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ADVANCED COMPUTATIONAL STRUCTURAL INFORMATICS BY STEREOLITHOGRAPHY – A 3D PRINTING

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Abstract:
Computational Structural Informatics is the discipline of science which investigates the structure and properties of scientific information, as well as the regularities and scientific information activity, its theory, history, methodology and organisation. The use of computers in solving information problems in the life sciences, mainly, it involves the creation of extensive electronic databases on structural informatics like 2D printing etc. Secondarily, it involves techniques such as the three-dimensional modelling of biomolecules and biologic systems. It is also used largely for the identification of new molecular targets for drug discovery. To explore computer graphics (1966/1967) as a means of coping with the 3D nature of chemistry and Physical models were useful accepted tools for chemists. This review explains about history, 3D printing like, 3D printing history, process, technologies and its applications.

Key words: ***bio-informatics, 3D printing process and technologies, spriatam.***

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INTRODUCTION:

Bio-Informatics

Bioinformatics is conceptualizing biology in terms of molecules (in the sense of physical- chemistry) and then applying "informatics" techniques (derived from disciplines such as applied math, CS, and statistics) to under standard organize the information associated with these molecules, on a large-scale. Bioinformatics is "MIS" for Molecular Biology Information.

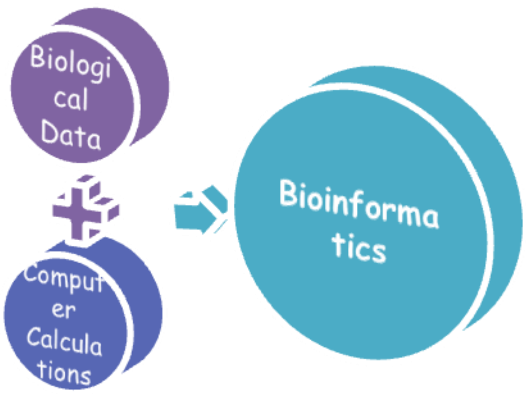

Fig. 1: introduction to bio informatics [1]

The use of computers in solving information problems in the life sciences, mainly, it involves the creation of extensive electronic databases on genomes, protein sequences, etc.

Secondarily, it involves techniques such as the three-dimensional modeling of biomolecules and biologic systems. It is also used largely for the identification of new molecular targets for drug discovery.

CHEMINFORMATICS:

Chem (o) informatics is a generic term that encompasses the design, creation, organization, storage, management, retrieval, analysis, dissemination, visualization and use of chemical information.

Is the mixing of those information resources to transform data into information and information into knowledge for the intended purpose of making better decisions faster in the area of drug lead identification and organization'' according to one view. Some groups generate hundreds of thousands to millions of compounds on a regular basis through combinatorial chemistry that are screened for biological activity[2].

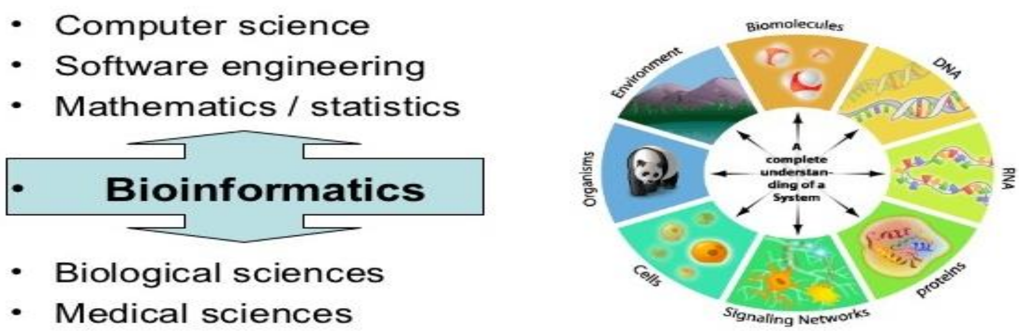

Fig 2: Bio informatics [3]

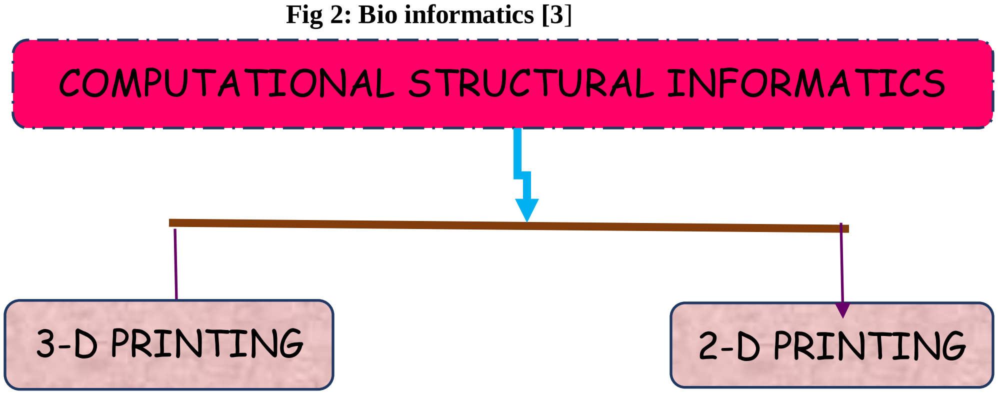

Fig 3: classification of computational structural informatics

2D PRINTING/ 2D GRAPHIC TECHNIQUE

2D printing models may combine geometric models (also called vector graphics), digital images (also called raster graphics), text to be typeset (defined by content, font style and size, color, position, and orientation), mathematical functions and equations, and more. These components can be modified and manipulated by two-dimensional geometric transformations such as translation, rotation, scaling. In object-oriented graphics, the image is described indirectly by an object endowed with a self-rendering method a procedure which assigns colors to the image pixels by an arbitrary algorithm. Complex models can be built by combining simpler objects, in the paradigms of object-oriented programming [4].

3D PRINTING

3D printing, also known as additive manufacturing, wasdeveloped in the 1980's as a process used to make three dimensionalobjects. Additive manufacturing creates partsfrom the ground up by fusing together layers of material. Its counterpart, subtractive manufacturing, begins with materialand removes excess until only the desired shape remains [5]. It is also known as rapid prototyping, is a mechanized method where by 3D objects are quickly made on a reasonably sized machine connected to a computer containing blueprints for the object. The 3D printing concept of custom manufacturing is exciting to nearly everyone. This revolutionary method for creating 3D models with the use of inkjet technology saves time and cost by eliminating the need to design; print and glue together separate model parts. Now, we can create a complete model in a single process using 3D printing. The basic principles include materials cartridges, flexibility of output, and translation of code into a visible pattern. 3D Printers are machines that produce physical 3D models from digital data by printing layer by layer. It can make physical models of objects either designed with a CAD program or scanned with a 3D Scanner. It is used in a variety of industries including jewelry, footwear, industrial design, architecture, engineering and construction, automotive, aerospace, dental and medical industries, education andconsumer products[6]. The term 3D printing covers a host of processes and technologies that offer a full spectrum of capabilities to produce parts and products in different materials. Essentially, what all processes and technologies have in common is the manner in which production is carried out layer by layer in an additive process which contrasts with traditional methods of production involving subtractive methods or molding/casting processes [7].

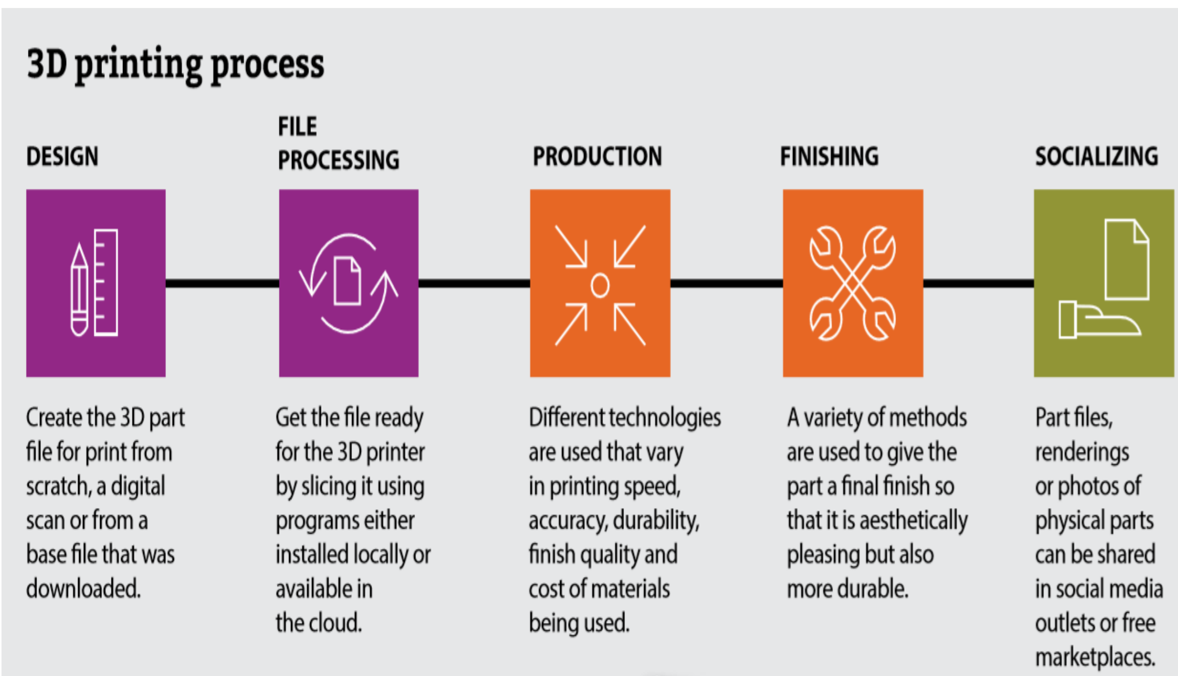

Fig 4: 3D printing process steps [5]

HISTORY

Early Additive Manufacturing (AM) equipment and materials were developed in the 1981. In1981, Hideo Kodama of Nagoya Municipal Industrial Research Institute invented two AMfabricating methods of a three-dimensional plastic model with photo-hardening polymer, where the UV exposure area is controlled by a mask pattern or the scanningfibertransmitter.

July 16, 1984 Alain Le Méhauté, Olivier de Witte and Jean Claude André filedtheir patent for the stereolithography process. The application of French inventor's wasabandoned by the French General Electric Company (now Alcatel-Alsthom) and CILAS (TheLaser Consortium). The claimed reason was "for lack of business perspective. It was threeweeks before Chuck Hullfiled his own patent for stereolithography.

Then in 1984, ChuckHull of 3D Systems Corporation developed a prototype system based on a process known as stereolithography, in which layers are added by curing photopolymers with ultraviolet lightlasers. Hull defined the process as a "system for generating three-dimensional objects bycreating a cross-sectional pattern of the object to be formed". His contribution is the design ofthe STL (Stereo Lithography) file format widely accepted by 3Dprinting software as well asthe digital slicing and infill strategies common to many processes today [8].

Charles Hull invented 3D printing, which he called "stereolithography," in the early 1980s. Hull, who has a bachelor's degree in engineering physics, was working on making plastic objects from photopolymers at the company Ultra Violet Products in California. Stereolithography uses a .stl file format to interpret the data in a CAD file, allowing these instructionsto be communicated electronically to the 3D printer. Along with shape, the instructions in the .stl file may also includeinformation such as the color, texture, and thickness of the object to be printed. Hull later founded the company 3D Systems, which developedthe first 3D printer, called a "stereolithographyapparatus."

In 1988, 3D Systems introducedthe first commercially available3D printer, the SLA-250. Many other companies have since developed 3D printers for commercial applications, such as DTM Corporation, Z Corporation, Solids cape, and Object Geometries. Hull's work, as well as advancesmade by other researchers,has revolutionized manufacturing,and is poised to do the same in many other fields including medicine [9].

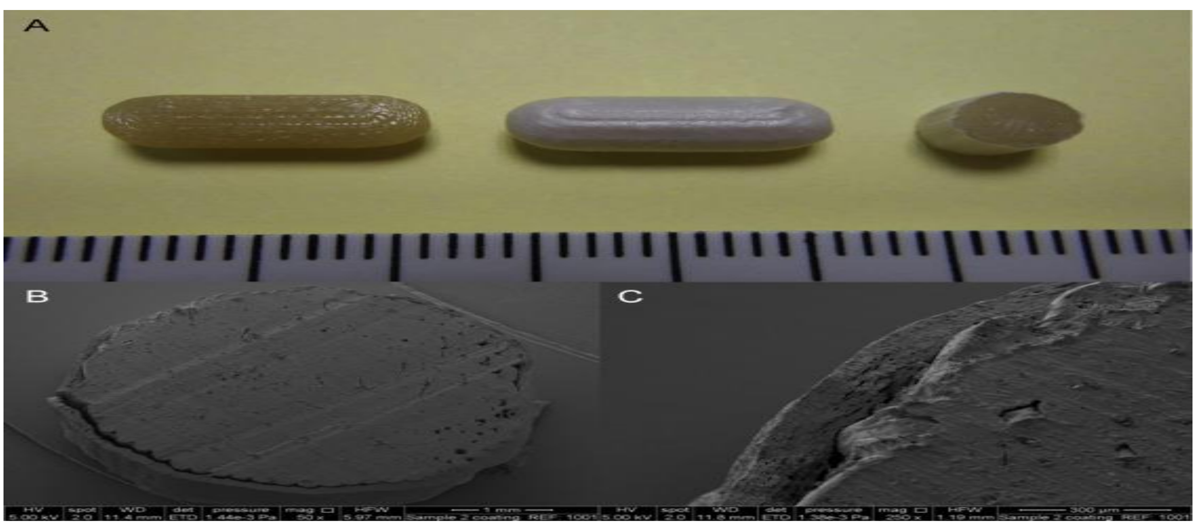

Fig 5:(A) from left to right, caplet prior to coating, caplet after coating and cross section of coated caplet (scale in cm); (B, C) SEM images of internal structure of cross-section of a coated-3D printed caplet. [10]

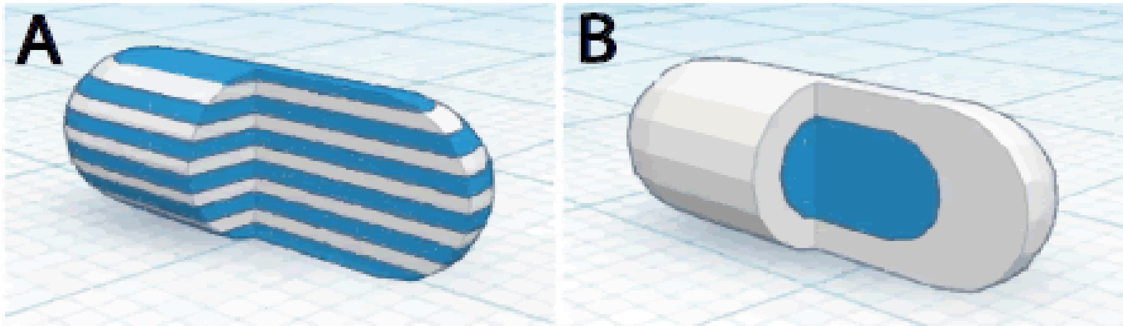

Fig 6: Schematic of tablets containing multiple drugs. (A) Multilayer device and (B) Duo Caplet. Reproduced with permission [11]

3D PRINTING TECHNOLOGIES:
Current 3D Printing Technologies Stereo lithography - Stereo lithographic 3D printers (known as SLAs or stereo lithography apparatus) position a perforated platform just below the surface of a vat of liquid photo curable polymer. A UV laser beam then traces the first slice of an object on the surface of this liquid, causing a very thin layer of photopolymer to harden. The perforated platform is then lowered very slightly, and another slice is traced out and hardened by the laser. Another slice is then created, and then another, until a complete object has been printed and can be removed from the vat of photopolymer, drained of excess liquid, and cured.

Fused deposition modelling - Here a hot thermoplastic is extruded from a temperature-controlled print head to produce fairly robust objects to a high degree of accuracy.

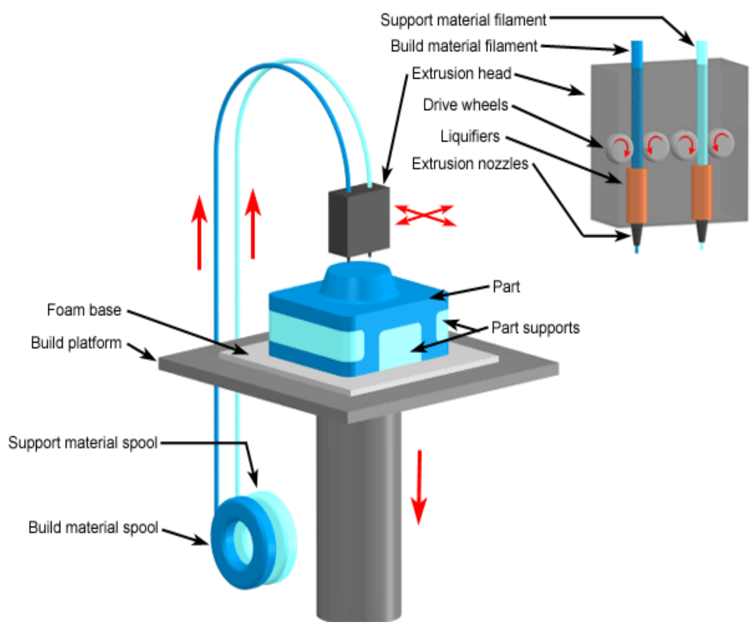

Fig 7: Fused deposition modeling [12]

Selective laser sintering (SLS) - This builds objects by using a laser to selectively fuse together successive layers of a cocktail of powdered wax, ceramic, metal, nylon or one of a range of other materials.

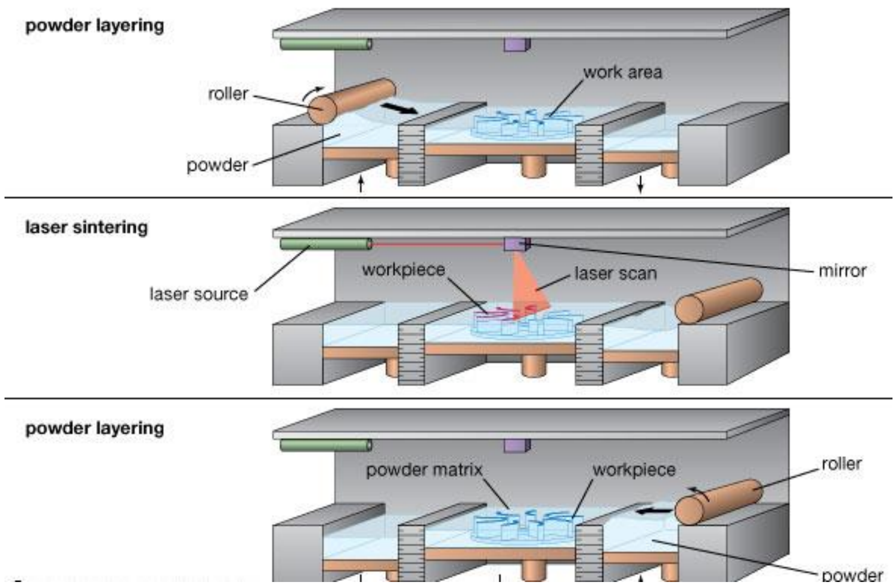

Fig 8: Selective laser sintering (SLS) process [13]

Multi-jet modeling (MJM) - This again builds up objects from successive layers of powder, with an inkjet-like print head used to spray on a binder solution that glues only the required granules together.

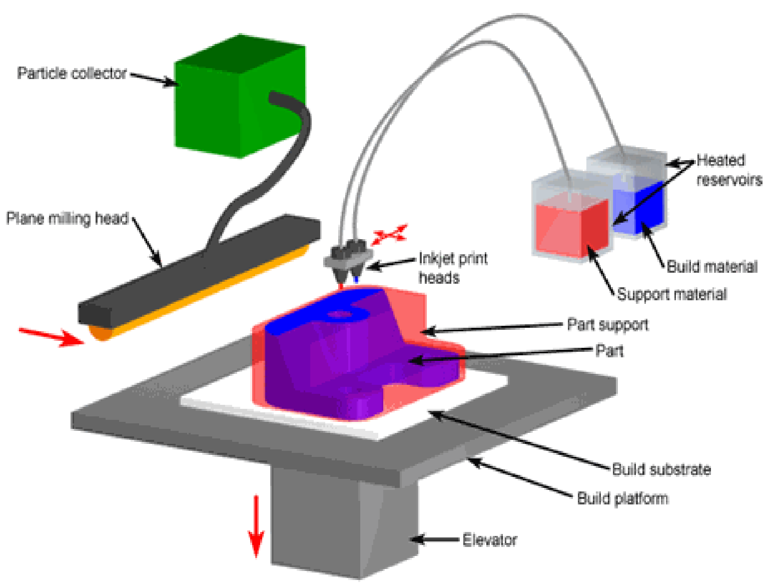

Fig 9: Multi-jet modeling (MJM) process [14]

The VFlash printer, manufactured by Canon, is low-cost 3D printer. It's known to build layers with a light-curable film. Unlike other printers, the VFlash builds its parts from the top down.

Recently, the Nano factory 3D printing technologies are introduced that are related to the nanotechnologies [6]

MATERIALS USED IN 3D PRINTING:

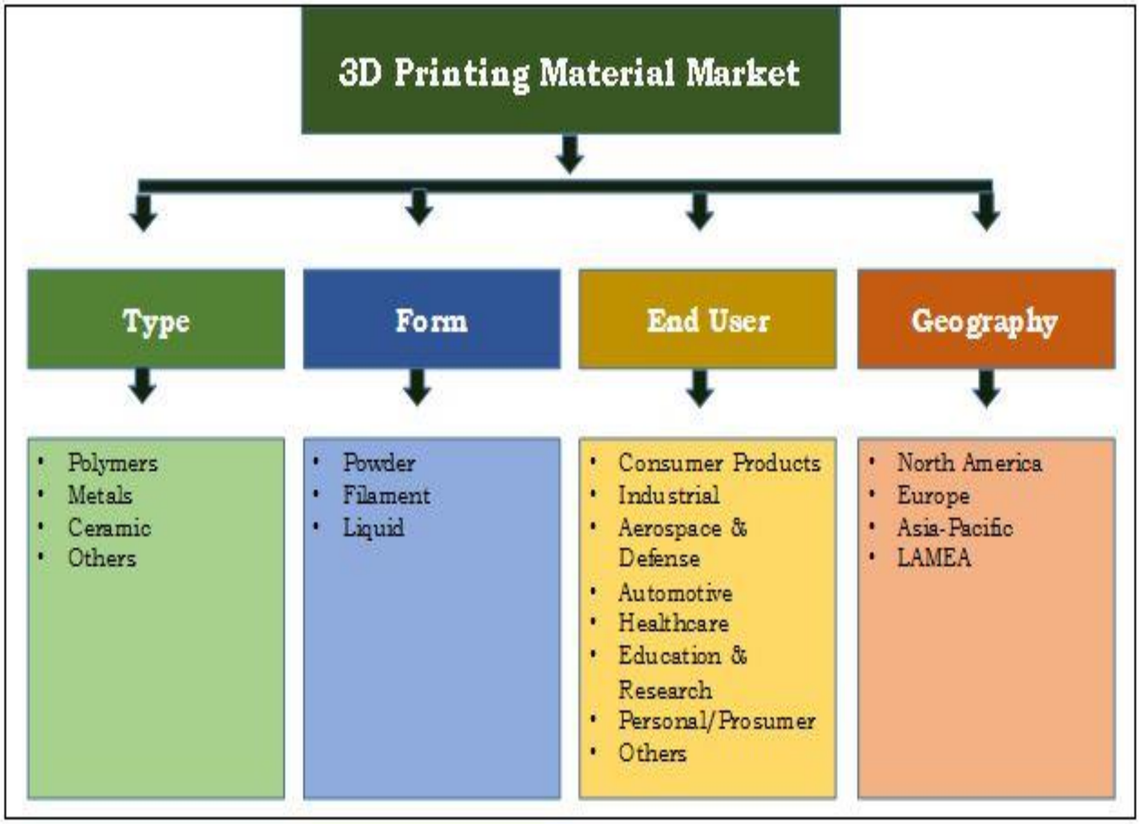

Fig 10: Materials Used In 3d Printing [15]

How 3D Printing works

When the user clicks 3D Print, the Printer warms up, fills the build chamber with build material, and, if necessary, automatically realigns its print heads. The Printer begins creating the model, depositing a layer ofpowder. The print carriage moves across that layer depositing binder (and inks for a color model) in the pattern of the first slice. Steps will be repeated until the model is complete the binder solidifies the powder in the cross-section of the model, leaving the rest of the powder dry for recycling. After each layer, the piston below the build chamber lowers the powder bed, preparing for the next layer. The cycle continues until the model is complete. When finished, the model is suspended in powder to cure. At the end of curing time, the machine automatically vacuums most of the powder from around the model and recycles it for use in subsequent builds.

Once all traces of powder are removed from the part, it can be used as is or undergo a postprocess treatment for further strengthening or improved finish. This process is referred to as infiltration, and deciding whether or how to infiltrate depends on our use of the model. Our infiltration options are all safe, clean, quick and effective.

Infiltrants are a secondary resin material that is typically drizzled or brushed onto the surface of the model. The infiltrant fills the microscopic pockets in the model, sealing its surface, enhancing color saturation and improving the mechanical properties of the model as it cures.

We have a variety of options for infiltrants depending on our needs. Options include water for basic requirements such as display models, Z-Bond for general purpose concept modeling and ZMax epoxy for functional prototypes or real-world parts. Z-Max-based prototypes have been used as production parts in underwater robotics applications, as pounding mechanical feet in footwear testing, and as functional auto parts in operating engine compartments [7].

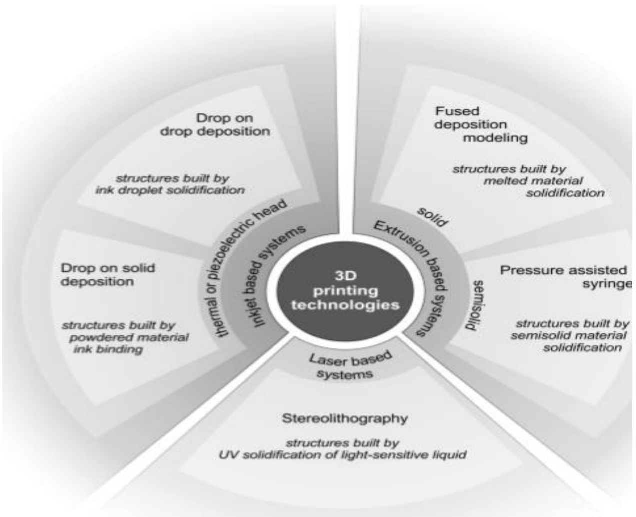

Fig 11: Stereo lithography [16]

3D printing set to revolutionize pharma

3D printing is revolutionizing pharma by allowing new substances to be tested directly on human tissues, and by changing the economies of scale, whereby any drug can be cost effective.

In 2012, Lee Cronin from the University of Glasgow shared his vision in a TED talk. In the future, he said, doctors will no longer write prescriptions, but will provide patients with algorithms that will allow them to print their own medication at home.

Two years ago, Cronin admitted that his vision was in the science fiction stage, but dream if in a slightly altered form might be turning into reality sooner than anticipated [7].

SPRITAM

A SPRITAM® (levetiracetam) tablet, for oral suspension, is now available as an adjunctive therapy in the treatment of partial onset seizures, myoclonic seizures and primary generalized tonic-clonic seizures. SPRITAM is the first prescription drug product approved by the U.S. Food and Drug Administration (FDA) that is manufactured using 3D printing technology. This innovative product disintegrates in the mouth with a sip of liquid and offers a new option for patients, including those who may struggle to take their medicine [17].

Spritam is the first 3D printed product approved by the FDA for use inside the human body. The company that developed it, Aprecia Pharmaceuticals, used powder-liquid three-dimensional printing (3DP) technology, which was developed by the Massachusetts Institute of Technology (MIT) in the late 1980s as a rapid-prototyping technique. Rapid prototyping is the same technique used in 3D printing.

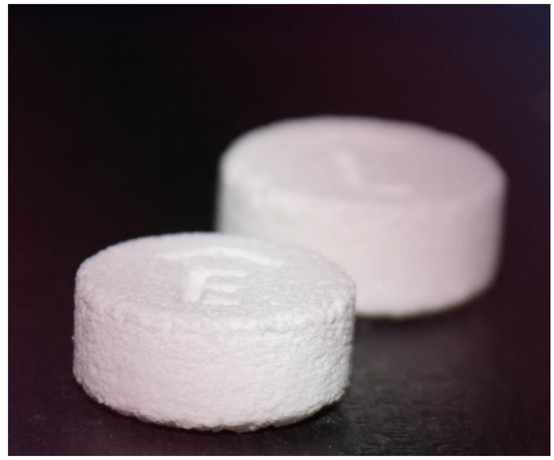

Fig 12: Spritam is the first 3D printed product prepared by Aprecia pharmaceuticals [18]

According to the company, this specific process was expanded into tissue engineering and pharmaceutical use from 1993 to 2003.

After acquiring exclusive license to MIT's 3DP process, Aprecia developed the ZipDose Technology platform. The medication delivery process allows high doses of up to 1,000 mg to rapidly disintegrate on contact with liquid. This is achieved by breaking the bonds that were created during the 3DP process.

The National Institute of Health (NIH) has a website with an extensive database of 3D printing applications in the medical field. This includes the NIH 3D Print Exchange special collection for prosthetics, which lets, print next generation prosthetics at a fraction of the cost of the ones now being sold in the marketplace.

The next evolution in the field of medicine is printing complex living tissues. Also known as bio-printing, the potential applications in regenerative medicine is incredible.

In conjunction with stem cell research, printing human organs is not as far-fetched as it sounds. Currently different body parts have been printed, and the days of long transplant waiting lists will eventually become a thing of the past.

It‘s important to remember that a lot more goes into the creation of a medication or other medical break-through than just being able to print drugs. Other costs include intensive research and development and then exhaustive testing.

So there's no reason to believe 3D printing alone will allow smaller drug firms to more effectively compete with huge pharmaceutical firms. But the breakthrough will certainly create more opportunities in the medical industry for companies of all sizes.

Outside of medicine, 3D printing has been used to print cars, clothes and even guns, which go to prove the only limitation of this technology is our imagination.

3D printing is one great example. It was invented in 1984, but its full potential is just now being realized.

In 2012, The Economist labeled this technology as, The Third Industrial Revolution, and that sentiment has been echoed by many since then. This has generated unrealistic expectations, even though it is evolving at an impressive rate [7].

APPLICATIONS OF 3D PRINTING:

INDUSTRIAL USES

- Rapid prototyping
- Rapid manufacturing
- Mass customization
- Mass production

DOMESTIC AND HOBBYIST USES

- Clothing
- 3D Bio-printing
- 3D printing for implant and medicinal device & 3D printing services [18].

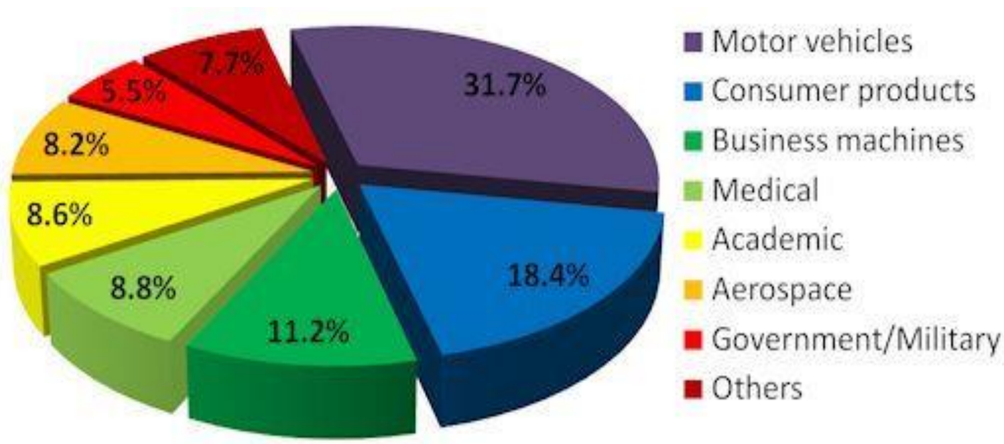

Fig 13: pie chart for 3D printing Applications [19]

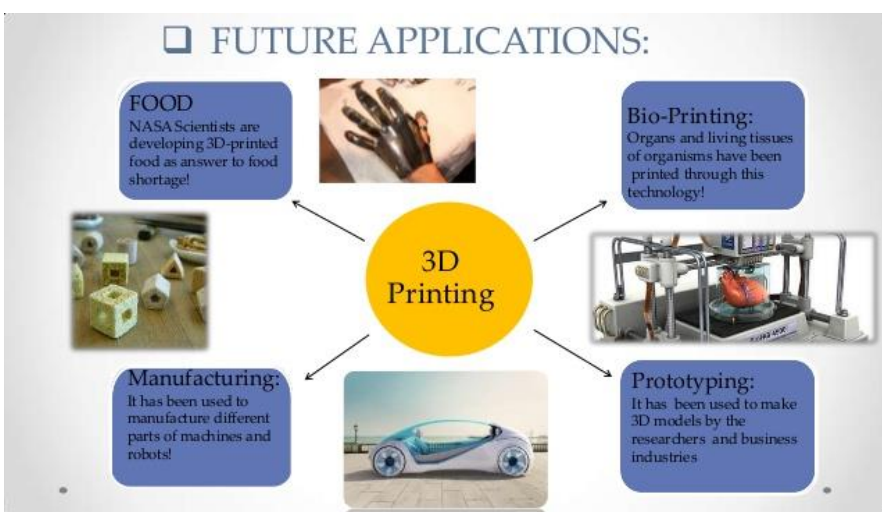

Fig 14: Future applications [20]

CONCLUSION:

- Computational intelligence (CI) comes up with more and more sophisticated, hierarchical learning machines. Running advanced techniques, including meta-learning, requires general data mining systems, capable of efficient management of machines.
- The capture results as static reports, or in the case of archives, as raw data. In both cases, the information is almost impossible to re-use. But computerized data re- use to make observations and draw conclusions.
- In contrast to purely sequence-based co receptor usage predictions, the proposed 3D structural representation captures the relative three-dimensional arrangement of chemical groups.
- The combination of methods from 3D structural bioinformatics with statistical learning methods allows for competitive performance as well as interpretation of co receptor usage at the structural level.
- SPRITAM® (levetiracetam) tablets, for oral suspension is an innovative product by 3D printing technology which disintegrates in the mouth with a sip of liquid and offers a new option for patients, including those who may struggle to take their medicine.

REFERENCES:

1.BIOINFORMATICS Introduction, Mark Gerstein, Yale University, bioinfo.mbb.yale.edu/mbb452a 5
2.Definition of informatics. http://en.wikipedia.org/ wiki/Informatics_(academic_field), http://www.bioinfcpcri.org/resources/definition.htm, www. Niobioinformatics .in/pdf /workshop /chemoinformatics_ IJITM.doc -Chemoinformatic in drug discovery By Tudor I. Oprea,
3.Bio-informatics, Wikipedia, on 27-12-2017.
niaz ahmad etal., a review on use of bio informatics tools in different spheres of life sciences,j.data mining genomics proeomics, 5(2), 2014.
4.https://en.wikipedia.org/wiki/2D_computer_graphics
5.An Introduction to 3D Printing Introduction, September 2015
6.Gaurav Tyagi, Technical Director/DIO, NIC-Muzaffarnagar, UP
7.Bhusnure O.G., et. al, 3D Printing & Pharmaceutical Manufacturing: Opportunities and Challenges, Ijppr.Human, 2015; Vol. 5 (1): 136-175.
8.Kazi Marzuka S, et. Al, 3D Printing: A New Avenue in Pharmaceuticals, Volume 5, Issue 5, 1686-1701., ISSN 2277– 7105
9.C. Lee Ventola, MS, Medical Applications for 3D Printing: Current and Projected Uses, October 2014 ,Vol. 39 No. 10, 704-711
10.Images of 3dp fabricated caplets in fabrication of controlled release budesonide tablets from science direct.com.
11.Giovanny F.Acosta –velez etal., 3D pharming :direct printing of personalized pharmaceutical tablets in polymer sciences, 1(2), 2016.
12.Fused deposition modelling (FDM), custompart.net. on 22-12-2017.
13.leslie langnau et al.,laser sintering -what is it,in make it fast, 2013.
14.Inkjet and multi jet printing , kyle stetz , rapid prototyping study.
15.3D printing materials market to reach in million globally, pitchegine.
16.Witold jamrz, printing techniques: recent developments in pharmaceutical technology, acta poloniae pharmaceutical and drug research, vol. 74 no. 3 pp. 753-763, 2017
17. First fda-approved medicine manufactured using 3d printing technology now available spritam® is designed to transform experience of taking epilepsy medication
18.https://www.slideshare.net/asertseminar/3d-printing-32339682
19.3D printing: medical applications in Disabled world.
20.3D printing steps: modelling printing finishing future applications, slide share.