

Digital oncology, the dawn of a new era turning the clock back on tumor mass

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Abstract

Evolutionary path of cancer therapeutics which started around eighty-two years ago, following serendipitous discovery of nitrogen mustard [1] has been guided by an accelerated pace of new discoveries, an ever-increasing depth of understanding of intracellular biological processes [2] and application of advances made in other fields of science [3].

Success in any field, especially in cancer medicine, is based on embracing evolution in understanding other scientific fields [4] and its application to the forward move in cancer therapeutics. As such, we have gone through discovery of a diverse group of therapeutics, targeting different sub compartments of growth and proliferation pathways [5] and taking advantage of their synergistic efficacy, in different combinations [6]. Dissection of immune regulatory pathways [7] and their interaction with cancer cell has led to the generation of modern immune therapeutic agents. Single-cell sequencing technology [8] has paved the way for the development of spatial omics [9], which has opened the way on deeper understanding of tumor evolutionary path [10]. This would give us the opportunity to design a new generation of cancer therapeutics [11] intercepting with the forward evolutionary path of tumor mass.

Along this path, we face insurmountable barriers in developing meaningful and game changing treatment strategies by directing single changes in a hyper complex biological system [12], manifested by complexities of genome [13], epigenome [14], microRNA network [15], gene regulatory mechanisms [16], and protein-protein interactions [17]. Consequently, we need to search for a solution that enables us to freeze or slow down the forward evolutionary path of tumor mass [18], by making a single change in a game changing variable of cancer cell.

Spatial Entropyomics and Artificial Intelligence (AI), as the Next Wave

In contradistinction to the published spatial omics, including spatial genomics [19], epigenomics [20], transcriptomics [21], and proteomics [22], which present a hyper complex set of data in each category, spatial entropyomics [23], presents only one value, number or digit that applies to one single step in evolution of tumor mass.

Available mathematical models [24] defining master regulator complex network entropy of malignant cells prove and provide a much higher value for malignant cells, as compared with their normal counterparts. Forward evolutionary move of tumor mass [25] along the thermodynamic arrow of time [26], necessitates an ever-increasing master regulator complex network entropy of driver zone [27]. This could be calculated by employing single-cell technology [28]. The artificial intelligence (AI) revolution [29], which has already permeated various disciplines within biology and medicine, will enable us to calculate both the current and future master regulator complex network entropy of tumor mass driver zones.

As such, we could generate an archive of a series of numbers [digits] which belong to different driver zones [30] at different time brackets along the thermodynamic arrow of time from past to future. This is akin to digital revolution [31] which has replaced analog system in electronics.

Conversion of Master Regulator Complex Network Entropy: The Final Stride

Major advances in nanotechnology [32], especially nano-delivery [33] and biological nanomachines [34] are expected to propel this venture to completion. Master regulator complex network entropy values of different malignant cells comprising the tumor mass [35] could get coded by a time value, as it relates to past, present, and future of tumor mass [36]. These numbers can be input into a specifically designed software program. This represents spatial entropyomics (Figure 1).

Modifications in these values, needed to convert current and future driver zones [37] to past and present driver zones respectively, would be calculated by employing AI. This data is handed to nano-technology and nano-delivery team, whose task is to design a physical or biological modification [38] needed and its delivery to driver zones of interest, so that the driver zones would be shifted back in time [39]. As such, we would reverse the thermodynamic arrow of time [40] in tumor mass, ie: we would drag tumor mass back in time (Figure 2).

On one occasion we might come in need of delivery of certain electrostatic force [41] to driver zone of interest and on another occasion we might come in need of delivery of a gene

editing mechanism [42] using clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9 to the zone of interest.

The common denominator among all different tasks is to take the driver zone to the past. This would freeze or significantly slow down the forward evolutionary speed of tumor mass [43] and would make cancer a chronic disease.

Conclusion

The history of cancer therapeutics which started eighty-two years ago, through serendipitous discovery of nitrogen mustard, has taken us through a tortuous path. Deep understanding of dynamics of tumor mass and its evolution has brought us to spatial entropyomics and digital age in modern oncology. Revolutions in AI, single-cell sequencing, nanotechnology and their application in the design of future cancer therapeutics, are expected to turn cancer into a chronic disease, even if not cured, without the toxicities associated with chemotherapy [44], radiation therapy [45], immunotherapy [46] and biological agents [47]. If we could make this historical achievement within one hundred years following introduction of nitrogen mustard into cancer therapeutics, our future generations would one day say, it took their ancestors one hundred years to solve one of the most complicated problems human race ever faced.

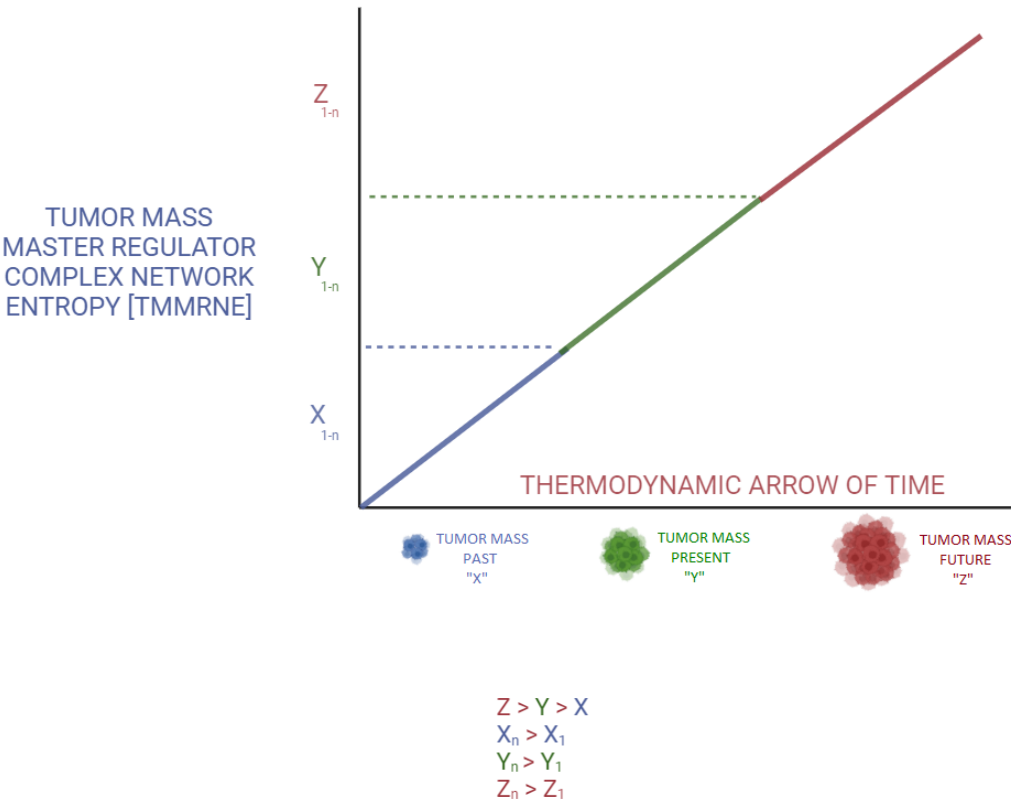


Figure 1: Tumor mass MRNE along the thermodynamic arrow of time. As tumor mass evolutionary path takes it from past to present and future, master regulator complex network entropy increases accordingly and to higher values.

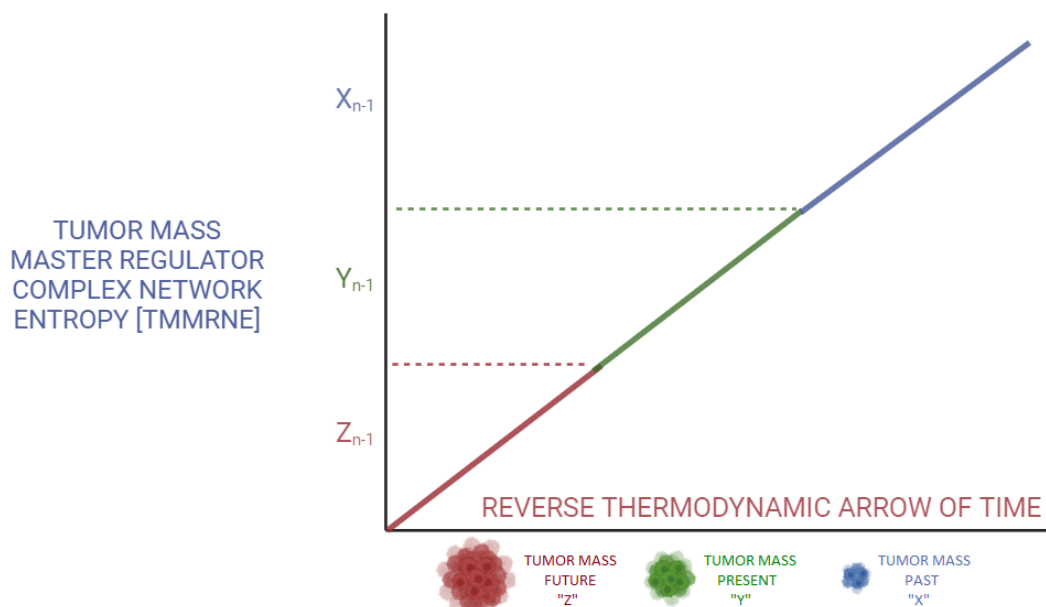


Figure 2: Dragging tumor mass back in time.

Taking master regulator network entropy of tumor mass back in time, i.e. changing MRNE [master regulator network entropy].

Value of Present to past and future to present.

By applying single cell sequencing technology and calculating MRNE of isolated cells, we could map tumor mass evolutinary path by those values. By using AI, we could predict the future drive zone MRNE. By employing nano-technology and nano-delivery through nanomachines, we could modify those values in reverse direction of themodynamic arrow of time.

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