blob loss: instance imbalance aware loss functions for semantic segmentation

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Abstract. Deep convolutional neural networks (CNN) have proven to be remarkably effective in semantic segmentation tasks. Most popular loss functions were introduced targeting improved volumetric scores, such as the Dice coefficient (DSC). By design, DSC can tackle class imbalance, however, it does not recognize instance imbalance within a class. As a result, a large foreground instance can dominate minor instances and still produce a satisfactory DSC. Nevertheless, detecting tiny instances is crucial for many applications, such as disease monitoring. For example, it is imperative to locate and surveil small-scale lesions in the follow-up of multiple sclerosis patients. We propose a novel family of loss functions, blob loss, primarily aimed at maximizing instance-level detection metrics, such as $F_1$ score and sensitivity. Blob loss is designed for semantic segmentation problems where detecting multiple instances matters. We extensively evaluate a DSC-based blob loss in five complex 3D semantic segmentation tasks featuring pronounced instance heterogeneity in terms of texture and morphology. Compared to soft Dice loss, we achieve 5% improvement for MS lesions, 3% improvement for liver tumor, and an average 2% improvement for microscopy segmentation tasks considering $F_1$ score.

Keywords: semantic segmentation loss function, instance imbalance awareness, multiple sclerosis, lightsheet microscopy

1 Introduction

In recent years convolutional neural networks (CNN) have gained increasing popularity for complex machine learning tasks, such as semantic segmentation. In semantic segmentation, one segments objects from different classes without differentiating multiple instances within a single class. In contrast, instance segmentation explicitly takes multiple instances into account, which involves simultaneous localization and segmentation. While U-net variants still represent the state-of-the-art to address semantic segmentation, Mask-RCNN and its variants dominate instance segmentation [12]. The scarcity of training data often hinders the application of back-bone-dependent Mask RCNNs, while U-Nets have proven to be less data-hungry [5].

However, many semantic segmentation tasks feature relevant instance imbalance, where large instances dominate over smaller ones within a class, as illustrated in Figure 1. Instances can vary not only with regard to size but also texture and other morphological features. U-nets trained with existing loss functions, such as Soft Dice [6,19,20,25,29], cannot address this. Instance imbalance is particularly pronounced and significant in medical applications: For example, even a single new multiple sclerosis (MS) lesion can impact the therapy decision. Despite many ways to compensate for class-imbalance [24,9,23,29], there is a notable void in addressing instance imbalance in semantic segmentation settings. Additionally, established metrics have been shown to correlate insufficiently with expert assessment [16].
**Contribution:** We propose *blob loss*, a novel framework to equip semantic segmentation models with instance imbalance awareness. This is achieved by dedicating a specific loss term to each instance without the necessity of instance-wise prediction. *Blob loss* represents a method to convert any loss function into a novel instance imbalance aware loss function for semantic segmentation problems designed to optimize detection metrics. We evaluate its performance on five complex three-dimensional (3D) semantic segmentation tasks, for which the discovery of miniature structures matters. We demonstrate that extending soft Dice loss to a *blob loss* improves detection performance in these multi-instance semantic segmentation tasks significantly. Furthermore, we also achieve volumetric improvements in some cases.

**Related work:** Sirinukunwattana et al. [28] suggested an instance-based Dice metric for evaluating segmentation performance. Salehi et al. [25] were among the first to propose a loss function, called *Tversky loss*, for semantic segmentation of multiple sclerosis lesions in magnetic resonance imaging (MR), trying to improve detection metrics. Similarly, Zhu et al. [33] introduced Focal Loss, initially designed for object detection tasks [18], into medical semantic segmentation tasks.

There have been few recent attempts aiming for a solution to instance imbalance. Zhang et al. [31] propose an auxiliary lesion-level sphere prediction task. However, they do not explicitly consider each instance separately. Shirokikh et al. [26] propose an instance-weighted loss function where a global weight map is inversely proportional to the size of the instances. However, unlike size, not all types of imbalance, such as morphology or texture, can be quantified easily, limiting the method’s applicability.
2 Methods

First, we introduce the problem of instance imbalance in semantic segmentation tasks. Then we present our proposed blob loss functions.

**Problem statement:** Large foreground areas dominate the calculation of established volumetric metrics (or losses); see Figure 1.

![Fig. 1. Problem statement (left): The Dice coefficient (DSC) for the segmentation with vs. without a lesion, encircled in green, is: 0.9806. Therefore, the segmentations are hardly distinguishable in terms of DSC. However, from a clinical perspective, the difference is important as the detection of a single lesion can affect treatment decisions. Comparison of segmentation performance (right): Maximum intensity projections of the FLAIR images overlayed with segmentations for *dice* and *blob dice*. Lesions are colored according to their detection status: Green for *true positive*; Blue for *false positive*; Red for *false negative*. For this particular patient, applying the transformation to a *blob loss* improves $F1$ from 0.74 to 1.0 and the volumetric Dice coefficient from 0.56 to 0.70 and the latter is caused by an increase in *volumetric precision* from 0.48 to 0.75, while the *volumetric sensitivity* remains constant at 0.66.](image)

This is because the volumetric measures only accumulate true or false predictions on a voxel level but not at the instance level. Therefore, training models with volumetry-based loss functions, such as soft Dice loss (*dice*), often leads to unsatisfactory instance detection performance. To achieve a better instance detection performance, it is necessary to take instance imbalance into account. Instance imbalance can be of many categories, such as morphology and texture. Importantly, instance imbalance often cannot be easily specified and quantified for use in CNN training, for example, as instance weights in the loss function. Thus, using conventional methods, it is difficult to incorporate instance imbalance in CNN training. Our objective is to design loss functions to compensate for the instance imbalance while being agnostic to the instance imbalance type. Therefore, we aim to dissect the image domain in an instance-wise fashion:

**blob loss formulation:** Consider a generic volumetric loss function $\mathcal{L}$ and image domain $\Omega$ and foreground domain $P$. Formally our objective is to find an
instance-specific subdomain $\Omega_n \subseteq \Omega$ corresponding to the $n^{th}$ instance such that $\mathcal{L}$ acting on $\Omega_n$ is aware of instance imbalance. The criteria to obtain these subsets $\{\Omega_n\}_{n=1}^N$ are such that $\Omega_i \cap \Omega_j \cap P = \emptyset; \forall (i,j)$, s.t. $1 \leq i, j \leq N, i \neq j$ and $\bigcup_{n=1}^N \Omega_n = \Omega$. In simple terms, the subsets $\{\Omega_n\}_{n=1}^N$ need to be mutually exclusive regarding foreground and collectively exhaustive with regard to the whole image domain.

To formalize blob loss, we address instance imbalance within a binary semantic segmentation framework. At the same time, we remain agnostic towards particular instance attributes and do not incorporate these in the loss function. To this extent, we propose to leverage the existing reference annotations and formally propose a novel family of instance-aware loss functions.

Consider a segmentation problem with $N$ instances; for different input images, $N$ can vary from few to many. Specifically, we propose to compute the instance-specific domain $\Omega_n$ by excluding all but the $n^{th}$ foreground from the whole image domain $\Omega$, see Equation (1):

$$\Omega_n = \Omega \setminus \bigcup_{j=1, j \neq n}^N P_j \quad (1)$$

where $P_j$ is the foreground domain for $j^{th}$ instances of $P$. This masking process is illustrated by Figure 2. It is worth noting that the background voxels are included in every $\Omega_n$.

Fig. 2. Masking process described in Equation (2). Left: the global ground truth label (GT), with the $n^{th}$ instance highlighted in green. Middle: The loss mask $\Omega_n$ for the $n^{th}$ instance (MASK) for multiplication with the network outputs. Right: the label used for the computation of the local blob loss for the $n^{th}$ instance. This process is repeated for every instance.

We propose to convert any loss function $\mathcal{L}$ for binary semantic segmentation into an instance-aware loss function $\mathcal{L}_{\text{blob}}$ defined as:

$$\mathcal{L}_{\text{blob}} ((p_i)_{i \in \Omega},(g_i)_{i \in \Omega}) = \frac{1}{N} \sum_{n=1}^N \mathcal{L} ((p_i)_{i \in \Omega_n},(g_i)_{i \in \Omega_n}) \quad (2)$$

where $\{(g_i)_{i \in \Omega}\}$ is the ground-truth segmentation, $\{(p_i)_{i \in \Omega}\}$ is the predicted segmentation, $N$ is the number of instances in the foreground.
As our goal is to assign equal importance to all instances irrespective of their size, shape, texture, and other topological attributes, we average over all instances.

To compute the total loss for a volume, we combine the instance-wise Loss component from Equation (2) with a global component to obtain the final Loss:

\[
L_{\text{total}} = \alpha L_{\text{global}} + \beta L_{\text{blob}}
\]

where \(\alpha\) and \(\beta\) denote the weights for the global and instance constraint \(L_{\text{blob}}\). We (anonymously) provide a sample Pytorch implementation of a dice-based blob loss on [GitHub]. In order to accelerate our training, we precompute the instances, here defined as connected components using cc3d [27], version 3.2.1.

**Model training:** For all our experiments, we use a basic 3D U-Net implemented via [MONAI] inspired by [8] and further depicted in supplementary materials. Furthermore, we use a dropout ratio of 0.1 and employ mish as activation function [21]. Otherwise, we stick to the default parameters of the U-Net implementation.

**Loss functions for comparison:** As baselines we use the MONAI implementations of soft Dice loss (dice) and Tversky loss (tversky) [25]. For tversky, we always use the standard parameters of \(\alpha = 0.3\) and \(\beta = 0.7\) suggested by the authors in the original publication [25]. For comparison we create blob dice, by transforming the standard dice into a blob loss using our conversion method Equation (2). The final loss is obtained by employing dice in the \(L_{\text{global}}\) and \(L_{\text{blob}}\) terms of the proposed total loss Equation (3). In analog fashion, we derive blob tversky. Furthermore, we compare against inverse weighting (iw), the globally weighted loss function of Shirokikh et al. [26]. For this, we use the official GitHub implementation to compute the weight maps and loss and deploy these in our training pipelines.

**Training procedure:** Our CNNs are trained on multiple cuboid-shaped crops per batch element, with higher resolution in the axial dimension, enabling the learning of contextual image features. The crops are randomly sampled around a center voxel that consists of foreground with a 95% probability. We consider one epoch as one full iteration of forward and backward passes through all batches of the training set. For all training, Ranger21 [30] serves as our optimizer. For each experiment, we keep the initial learning rate (lr) constant between training runs. Depending on the segmentation task, we deploy varying suitable image normalization strategies. For comparability, we keep all training parameters except for the loss functions constant on a segmentation task basis and stick to this standard training procedure.

**Training-test split and model selection:** Given the high heterogeneity of our bio-medical datasets and the limited availability of high-quality ground truth annotations due to the very costly labeling procedures requiring domain experts, we do not set aside data for validation and therefore do not conduct model selection. Instead, inspired by [14], we split our data 80:20 into training and test set and evaluate on the last checkpoint of the model training. As an exception, the MS dataset comes with predefined training, validation, and test set splits;
therefore, we additionally evaluate the best model checkpoint, meaning the model with the lowest loss on the validation set. As we are more interested in blob loss’ generalization capabilities than exact quantification of improvements on particular datasets, we prioritize a broad validation on multiple datasets over cross-validation.

**Technical details:** Our experiments were conducted using NVIDIA RTX8000, RTX6000, RTX3090, and A6000 GPUs using CUDA version 11.4 in conjunction with Pytorch version 1.9.1 and MONAI version 0.7.0.

### 2.1 Evaluation Metrics and Interpretation

**Metrics:** We obtain global, volumetric performance measures from pymia [15]. In addition to DSC, we also evaluate volumetric sensitivity ($S$), volumetric precision ($P$), and the Surface Dice similarity coefficient (SDSC). To compute instance-wise detection metrics, namely instance F1 ($F1$), instance sensitivity ($IS$) and instance precision ($IP$), we employ a proven evaluation pipeline from Pan et al. [22].

**Interpretation:** By design, human annotators tend to overlook tiny structures. For comparison, human annotators initially missed 29% of micrometastases when labeling the DeepMACT light-sheet microscopy dataset [22]. Therefore, the likelihood of a structure being correctly labeled in the ground truth is much higher for foreground than for background structures. Additionally, human annotators have a tendency to label a structure’s center but do not perfectly trace its contours. Both phenomena are illustrated in Figure 3. These effects are particularly pronounced for microscopy datasets, which often feature thousands of blobs. These factors are important to keep in mind when interpreting the results. Consequently, volumetric - and instance sensitivity are much more informative than volumetric and instance precision.
3 Experiments

To validate blob loss, we train segmentation models on a selection of datasets from different 3D imaging modalities, namely brain MR, thorax CT, and light-sheet microscopy. We select datasets featuring a variety of fragmented semantic segmentation problems. Figure 12 features an overview over blob counts, volumetrics, and shape features in the datasets. For simplicity, we use the default values $\alpha = 2.0$ and $\beta = 1.0$ across all experiments.

Multiple Sclerosis (MRI): The Multiple Sclerosis (MS) dataset, comprising 521 single timepoint MRI examinations of patients with MS, was collected for internal validation of MS lesion segmentation algorithms. The patients come from a representative, institutional cohort covering all stages (in terms of time from disease onset) and forms (relapsing-remitting, progressive) of MS. A 3D T1w and a 3D FLAIR sequence were acquired on a 3 Tesla Philips Achieva scanner. All 3D volumes feature $193 \times 193 \times 229$ voxels in 1mm isotropic resolution. The dataset divides into a fixed training set of 200, a validation set of 21, and a test set of 200 cases. The annotations feature a total of 4791 blobs, with $25.69 \pm 23.01$ blobs per sample. Expert neuroradiologists annotated the MS lesions manually and ensured pristine ground truth quality with consensus voting.

For all training runs of 500 epochs, we set the initial learning rate to $1e^{-2}$ and the batch size to 4. The networks are trained on a single GPU using 2 random crops with a patch size of $192 \times 192 \times 32$ voxels per batch element after applying a min/max normalization. As the MS dataset comes with a predefined validation set of 21 images, we also save the checkpoint with the lowest loss on the validation set and compare it to the respective last checkpoint of the training. In addition to the standard dice, we also compare against tversky. Furthermore, we conduct an ablation study to find out how the performance metrics are affected by choosing different values for $\alpha$ and $\beta$.

Liver Tumors - LiTS (CT): To develop an understanding of blob loss performance on other imaging modalities, we train a model for segmenting liver tumors on CT images of the LiTS challenge [4]. The dataset consists of varying high-resolution CT images of the abdomen. The challenge’s original task was segmenting liver and liver tumor tissue. As we are primarily interested in segmenting small fragmented structures, we limit our experiments to the liver area and segment only liver tumor tissue (in contrast to tumors, the liver represents a huge solid structure, and we are interested in blobs). We split the publicly available training set into 104 images for training and 27 for testing. The annotations were created by expert radiologists and feature a total of 908 blobs, with $12.39 \pm 14.92$ blobs per sample.

For all training runs of 500 epochs, we set the initial learning rate to $1e^{-2}$ and the batch size to 2. The networks are trained on two GPUs in parallel using 2 random crops with a patch size of $192 \times 192 \times 64$ voxels per batch element. We apply normalization based on windowing on the Hounsfield (HU) scale. Therefore, we define a normalization window suitable for liver tumor segmentation around center 30 HU with a width of 150 HU, and 20% added tolerance.
**DISCO-MS (light-sheet microscopy)** To develop an understanding for blob loss performance on other imaging modalities, we train a model for segmenting Amyloid plaques in light-sheet microscopy images of the DISCO-MS dataset [3].

The volumes of 300x300x300 voxels resolution contain cleared tissue of mouse brain. We split the publicly available dataset into 41 volumes for training and six for testing. The annotations feature a total of 988 blobs, with 28.32±24.44 blobs per sample. Even though the label quality is very high, the results should still be interpreted with care following the guidelines in Section 2.1.

For all training runs of 800 epochs, we set the initial learning rate to 1e-3 and the batch size to 6. As our initial model trained with dice does not produce satisfactory results, we furthermore try learning rates of 1e-2, 3e-4 and 1e-4, following the heuristics suggested by [1] without success. The networks are trained on two GPUs in parallel using 2 random crops with a patch size of 192x192x64 per batch element. The images are globally normalized, using a minimum and maximum threshold defined by the 0.5 and 99.5 percentile.

**SHANEL (light-sheet microscopy)** For further validation, we evaluate neuron segmentation in light-sheet microscopy images of the SHANEL dataset [32]. The volumes of 200x200x200 voxels resolution contain cleared human brain tissue from the primary visual cortex, the primary sensory cortex, the primary motor cortex, and the hippocampus. We split this publicly available dataset into nine volumes for training and three for testing. The annotations feature a total of 20684 blobs, with 992.14±689.39 blobs per sample. As the data is more sparsely annotated than DISCO-MS, F1 and especially DSC should be interpreted with great care, as described in Section 2.1.

For all training runs of 1000 epochs, we set the initial learning rate to 1e-3 and the batch size to 3. The networks are trained on two GPUs in parallel using 6 random crops with a patch size of 128x128x32 per batch element, with min/max normalization.
DeepMACT (light-sheet microscopy) For further validation, we evaluate the segmentation of micrometastasis in light-sheet microscopy images of the DeepMact dataset [22]. The volumes of 350x350x350 resolution contain cleared tissue featuring different body parts of a mouse. We split the publicly available dataset into 115 images for training and 19 for testing. The annotations feature a total of 484 blobs, with 6.99±8.14 blobs per sample. As the data is sparsely annotated, F1 and especially DSC should be interpreted with great care, as described in Section 2.1.

For all training runs of 500 epochs, we set the initial learning rate to 1e-2 and the batch size to 4. The networks are trained on a single GPU using 2 random crops with a patch size of 192x192x48. The images are globally normalized based using a minimum and maximum threshold defined by the 0.0 and 99.5 percentile.
4 Results

Table 1 summarizes the quantitative results of our experiments and Figures 43 and 44 (Appendix) visualize qualitative results. Across all datasets, we find that extending dice to a blob loss helps to improve detection metrics. Furthermore, in some cases, we also observe improvements in volumetric performance measures. While model selection seems not beneficial on this dataset, employing blob loss produces more robust results, as both the dice and tversky models suffer performance drops for the best checkpoints. Notably, even though tversky was explicitly proposed for MS lesion segmentation, it is clearly outperformed by dice, as well as blob dice and blob tversky. Further, even with the mitigation strategies suggested by the authors, inverse weighting produced over-segmentations.

Table 1. Experimental results for five datasets. For all training runs with blob loss we use $\alpha = 1$ and $\beta = 2$. Note that the results for LiTS are based on a different, more challenging test set and are therefore not comparable with the public leaderboard of the LiTS challenge. For DISCO-MS, the dice model completely over-segments and produces dissatisfactory results. Therefore, we try two additional training runs with reduced learning rates following the heuristics suggested by [1], resulting in similar over-segmentation. The same problem is observed for inverse weighting (iw). Shirokikh et al. [26] themselves note the stability problems of the method and suggest lowering the learning rate to $1 - e^{-3}$.

| dataset   | loss            | lr  | DSC  | SDSC | F1   | IS   | IP   |
|-----------|-----------------|-----|------|------|------|------|------|
| MS        | blob dice       | 1e-2| 0.680| 0.848| 0.810| 0.822| 0.828|
|           | dice            | 1e-2| 0.660| 0.820| 0.758| 0.854| 0.711|
|           | iw [26]         | 1e-2| 0.153| 0.167| 0.278| 0.801| 0.188|
|           | iw [26]         | 1e-3| 0.243| 0.273| 0.282| 0.819| 0.189|
|           | blob tversky    | 1e-2| 0.690| 0.852| 0.804| 0.829| 0.804|
|           | tversky         | 1e-2| 0.601| 0.697| 0.566| 0.854| 0.459|
| LiTS      | blob dice       | 1e-2| 0.663| 0.542| 0.657| 0.861| 0.631|
|           | dice            | 1e-2| 0.659| 0.546| 0.623| 0.801| 0.599|
| SHANEL    | blob dice       | 1e-3| 0.543| 0.808| 0.792| 0.874| 0.724|
|           | dice            | 1e-3| 0.539| 0.794| 0.783| 0.854| 0.723|
| DISCO-MS  | blob dice       | 1e-3| 0.546| 0.678| 0.589| 0.760| 0.481|
|           | dice            | 1e-3| 0.095| 0.083| 0.012| 0.870| 0.006|
|           |                 | 3e-4| 0.016| 0.036| 0.379| 0.896| 0.240|
|           |                 | 1e-4| 0.007| 0.011| 0.228| 0.825| 0.132|
| DeepMACT  | blob dice       | 1e-2| 0.357| 0.393| 0.391| 0.871| 0.276|
|           | dice            | 1e-2| 0.353| 0.372| 0.367| 0.801| 0.254|

Table 2 summarizes the results of the ablation study on $\alpha$ and $\beta$ parameters of blob loss. We find that assigning higher importance to the global parameter by choosing $\alpha = 2$ and $\beta = 1$ seems to produce the best results. Overall, we
Table 2. Ablation analysis on the blob loss’ hyperparameters $\alpha$ and $\beta$ for the MS lesions dataset. We observe that blob loss seems to be quite robust with regard to hyperparameter choice, as long as the global term remains present, compare Equation (3). The default parameters $\alpha = 2$ and $\beta = 1$ provide the best results.

| loss     | $\alpha$ | $\beta$ | DSC   | S     | P     | SDSC  | F1    | IS    | IP    |
|----------|----------|----------|-------|-------|-------|-------|-------|-------|-------|
|blob dice | 3        | 1        | 0.674 | 0.629 | 0.765 | 0.833 | 0.790 | 0.796 | 0.815 |
|blob dice | 2        | 1        | **0.680** | 0.626 | 0.782 | **0.848** | **0.810** | 0.822 | **0.828** |
|blob dice | 1        | 1        | 0.658 | 0.580 | 0.802 | 0.839 | 0.804 | 0.840 | 0.801 |
|blob dice | 1        | 2        | 0.630 | 0.552 | 0.803 | 0.819 | 0.792 | 0.832 | 0.786 |
|dice      | 1        | 0        | 0.660 | **0.704** | 0.656 | 0.820 | 0.758 | **0.854** | 0.711 |
|blob      | 0        | 1        | 0.522 | 0.409 | **0.837** | 0.728 | 0.744 | 0.805 | 0.727 |

find that blob loss seems quite robust regarding the choice of hyperparameters as long as the global term remains included by choosing a $\alpha$ greater than $0$. 
5 Discussion

**Contribution:** blob loss can be employed to provide existing loss functions with instance imbalance awareness. We demonstrate that the application of blob loss improves detection- and in some cases, even volumetric segmentation performance across a diverse set of complex 3D bio-medical segmentation tasks. We evaluate blob loss’ performance in the segmentation of multiple sclerosis (MS) lesions in MR, liver tumors in CT, and segmentation of different biological structures in 3D light-sheet microscopy datasets. Depending on the dataset, it achieves these improvements either due to better detection of foreground objects, better suppression of background objects, or both. We provide an implementation of blob loss leveraging on a precomputed connected component analysis for fast processing times.

**Limitations:** Certainly, the biggest disadvantage of blob loss is the dependency on instance segmentation labels; however, in many cases, these can be simply obtained by a connected component analysis, as demonstrated in our experiments. Another disadvantage of blob loss compared to other loss functions are the more extensive computational requirements. By definition, the user is required to run computations with large patch sizes that feature multiple instances. This results in an increased demand for GPU memory, especially when working with 3D data (as in our experiments). However, larger patch sizes have proven helpful for bio-medical segmentation problems, in general. Furthermore, according to our formulation, blob loss possesses an interesting mathematical property, it penalizes false positives proportionally to the number of instances in the volume. Additionally, even though blob loss can easily be reduced to a single hyperparameter, and it proved quite robust in our experiments, it might be sensitive to hyperparameter tuning. Moreover, by design blob loss can only improve performance for multi-instance segmentation problems.

**Interpretation:** One can only speculate why blob loss improves performance metrics. CNNs learn features that are very sensitive to texture. Unlike conventional loss functions, blob loss adds attention to every single instance in the volume. Thus the network is forced to learn the instance imbalanced features such as, but not limited to morphology and texture, which would not be well represented by optimizing via dice and alike. Such instance imbalance was observed in the medical field, as it has been shown that MS lesions change their imaging phenotype over time, with recent lesions looking significantly different from older ones. These aspects might explain the gains in instance sensitivity. Furthermore, adding the multiple instance terms leads to heavy penalization on background, which might explain why we often observe an improvement in precision, see supplementary materials.

**Outlook:** Future research will have to reveal to which extent transformation to blob loss can be beneficial for other segmentation tasks and loss functions. A first and third place in recent public segmentation challenges using a compound-based variant blob loss indicate that blob loss might possess broad applicability towards other instance imbalanced semantic segmentation problems.
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6 Supplementary Materials

In the supplementary materials we use the acronyms introduced in the main text. For easier understanding we repeat the ones used in the tables: learning-rate (lr); Sørensen-Dice similarity coefficient (DSC); Surface Dice similarity coefficient (SDSC); Instance sensitivity (IS); Instance Precision (IP)

6.1 Data Set Description

Fig. 42. Dataset heterogeneity and instance imbalance. Boxplot left: blob count per sample; Boxplot right: volume per blob. For visualization purposes, the boxplots are cut off at the 95% percentile. The four kernel density plots on the bottom depict four shape features, defined as: Compactness: Volume of blob divided by the volume of a hypothetical enclosing sphere. Sphereness: Ratio of the maximum distance within a blob to the diameter of a hypothetical sphere with the same volume as the blob. Stringness: Equals 1 − Sphereness and approaches 1 for string-like shapes. Skewness: Approaches 1 if a blob is thick or dense on one end and has a large tail on the other side.
6.2 Data Availability Statements

As the MS dataset contains sensitive patient information, requests for the MS data will be reviewed by an ethical committee to determine whether the request is subject to any confidentiality obligations. Requests should contain a research proposal, an ethics statement, and a data transfer agreement. LiTS challenge data is publicly available at [codalab.org](http://codalab.org). SHANEL, DISCO-MS, and DeepMACT datasets are available upon request via [discotechnologies.org](http://discotechnologies.org).

6.3 Why the two hyper-parameters $\alpha$ and $\beta$?

One might wonder why *blob loss* is defined with $\alpha$ and $\beta$, while $\beta$ could easily be defined as $1 - \alpha$. Assume one would want to extend a conventional soft dice loss (this equals $\alpha = 1$ and $\beta = 0$) to a *blob dice* with equal weights to see if it aids segmentation performance. In this case, $\alpha$ and $\beta$ would both become 0.5. As the initial soft dice loss is now halved, one needs to double the learning rate to maintain comparability between training runs. These learning rate adjustments can become cumbersome, especially when operating with non equal weighted loss candidates.

6.4 Why do we need masking?

To explore the effect of the masking defined in Equation (2), we train another model on the MS dataset. Therefore, we keep all training parameters constant except for the loss. Here, we skip the masking inside the loss computation. We find that the masking is crucial for achieving a high segmentation performance, see Table 42.

### Table 42. Segmentation performance when computing the loss without masking.

| dataset | architecture | loss            | lr   | DSC  | SDSC  | F1   | IS   | IP   |
|---------|--------------|-----------------|------|------|-------|------|------|------|
| MS      | BasicUnet    | blob dice       | 1e-2 | 0.680| 0.848 | 0.810| 0.822| 0.828|
| MS      | BasicUnet    | dice            | 1e-2 | 0.660| 0.820 | 0.758| 0.854| 0.711|
| MS      | BasicUnet    | no_masking      | 1e-2 | 0.358| 0.382 | 0.297| 0.829| 0.201|
6.5 Qualitative Segmentation Performance

Fig. 43. Comparison of detection performance. Maximum intensity projections of the FLAIR images overlayed with segmentations for dice and blob dice. Lesions are colored according to their detection status: Green for true positive; Blue for false positive; Red for false negative. In this case, transformation to a blob loss improves $F1$ from 0.74 to 1.0. This is driven by an increase in instance-sensitivity from 0.83 to 1.0 and instance-precision from 0.67 to 1.0. Therefore, for this particular patient blob loss boosts $F1$ by simultaneously improving detection of foreground and suppression of background signal. This seems to be a regular pattern across multiple segmentation problems, compare Table 1. Refer to Figure 44 for a volumetric analysis.
Fig. 44. Comparison of volumetric segmentation performance. Maximum intensity projections of the FLAIR images overlayed with segmentations for dice and blob dice. Lesions are colored according to their detection status: Green for true positive; Blue for false positive; Red for false negative. For this particular patient, applying the transformation to a blob loss improves the volumetric Dice coefficient from 0.56 to 0.70. This is caused by an increase in volumetric precision from 0.48 to 0.75, while the volumetric sensitivity remains constant at 0.66. Thus, unlike on the detection level, the improvement is solely reached due to better suppression of background signal, compare Figure 43.

6.6 MS model selection experiment

Table 43. Results for the model selection experiment on MS data. We evaluate the checkpoint with the lowest loss on the validation set of 21 patients. As dice and especially tversky suffer big performance drops, conducting model selection seems to hurt the networks’ generalization ability. Training with blob loss leads to more robust performance.

| dataset | architecture | loss       | DSC  | SDSC | F1   | IS   | IP   |
|---------|--------------|------------|------|------|------|------|------|
| MS      | BasicUnet    | blob dice  | 0.678| 0.849| 0.800| 0.859| 0.775|
| MS      | BasicUnet    | dice       | 0.640| 0.800| 0.759| 0.810| 0.748|
| MS      | BasicUnet    | blob tversky| 0.692| 0.857| 0.796| 0.848| 0.775|
| MS      | BasicUnet    | tversky    | 0.405| 0.461| 0.413| 0.851| 0.302|
6.7 Multi-class Segmentation Extension of blob loss

Extension to multi-class segmentation problems can be achieved by summing across the foreground classes. Let \( \mathcal{L} \) a loss function for binary segmentation, and let \( p = (p^c_i)_{i \in \Omega, c=0...C} \) be the predicted segmentation and \( g = (g^c_i)_{i \in \Omega, c=0...C} \) the one-hot encoding of the ground-truth segmentation, where \( \Omega \) is the image domain and \( C \geq 1 \) is the number of foreground classes. We assume without loss of generality that the background corresponds to the class \( c = 0 \).

We propose to define the instance-aware loss function \( \mathcal{L}_{\text{blob}} \) associated with \( \mathcal{L} \) as

\[
\mathcal{L}_{\text{blob}}(p, g) = \frac{1}{C} \sum_{c=1}^{C} \left( \frac{1}{N_c} \sum_{n=1}^{N_c} \mathcal{L}((p^c_i)_{i \in \Omega_{c,n}}, (g^c_i)_{i \in \Omega_{c,n}}) \right)
\]

where \( \Omega_{c,n} \) is the image domain after excluding the voxels labeled as \( c \) in the ground-truth segmentation, and that does not belong to the instance \( n \).

The final loss for multi-class segmentation has the same form as for the binary segmentation case

\[
\mathcal{L} = \alpha \mathcal{L}_{\text{global}} + \beta \mathcal{L}_{\text{blob}}
\]

where \( \alpha \geq 0 \) and \( \beta \geq 0 \). Depending on the segmentation task at hand, one could further consider the introduction of class-specific \( \alpha \) and \( \beta \).

6.8 Dependency on Network architecture

U-Nets are the state-of-the-art architecture for bio-medical semantic segmentation \cite{ronneberger2015u}. As our primary goal is to evaluate a novel loss function, we choose the most standard U-Net architecture we could find for our experiments, see Figure 45. To investigate whether blob loss is dependent on the architecture we conduct a network architecture ablation study on the MS dataset. Despite exchanging the network architecture, we set the learning rate to \( 1e^{-3} \) and keep

![Fig. 45. The U-Net architecture used in the experiments, consisting of encoder and decoder parts. The numbers under the convolutional layers represent the channel count. The implementation is available via MONAI and is inspired by Falk et al. \cite{falk2021}.](image-url)
the other parameters constant to the previous training runs. We compare a blob dice and dice dice baseline with UNETR [11]. Unlike our basic U-Net implementation UNETR features transformers. The implementation is available via MONAI. Table 44 summarizes the results of the model selection ablation study.

**Table 44.** Architecture ablation study. We compare dice against blob dice for training runs with UNETR [11]. The results indicate that the performance improvements of blob loss are architecture agnostic.

| dataset | architecture | loss       | lr  | DSC  | SDSC | F1   | IS   | IP   |
|---------|--------------|------------|-----|------|------|------|------|------|
| MS      | UNETR        | dice       | 1e-3| 0.380| 0.386| 0.383| 0.870| 0.272|
| MS      | UNETR        | blob dice  | 1e-3| **0.632** | **0.789** | **0.691** | **0.889** | **0.600** |

### 6.9 Increased Instance-wise Penalization of False Positives for Soft Dice Loss

Applying blob loss leads to increased instance-wise penalization of false positives. Let $Y$ be the predicted segmentation, $L$ be the ground-truth binary segmentation, and $N > 0$ the number of instances. Reasonably, we can assume that our ground truth is perfect and can be used for accurate false-positives and false-negatives categorization. Let $\{L_i\}_{i=1}^N$ be the masks of the binary instances. Hence, by construction we have $\sum_{i=1}^N L_i = L$. Further, we define the domain mask for each instance $L_i$ as follows

$$\Omega_i = I - \sum_{j=1,j\neq i}^N L_j$$ (6)

where $I$ is the mask on the image domain $\Omega$ with all its values equal to 1.

Although we predict all instances in a single channel, one can decompose it into $N + 1$ number of channel

$$Y = \sum_{i=1}^N L_i \odot Y + \left(I - \sum_{i=1}^N L_i\right) \odot Y$$ (7)

where $\odot$ denotes Hadamard product. We denote $L_i \odot Y$ as $Y_i$ and $(I - \sum_{i=1}^N L_i) \odot Y$ as $Y_{fp}$. Note that $Y_i$ consists of voxel-wise true-positives and $Y_{fp}$ consists of false-positives. Using the definition of the blob loss in Equation 2, with $\mathcal{L}$ the
soft Dice loss, \( g = L_i \) and \( p = Y \odot \Omega_i \)

\[
\mathcal{L} ( (p^j)_{j \in \Omega_i}, (g^j)_{j \in \Omega_i} ) = \frac{2 \times \sum_{j \in \Omega_i} \sum_{j \in \Omega_i} g^j p^j}{\sum_{j \in \Omega_i} g^j + \sum_{j \in \Omega_i} p^j}; \quad \text{[superscript } j \text{ denotes each voxel]} \\
= \frac{2 \times \sum_{j=1}^{M} L_i^j Y_j^i \Omega_i^j}{\sum_{j=1}^{M} L_i^j + \sum_{j=1}^{M} (Y_j^i \odot \Omega_i^j)} \\
= \frac{2 \times \sum_{j=1}^{M} (L_i \odot Y_j)^j}{\sum_{j=1}^{M} L_i^j + \sum_{j=1}^{M} (Y \odot \Omega_i)^j}; \quad \text{[using the fact } L_i \odot \Omega_i = L_i] 
\]

(8)

considering only \( Y \odot \Omega_i \) we have

\[
Y \odot \Omega_i = Y \odot \Omega_i \odot L_i + Y \odot \Omega_i \odot (I - L_i) \\
= Y \odot L_i + Y \odot (I - \sum_{i=1, i\neq j}^{N} L_j) \odot (I - L_i) \\
= Y \odot L_i + Y \odot (I - \sum_{i=1, i\neq j}^{N} L_j) - Y \odot L_i; \quad \text{[since } L_i \odot L_j = 0 \text{ for } i \neq j] \\
= Y \odot L_i + Y \odot (I - \sum_{i=1}^{N} L_j) \\
= \sum_{j=1}^{M} Y_i^j + \sum_{j=1}^{M} Y_j^i 
\]

(9)

Replacing Eq. (9) in Eq. (8) we get

\[
\mathcal{L} ( (p^j)_{j \in \Omega_i}, (g^j)_{j \in \Omega_i} ) = \frac{2 \times \sum_{j=1}^{M} Y_i^j}{\sum_{j=1}^{M} L_i^j + \sum_{j=1}^{M} Y_i^j + \sum_{j=1}^{M} Y_j^i} 
\]

(10)

The term \( \sum_{j=1}^{M} Y_j^i \) in the denominator penalizes the false positive and is present for every instance \( i \). Therefore, the instance-aware soft Dice loss penalizes more the false positives than the soft Dice loss. Also note that the degree of false-positives penalty is proportional to the number of instances. This dynamic penalty is beneficial in preventing network from over-predicting in case of many instances while it does not affect much for fewer instances.
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