours, 4D scaffolds were actuated and 3 days later, when was measured from pictures using ImageJ.<br>
TABLE II: GEOMETRICAL PARAMETERS<br>  $\frac{h2(\mu m)}{50-160\pm5}$   $\frac{h1(\mu m)}{31 \pm 14.1}$   $\frac{D(\mu m)}{1.0\pm 0.1}$   $\frac{D(\lambda + 0.4)}{1.2 \pm 0.4}$ <br>
Values are written as mean  $\pm$  standard deviation driven to differentiation for 4 days, by adding neural differentiation supplemented with the neurotrophin BDNF. **Example 11** (um) 11 (um) 11 (um) 11 (um) 11 (um) 11 (um) 11 (un) 11 **SURES**<br> **SURES** are written as mean ± standard deviation, 30 samples are written as mean ± standard deviation, 30 samples are used to obtain h1, D and W measures E. *Biological application* Scaffolds used to validate the immunoassayed 4D scaffold revealed homogeneous positivity E. *Biological application*<br>
E. *Biological application*<br>
explore the effects of 4D bioprinting in cell differentiation and<br>
explore the effects of 4D bioprinting in cell differentiation and<br>
eromaton was explored. A cust *E. Biological application*<br>Scaffolds used to Scaffolds used to evalidate the model have been also used to evaly<br>of the effects of 4D bioprinting in cell differentiation and<br>growth. More in detail, *in vitro* modelling of Scaffolds used to validate the model have been also used to explore the effects of 4D biopirinting in cell differentiation and growth. More in detail, *in vitro* modelling of neural tube formation was explored. A customiz I, *in vitro* modelling of neural tube<br>
. A customized holder was put on the<br>
ill flat in water-based solution to kept<br>
reator just needed to remove the holder<br>
novement. Holder was needed to give<br>
novement. Holder was ne scaffold while it was still flat in water-based solution to kept<br>the scaffold flat. The operator just needed to remove the holder<br>to actuate the folding movement. Holder was needed to give<br>time to cell to attach on the sc e scaffold flat. The operator just needed to remove the holder<br>actuate the folding movement. Holder was needed to give<br>ne to cell to attach on the scaffold, otherwise shape changing<br>ould start too early and the cells would

# A. Predicted and measured radius comparison

Radius of curvature values are plotted as function of the total thickness as shown in Fig.5.



Mean values of the model (continuous green line) are<br>calculated using mean value of measured material and mathematical model itself, it needs to be improved by adding<br>geometrical parameters (*i.e.*, Young's modulus, expans Mean values of the model (continuous green line) are<br>calculated using mean value of measured material and<br>mathematical model itself, it needs to be<br>geometrical parameters (*i.e.*, Young's modulus, expansion<br>the time depend Mean values of the model (continuous green line) are diameter and degree of curve<br>calculated using mean value of measured material and mathematical model itself, it<br>geometrical parameters (*i.e.*, Young's modulus, expansio Mean values of the model (continuous green line) are diameter and degree of curvature as a result. Looking at the calculated using mean value of measured material and mathematical model itself, it needs to be improved by a Mean values of the model (continuous green line) are<br>
diameter and degree of curvature as a result. Looking at the<br>
calculated using mean value of measured material and mathematical model itself, it needs to be improved b Mean values of the model (continuous green line) are diameter and degree of curvature as calculated using mean value of measured material and mathematical model itself, it needs to lgeometrical parameters (*i.e.*, Young's Mean values of the model (continuous green line) are diameter and degree of curvature calculated using mean value of measured material and mathematical model itself, it needs geometrical parameters (*i.e.*, Young's modulu Mean values of the model (continuous green line) are<br>
diameter and degree of curvature as a result. Looking at the<br>
calculated using mean value of measured material and mathematical model itself, it needs to be improved by in the same region, when the total thickness of the 4D printed change seems to sustain neural differentiation as showed by Mean values of the model (continuous green line) are<br>
calculated using mean value of measured material and<br>
mathematical model<br>
geometrical parameters (*i.e.*, Young's modulus, expansion the time dependent<br>
coefficients, Mean values of the model (continuous green line) are diameter and degree of curvature as a value of measured material and mathematical model itself; it needs to committed by more them of measured material and mathematical

changes occurring during neural induction phase suggest



homogeneously distributed on scaffold surface during neural No. 4. MARY ANN LIEBERT INC., PP. 159–167, DEC. 01, 2015<br>[2] Q. GE, C. K. DUNN, H. J. QI, AND M. L. DUNN, "ACTIVE ORIGAMI BY 4D induction showing morphological change due to neural commitment

express Nestin and SOX2 neural progenitor typical markers  $A_{PR, 2016}$ to be oriented along the thickness of the scaffold, showing a [5] Y. WANG ET AL., "THREE-DIMENSIONAL PRINTING OF SHAPE MEMORY HYDROGELS neural tube (Fig.7b).



structure expressing Nestin and SOX2 (DIV12) B) maintenance of the [12] A. LAPOMARDA ET AL., "PECTIN AS RHEOLOGY MODIFIER OF A GELATIN-BASED

Mean values of the model (continuous green line) are diameter and degree of curvature as a result. Looking at the 4<br>diameter and degree of curvature as a result. Looking at the<br>mathematical model itself, it needs to be improved by adding<br>the time dependent behaviour. In this way, we can achieve a<br>model capable to predict the change in mathematical model itself, it needs to be improved by adding <sup>4</sup><br>diameter and degree of curvature as a result. Looking at the<br>mathematical model itself, it needs to be improved by adding<br>the time dependent behaviour. In this way, we can achieve a<br>model capable to predict the change model capable to predict the change in shape through space and time.

aan values of the model (continuous green line) are diameter and degree of curvature as a result. Looking at the duted using mean value of measured material and mathematical model isself, it needs to be improved by addite Cells attached to the scattold within 24h atter seeding<br>(Fig.6a, top panels). After holder removal, cells still adhere<br>exhaustive gene characterization in longer period of to scaffold surface and within 48h colonize the whole<br>differentiation is ongoing, to evaluate if 4D printed scaffolds scaffold surface (Fig.6a, bottom panels). Morphological can support neural progenitor differentiation into mature <sup>4</sup><br><sup>4</sup><br>ameter and degree of curvature as a result. Looking at the<br>athematical model itself, it needs to be improved by adding<br>e time dependent behaviour. In this way, we can achieve a<br>odel capable to predict the change in <sup>4</sup><br>diameter and degree of curvature as a result. Looking at the<br>mathematical model itself, it needs to be improved by adding<br>the time dependent behaviour. In this way, we can achieve a<br>model capable to predict the change scaffold recapitulate the formation of neural tube in vitro. The <sup>4</sup><br>diameter and degree of curvature as a result. Looking at the<br>mathematical model itself, it needs to be improved by adding<br>the time dependent behaviour. In this way, we can achieve a<br>model capable to predict the change <sup>4</sup><br>diameter and degree of curvature as a result. Looking at the<br>mathematical model itself, it needs to be improved by adding<br>the time dependent behaviour. In this way, we can achieve a<br>model capable to predict the change <sup>4</sup><br>diameter and degree of curvature as a result. Looking at the<br>mathematical model itself, it needs to be improved by adding<br>the time dependent behaviour. In this way, we can achieve a<br>model capable to predict the change <sup>4</sup><br>
diameter and degree of curvature as a result. Looking at the<br>
mathematical model itself, it needs to be improved by adding<br>
the time dependent behaviour. In this way, we can achieve a<br>
model capable to predict the cha <sup>4</sup><br>diameter and degree of curvature as a result. Looking at the<br>mathematical model itself, it needs to be improved by adding<br>the time dependent behaviour. In this way, we can achieve a<br>model capable to predict the change <sup>4</sup><br><sup>4</sup><br>diameter and degree of curvature as a result. Looking at the<br>mathematical model itself, it needs to be improved by adding<br>the time dependent behaviour. In this way, we can achieve a<br>model capable to predict the cha <sup>4</sup><br>4<br>diameter and degree of curvature as a result. Looking at the<br>mathematical model itself, it needs to be improved by adding<br>model capable to predict the change in shape through space<br>and time.<br>The 4D printed scaffold w <sup>4</sup><br>4<br>diameter and degree of curvature as a result. Looking at the<br>mathematical model itself, it needs to be improved by adding<br>the time dependent behaviour. In this way, we can achieve a<br>model capable to predict the chang <sup>4</sup><br>4<br>mathematical model itself, it needs to be improved by adding<br>the time dependent behaviour. In this way, we can achieve a<br>model capable to predict the change in shape through space<br>and time.<br>The 4D printed scaffold wa neurons. meter and degree of curvature as a result. Looking at the unhematical model itself, it needs to be improved by adding time dependent behaviour. In this way, we can achieve a due time dependent behaviour. In this way, we ca the time dependent behaviour. In this way, we can achieve a<br>model capable to predict the change in shape through space<br>and time.<br>The 4D printed scaffold was then used to develop a neural<br>tube in vitro model. Indeed, the se model capable to predict the change in shape through space<br>
The 4D printed scaffold was then used to develop a neural<br>
tube in vitro model. Indeed, the self-folding movement of the<br>
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